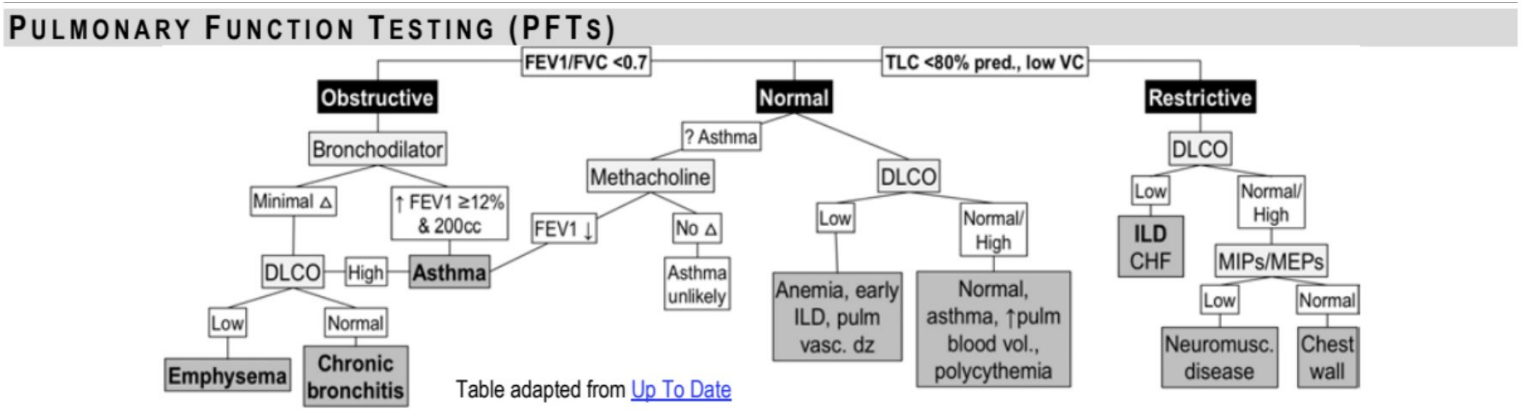
Asthma Management



Symptoms (wheezing SOB nocturnal)
TEST BEFORE TREATING
Spirometry Reversible obstructive airway disease FEV1 decreased FEV1/FVC < 70%
Bronchodilator challenge FEV_1 increase ≥12% AND ≥200 mL from baseline (or PEF ≥20%) Specific test, not sensitive test
Methacholine Challenge - >20% fall in FEV1 at a methacholine Concentration of < 8mg/ml Sensitive test, not specific
Type 2 asthma FENO > 50ppb, Eosinophils, IgE
Step up 1/2. SABA ICS PRN 3 Scheduled SABA ICS 4 SABA medium ICS 5. High dose ICS LABA LAMA 6. Biologics
<2 a week < 2 nocturnal symptoms a month

ASTHMA (GINA 2023, NAEPP 2020)

Definition: heterogeneous condition with resp sx (wheeze, SOB, chest tightness, cough) and variable expiratory airflow limitation

Symptoms	Resp sx (wheeze, SOB, cough, chest tightness) that vary over time & intensity, worse @ night/early AM
Triggers	Exercise, cold air, allergens, irritants (smoke, perfume), viral respiratory infections, drugs (ASA, NSAIDS, β-blockers)
Spirometry	Obstructive (FEV1/FVC < LLN or 0.7), reverses w/ bronchodilator (↑0.12 or >200mL), worsens w/ methacholine (can be nl before provocation, FEV1 ↓ 0.2)
Endotypes	T2-high (atopic triad, ↑Th-2/eosinophil response; steroid-sensitive), T2-low (poorly understood, often steroid-refractory)
New-onset adult cases ddx: systemic disease (ABPA, EGPA, systemic mastocytosis), occupational asthma (10-25%; NEJM 2014;370:640), ASA-exacerbated resp. disease (7%, esp. if nasal polyps; J Allergy Clin Immunol 2015;135:676)	

Outpatient Care

- **Controller + reliever**: stepwise based on severity (*below*); step up if not controlled; step down if well controlled 2-3mo
  - Note: *GINA guidelines rec ICS-containing controller*; no longer rec. tx w/ SABA a/w ↑allergic responses & airway inflammation, ↓response, & overuse a/w ↑severe exacerbations, though NAEPP still recs SABA PRN
  - May be some phenotypes w/ low eos. inflamm. (<2% in sputum) in whom ICS ↓effective (NEJM 2019;380:2009)
- **Non-pharm interventions**: smoking cessation, regular physical activity, vaccines, breathing exercises, weight loss if obese

NEJM 2019;238:2020; NEJM 2018;378:1865; NEJM 2018;378:1877; AJRCCM 2005;171:129; Chest 2006;129:246; Lancet 2011;377:650

Adapted from GINA 2023	**Mild intermittent STEP 1**	**Mild persistent STEP 2**	**Moderate persistent STEP 3**	**Severe persistent STEP 4**	**Severe STEP 5**
Symptom frequency	Infrequent	2-7d/week	Most days	All day	All day
Nighttime awakenings	<2/month	3-4n/month	>1/week	Nightly	Nightly
Exacerbations	0-1/year	>2/year	>2/year	>2/year	>2/year
Baseline FEV1	Normal	Normal	60-80% predicted	<60%	<60%
Controller (Preferred)	**None**	**None**	**Low dose ICS-formoterol**	**Med dose ICS-formoterol**	**Med dose ICS-formoterol and LAMA** *Consider: phenotypic assessment and biologics**
Controller alternative	*Low-dose ICS whenever using PRN SABA*	*Low dose ICS*	*Low dose ICS-LABA***	*Med/high dose ICS-LABA*	*Same as above, can consider LTRA, azithro*
Reliever (Preferred)	PRN low dose ICS-formoterol				
Reliever alternative	*PRN SABA or ICS-SABA*				

***Biologics**: anti-IL4R-alpha, anti-IgE, anti-IL5, anti-TSLP. **LABA w/o ICS ↑ rates of death (CHEST 2006;129:15; NEJM 2010;362:1169).

- **As-needed low-dose ICS-formoterol** (anti-inflammatory reliever/AIR)
- Examples: **Symbicort** (budesonide-formoterol 80/4.5 mcg) or **AirSupra** (albuterol-budeson 80/90 mcg)

Pulmicort Flexhaler, **Asmanex**, **QVAR Redihaler**, **Arnuity Ellipta**

Step 3 - Moderate persistent asthma:

- **Low-dose ICS-formoterol as MART** (maintenance and reliever therapy)
- Daily maintenance: **Symbicort** 80/4.5 mcg or **Dulera** 100/5 mcg
- Plus same inhaler as-needed for symptoms
- Alternative: Low-dose ICS-LABA + as-needed SABA

STEP 4 Medium-dose ICS-formoterol as MART

- Daily maintenance: **Symbicort** 160/4.5 mcg or **Dulera** 200/5 mcg
- Plus same inhaler as-needed for symptoms
- Alternative: Medium-dose ICS-LABA combinations like **Advair**, **Breo Ellipta**, **Wixela**

Step 5 - Severe persistent asthma:

- **High-dose ICS-LABA + LAMA** (triple therapy preferred)
- Triple therapy options: **Trelegy Ellipta** (fluticasone-vilanterol-umeclidinium) or **Breztri Aerosphere** (budesonide-glycopyrrolate-formoterol)
- **LTRA**: montelukast (**Singulair**)
-

STEP 1 / 2 PRN ICS FORMOTEROL

Quick Reliever Medicines

Short-Acting Beta$_2$-Agonists (SABA)

Albuterol Sulfate HFA
albuterol sulfate
90 mcg
G

Albuterol Sulfate Neb
0.64 mg/3 ml; 1.25 mg/3 ml; 2.5 mg/3 ml

ProAir® RespiClick
albuterol sulfate
117 mcg

Proventil® HFA
albuterol sulfate
120 mcg
G

Ventolin® HFA
albuterol sulfate
90 mcg

Xopenex HFA®
levalbuterol tartrate
50 mcg
G

Xopenex® Neb
levalbuterol hydrochloride
0.31 mg/3 ml; 0.63 mg/3 ml; 1.25 mg/3 ml
G

Short-Acting Muscarinic Antagonists (SAMA)

Atrovent® HFA
ipratropium bromide
17 mcg
C

Atrovent® Neb
ipratropium bromide
250/500 mcg
G

AIR

Short-Acting Combinations (SABA-ICS)

AirSupra®
(albuterol and budesonide)
80, 90 mcg
AIR

Short-Acting Combinations (SABA-SAMA)

Combivent® Respimat®
ipratropium bromide and albuterol
20/100 mcg
C

DuoNeb®
ipratropium bromide and albuterol sulfate
0.5 mg-3 mg/3 ml
G

Maintenance/Controller Medicines

Inhaled Corticosteroids (ICS) asthma only

Alvesco® HFA
ciclesonide
80/160 mcg

ArmonAir™ RespiClick®
fluticasone propionate
55/113/232 mcg

Arnuity® Ellipta®
fluticasone furoate
100/200 mcg

Asmanex® HFA
mometasone furoate
100/200 mcg

Asmanex® Twisthaler®
mometasone furoate
110/220 mcg

Budesonide Inhalation Suspension
0.25 mg/2 ml/.5 mg/2 ml/1 mg/2 ml

Fluticasone Propionate Diskus®
fluticasone propionate
50/100/250 mcg

Fluticasone Propionate HFA
fluticasone propionate
44/110/220 mcg

Pulmicort® Flexhaler®
budesonide
90/180 mcg

Pulmicort Respules®
budesonide inhalation suspension
0.25 mg/2 ml, 0.5 mg/2 ml, 1 mg/2 ml

QVAR® Redihaler™
beclomethasone dipropionate
40/80 mcg

Combination Therapy (Inhaled Corticosteroid - Long-Acting Beta$_2$-Agonists) (ICS-LABA)

Advair Diskus®
fluticasone propionate and salmeterol
100/50, 250/50, 500/50 mcg
G
Milk

Advair® HFA
fluticasone propionate and salmeterol xinafoate
45/21, 115/21, 230/21 mcg

AirDuo® RespiClick®
fluticasone propionate and salmeterol
55/14, 113/14, 232/14 mcg
G

Breo® Ellipta®
fluticasone and vilanterol
100/25, 200/25 mcg
G
Milk

Wixela™ Inhub™
fluticasone propionate and salmeterol xinafoate
100/50, 250/50, 500/50 mcg

SMART/MART

Symbicort®
budesonide and formoterol fumarate dihydrate
80/4.5, 160/4.5 mcg
G
S

ulera®
ometasone furoate and formoterol fumarate dihydrate
5, 100/5, 200/5 mcg

Triple Therapy (ICS-LABA-LAMA)

Trelegy Ellipta
fluticasone/vilanterol/umeclidinium
100 mcg/62.5 mcg/25 mcg A C
200 mcg/62.5 mcg/25 mcg A

Breztri Aerosphere®
budesonide glycopyrrolate formoterol fumarate
160/9/4.8 mcg
C

Long-Acting Muscarinic Antagonists (LAMA)

Incruse® Ellipta®
umeclidinium
62.5 mcg
C

Lonhala Magnair®
glycopyrrolate
25 mcg/1 ml
C

Spiriva® HandiHaler®
tiotropium bromide
18 mcg
C

Spiriva® Respimat®
tiotropium bromide
1.25 mcg
A C

Tudorza™ Pressair™
aclidinium bromide
400 mcg
C

Yupelri® Neb
revefenacin
175 mcg/3 ml
C

Long-Acting Beta$_2$-Agonists (LABA) COPD only

Brovana® Neb
arformoterol
15 mcg

Perforomist® Neb
formoterol fumarate dihydrate
20 mcg

Serevent® Diskus®
salmeterol xinafoate
50 mcg

Striverdi® Respimat®
olodaterol hydrochloride
2.5 mcg

LAMA-LABA COPD only

Anoro® Ellipta
umeclidinium and vilanterol
55/22, 62.5/25 mcg

Bevespi Aerosphere®
glycopyrrolate and formoterol
9/4.8 mcg

Duaklir® Pressair®
aclidinium and formoterol
400/12 mcg

Stiolto® Respimat®
olodaterol and tiotropium bromide
2.5/2.5 mcg

Add-On Medicines

Monoclonal Antibody (biologics, injection)

Cinqair®
reslizumab
100 mg
A

Dupixent®
dupilumab
100/200/300 mg
A C

Fasenra™
benralizumab
30 mg
A

Nucala®
mepolizumab
100 mg
A

Tezspire™
tezepelumab-ekko
210 mg
A

Xolair®
omalizumab
75/150 mg
A

PDE Inhibitors

PDE4 Daliresp®
roflumilast
250/500 mcg
C

PDE3/4 Ohtuvayre™
ensifentrine
3mg/2.5mL
C

Leukotriene Receptor Antagonists (LTRA)

Singulair®
montelukast sodium
4/5/10 mg

Zyflo®
zileuton ER
600 mg

Use a valved holding chamber/spacer

All HFA inhalers should be used with a compatible valved holding chamber/spacer.

You can also connect with a lung health navigator for one-on-one, free support from the American Lung Association's Lung HelpLine at 1-800-LUNGUSA.

How-To Videos

STEP 3 SCHEDULED LOW DOSE ICS FORMOTEROL

Quick Reliever Medicines

Short-Acting Beta$_2$-Agonists (SABA)

Albuterol Sulfate HFA
albuterol sulfate
90 mcg
G

Albuterol Sulfate Neb
0.64 mg/3 ml; 1.25 mg/3 ml; 2.5 mg/3 ml

ProAir® RespiClick
albuterol sulfate
117 mcg

Proventil® HFA
albuterol sulfate
120 mcg
G

Ventolin® HFA
albuterol sulfate
90 mcg

Xopenex HFA®
levalbuterol tartrate
50 mcg
G

Xopenex® Neb
levalbuterol hydrochloride
0.31 mg/3 ml; 0.63 mg/3 ml; 1.25 mg/3 ml
G

Short-Acting Muscarinic Antagonists (SAMA)

Atrovent® HFA
ipratropium bromide
17 mcg
C

Atrovent® Neb
ipratropium bromide
250/500 mcg
G

AIR

Short-Acting Combinations (SABA-ICS)

AirSupra®
(albuterol and budesonide)
80, 90 mcg
AIR

Short-Acting Combinations (SABA-SAMA)

Combivent® Respimat®
ipratropium bromide and albuterol
20/100 mcg
C

DuoNeb®
ipratropium bromide and albuterol sulfate
0.5 mg-3 mg/3 ml
G

Maintenance/Controller Medicines

Inhaled Corticosteroids (ICS) asthma only

Alvesco® HFA
ciclesonide
80/160 mcg

ArmonAir™ RespiClick®
fluticasone propionate
55/113/232 mcg

Arnuity® Ellipta®
fluticasone furoate
100/200 mcg

Asmanex® HFA
mometasone furoate
100/200 mcg

Asmanex® Twisthaler®
mometasone furoate
110/220 mcg

Budesonide Inhalation Suspension
0.25 mg/2 ml/.5 mg/2 ml/1 mg/2 ml

Fluticasone Propionate Diskus®
fluticasone propionate
50/100/250 mcg

Fluticasone Propionate HFA
fluticasone propionate
44/110/220 mcg

Pulmicort® Flexhaler®
budesonide
90/180 mcg

Pulmicort Respules®
budesonide inhalation suspension
0.25 mg/2 ml, 0.5 mg/2 ml, 1 mg/2 ml

QVAR® Redihaler™
beclomethasone dipropionate
40/80 mcg

Combination Therapy (Inhaled Corticosteroid - Long-Acting Beta$_2$-Agonists) (ICS-LABA)

Advair Diskus®
fluticasone propionate and salmeterol
100/50, 250/50, 500/50 mcg
G
Milk

Advair® HFA
fluticasone propionate and salmeterol xinafoate
45/21, 115/21, 230/21 mcg

AirDuo® RespiClick®
fluticasone propionate and salmeterol
55/14, 113/14, 232/14 mcg
G

Breo® Ellipta®
fluticasone and vilanterol
100/25, 200/25 mcg
G
Milk

Wixela™ Inhub™
fluticasone propionate and salmeterol xinafoate
100/50, 250/50, 500/50 mcg

SMART/MART

Symbicort®
budesonide and formoterol fumarate dihydrate
80/4.5, 160/4.5 mcg
G
S

…ulera®
…metasone furoate and …moterol fumarate dihydrate
…5, 100/5, 200/5 mcg

…riple Therapy (ICS-LABA-LAMA)

…relegy Ellipta
…icasone/vilanterol/umeclidinium
… mcg/62.5 mcg/25 mcg A C
… mcg/62.5 mcg/25 mcg A C

Breztri Aerosphere®
budesonide glycopyrrolate formoterol fumarate
160/9/4.8 mcg
C

Long-Acting Muscarinic Antagonists (LAMA)

Incruse® Ellipta®
umeclidinium
62.5 mcg
C

Lonhala Magnair®
glycopyrrolate
25 mcg/1 ml
C

Spiriva® HandiHaler®
tiotropium bromide
18 mcg
C

Spiriva® Respimat®
tiotropium bromide
1.25 mcg
A C

Tudorza™ Pressair™
aclidinium bromide
400 mcg
C

Yupelri® Neb
revefenacin
175 mcg/3 ml
C

Long-Acting Beta$_2$-Agonists (LABA) COPD only

Brovana® Neb
arformoterol
15 mcg

Perforomist® Neb
formoterol fumarate dihydrate
20 mcg

Serevent® Diskus®
salmeterol xinafoate
50 mcg

Striverdi® Respimat®
olodaterol hydrochloride
2.5 mcg

LAMA-LABA COPD only

Anoro® Ellipta
umeclidinium and vilanterol
55/22, 62.5/25 mcg

Bevespi Aerosphere®
glycopyrrolate and formoterol
9/4.8 mcg

Duaklir® Pressair®
aclidinium and formoterol
400/12 mcg

Stiolto® Respimat®
olodaterol and tiotropium bromide
2.5/2.5 mcg

Add-On Medicines

Monoclonal Antibody (biologics, injection)

Cinqair®
reslizumab
100 mg
A

Dupixent®
dupilumab
100/200/300 mg
A C

Fasenra™
benralizumab
30 mg
A

Nucala®
mepolizumab
100 mg
A

Tezspire™
tezepelumab-ekko
210 mg
A

Xolair®
omalizumab
75/150 mg
A

PDE Inhibitors

PDE4 Daliresp®
roflumilast
250/500 mcg
C

PDE3/4 Ohtuvayre™
ensifentrine
3mg/2.5mL
C

Leukotriene Receptor Antagonists (LTRA)

Singulair®
montelukast sodium
4/5/10 mg

Zyflo®
zileuton ER
600 mg

Use a valved holding chamber/spacer

All HFA inhalers should be used with a compatible valved holding chamber/spacer.

You can also connect with a lung health navigator for one-on-one, free support from the American Lung Association's Lung HelpLine at 1-800-LUNGUSA.

How-To Videos

STEP 4 SCHEDULED MEDIUM DOSE ICS FORMOTEROL

Quick Reliever Medicines

Short-Acting Beta$_2$-Agonists (SABA)

- **Albuterol Sulfate HFA** — albuterol sulfate, 90 mcg — G
- **Albuterol Sulfate Neb** — 0.64 mg/3 ml; 1.25 mg/3 ml; 2.5 mg/3 ml
- **ProAir® RespiClick** — albuterol sulfate, 117 mcg
- **Proventil® HFA** — albuterol sulfate, 120 mcg — G
- **Ventolin® HFA** — albuterol sulfate, 90 mcg
- **Xopenex HFA®** — levalbuterol tartrate, 50 mcg — G
- **Xopenex® Neb** — levalbuterol hydrochloride, 0.31 mg/3 ml; 0.63 mg/3 ml; 1.25 mg/3 ml — G

Short-Acting Muscarinic Antagonists (SAMA)

- **Atrovent® HFA** — ipratropium bromide, 17 mcg — C
- **Atrovent® Neb** — ipratropium bromide, 250/500 mcg — G

AIR

- **Short-Acting Combinations (SABA-ICS)**
  - **AirSupra®** — (albuterol and budesonide), 80, 90 mcg — AIR

Short-Acting Combinations (SABA-SAMA)

- **Combivent® Respimat®** — ipratropium bromide and albuterol, 20/100 mcg — C
- **DuoNeb®** — ipratropium bromide and albuterol sulfate, 0.5 mg-3 mg/3 ml — G

Maintenance/Controller Medicines

Inhaled Corticosteroids (ICS) asthma only

- **Alvesco® HFA** — ciclesonide, 80/160 mcg
- **ArmonAir™ RespiClick®** — fluticasone propionate, 55/113/232 mcg
- **Arnuity® Ellipta®** — fluticasone furoate, 100/200 mcg
- **Asmanex® HFA** — mometasone furoate, 100/200 mcg
- **Asmanex® Twisthaler®** — mometasone furoate, 110/220 mcg
- **Budesonide Inhalation Suspension** — 0.25 mg/2 ml/.5 mg/2 ml/1 mg/2 ml
- **Fluticasone Propionate Diskus®** — fluticasone propionate, 50/100/250 mcg
- **Fluticasone Propionate HFA** — fluticasone propionate, 44/110/220 mcg
- **Pulmicort® Flexhaler®** — budesonide, 90/180 mcg
- **Pulmicort Respules®** — budesonide inhalation suspension, 0.25 mg/2 ml, 0.5 mg/2 ml, 1 mg/2 ml
- **QVAR® Redihaler™** — beclomethasone dipropionate, 40/80 mcg

Combination Therapy (Inhaled Corticosteroid - Long-Acting Beta$_2$-Agonists) (ICS-LABA)

- **Advair Diskus®** — fluticasone propionate and salmeterol, 100/50, 250/50, 500/50 mcg — G — Milk
- **Advair® HFA** — fluticasone propionate and salmeterol xinafoate, 45/21, 115/21, 230/21 mcg
- **AirDuo® RespiClick®** — fluticasone propionate and salmeterol, 55/14, 113/14, 232/14 mcg — G
- **Breo® Ellipta®** — fluticasone and vilanterol, 100/25, 200/25 mcg — G — Milk
- **Wixela™ Inhub™** — fluticasone propionate and salmeterol xinafoate, 100/50, 250/50, 500/50 mcg

SMART/MART

- **Symbicort®** — budesonide and formoterol fumarate dihydrate, 80/4.5, 160/4.5 mcg — G — S
- **…ulera®** — …ometasone furoate and …rmoterol fumarate dihydrate …5, 100/5, 200/5 mcg

…riple Therapy (ICS-LABA-LAMA)

- **…relegy Ellipta** — …icasone/vilanterol/umeclidinium …0 mcg/62.5 mcg/25 mcg — A — C
- **Breztri Aerosphere®** — budesonide glycopyrrolate formoterol fumarate, 160/9/4.8 mcg — C

Long-Acting Muscarinic Antagonists (LAMA)

- **Incruse® Ellipta®** — umeclidinium, 62.5 mcg — C
- **Lonhala Magnair®** — glycopyrrolate, 25 mcg/1 ml — C
- **Spiriva® HandiHaler®** — tiotropium bromide, 18 mcg — C
- **Spiriva® Respimat®** — tiotropium bromide, 1.25 mcg — A — C
- **Tudorza™ Pressair™** — aclidinium bromide, 400 mcg — C
- **Yupelri® Neb** — revefenacin, 175 mcg/3 ml — C

Long-Acting Beta$_2$-Agonists (LABA) COPD only

- **Brovana® Neb** — arformoterol, 15 mcg
- **Perforomist® Neb** — formoterol fumarate dihydrate, 20 mcg
- **Serevent® Diskus®** — salmeterol xinafoate, 50 mcg
- **Striverdi® Respimat®** — olodaterol hydrochloride, 2.5 mcg

LAMA-LABA COPD only

- **Anoro® Ellipta** — umeclidinium and vilanterol, 55/22, 62.5/25 mcg
- **Bevespi Aerosphere®** — glycopyrrolate and formoterol, 9/4.8 mcg
- **Duaklir® Pressair®** — aclidinium and formoterol, 400/12 mcg
- **Stiolto® Respimat®** — olodaterol and tiotropium bromide, 2.5/2.5 mcg

Add-On Medicines

Monoclonal Antibody (biologics, injection)

- **Cinqair®** — reslizumab, 100 mg — A
- **Dupixent®** — dupilumab, 100/200/300 mg — A — C
- **Fasenra™** — benralizumab, 30 mg — A
- **Nucala®** — mepolizumab, 100 mg — A
- **Tezspire™** — tezepelumab-ekko, 210 mg — A
- **Xolair®** — omalizumab, 75/150 mg — A

PDE Inhibitors

- **PDE4 Daliresp®** — roflumilast, 250/500 mcg — C
- **PDE3/4 Ohtuvayre™** — ensifentrine, 3mg/2.5mL — C

Leukotriene Receptor Antagonists (LTRA)

- **Singulair®** — montelukast sodium, 4/5/10 mg
- **Zyflo®** — zileuton ER, 600 mg

Use a valved holding chamber/spacer

All HFA inhalers should be used with a compatible valved holding chamber/spacer.

You can also connect with a lung health navigator for one-on-one, free support from the American Lung Association's Lung HelpLine at 1-800-LUNGUSA.

How-To Videos

STEP 5 SCHEDULED HIGH DOSE ICS FORMOTEROL / LAMA

Quick Reliever Medicines

Short-Acting Beta$_2$-Agonists (SABA)

- **Albuterol Sulfate HFA** — albuterol sulfate, 90 mcg — G
- **Albuterol Sulfate Neb** — 0.64 mg/3 ml; 1.25 mg/3 ml; 2.5 mg/3 ml
- **ProAir® RespiClick** — albuterol sulfate, 117 mcg
- **Proventil® HFA** — albuterol sulfate, 120 mcg — G
- **Ventolin® HFA** — albuterol sulfate, 90 mcg
- **Xopenex HFA®** — levalbuterol tartrate, 50 mcg — G
- **Xopenex® Neb** — levalbuterol hydrochloride, 0.31 mg/3 ml; 0.63 mg/3 ml; 1.25 mg/3 ml — G

Short-Acting Muscarinic Antagonists (SAMA)

- **Atrovent® HFA** — ipratropium bromide, 17 mcg — C
- **Atrovent® Neb** — ipratropium bromide, 250/500 mcg — G

AIR

- **Short-Acting Combinations (SABA-ICS)**
  - **AirSupra®** — (albuterol and budesonide), 80, 90 mcg — AIR

Short-Acting Combinations (SABA-SAMA)

- **Combivent® Respimat®** — ipratropium bromide and albuterol, 20/100 mcg — C
- **DuoNeb®** — ipratropium bromide and albuterol sulfate, 0.5 mg-3 mg/3 ml — G

Maintenance/Controller Medicines

Inhaled Corticosteroids (ICS) asthma only

- **Alvesco® HFA** — ciclesonide, 80/160 mcg
- **ArmonAir™ RespiClick®** — fluticasone propionate, 55/113/232 mcg
- **Arnuity® Ellipta®** — fluticasone furoate, 100/200 mcg
- **Asmanex® HFA** — mometasone furoate, 100/200 mcg
- **Asmanex® Twisthaler®** — mometasone furoate, 110/220 mcg
- **Budesonide Inhalation Suspension** — 0.25 mg/2 ml/.5 mg/2 ml/1 mg/2 ml
- **Fluticasone Propionate Diskus®** — fluticasone propionate, 50/100/250 mcg
- **Fluticasone Propionate HFA** — fluticasone propionate, 44/110/220 mcg
- **Pulmicort® Flexhaler®** — budesonide, 90/180 mcg
- **Pulmicort Respules®** — budesonide inhalation suspension, 0.25 mg/2 ml, 0.5 mg/2 ml, 1 mg/2 ml
- **QVAR® Redihaler™** — beclomethasone dipropionate, 40/80 mcg

Combination Therapy (Inhaled Corticosteroid - Long-Acting Beta$_2$-Agonists) (ICS-LABA)

- **Advair Diskus®** — fluticasone propionate and salmeterol, 100/50, 250/50, 500/50 mcg — G — Milk
- **Advair® HFA** — fluticasone propionate and salmeterol xinafoate, 45/21, 115/21, 230/21 mcg — G
- **AirDuo® RespiClick®** — fluticasone propionate and salmeterol, 55/14, 113/14, 232/14 mcg — G
- **Breo® Ellipta®** — fluticasone and vilanterol, 100/25, 200/25 mcg — G — Milk
- **Wixela™ Inhub™** — fluticasone propionate and salmeterol xinafoate, 100/50, 250/50, 500/50 mcg

SMART/MART

- **Symbicort®** — budesonide and formoterol fumarate dihydrate, 80/4.5, 160/4.5 mcg — G — S
- **…ulera®** — …ometasone furoate and …moterol fumarate dihydrate …5, 100/5, 200/5 mcg

…riple Therapy (ICS-LABA-LAMA)

- **…relegy Ellipta** — …icasone/vilanterol/umeclidinium …0 mcg/62.5 mcg/25 mcg — A — C …0 mcg/62.5 mcg/25 mcg — A
- **Breztri Aerosphere®** — budesonide glycopyrrolate formoterol fumarate, 160/9/4.8 mcg — C

Long-Acting Muscarinic Antagonists (LAMA)

- **Incruse® Ellipta®** — umeclidinium, 62.5 mcg — C
- **Lonhala Magnair®** — glycopyrrolate, 25 mcg/1 ml — C
- **Spiriva® HandiHaler®** — tiotropium bromide, 18 mcg — C
- **Spiriva® Respimat®** — tiotropium bromide, 1.25 mcg — A C
- **Tudorza™ Pressair™** — aclidinium bromide, 400 mcg — C
- **Yupelri® Neb** — revefenacin, 175 mcg/3 ml — C

Long-Acting Beta$_2$-Agonists (LABA) COPD only

- **Brovana® Neb** — arformoterol, 15 mcg
- **Perforomist® Neb** — formoterol fumarate dihydrate, 20 mcg
- **Serevent® Diskus®** — salmeterol xinafoate, 50 mcg
- **Striverdi® Respimat®** — olodaterol hydrochloride, 2.5 mcg

LAMA-LABA COPD only

- **Anoro® Ellipta** — umeclidinium and vilanterol, 55/22, 62.5/25 mcg
- **Bevespi Aerosphere®** — glycopyrrolate and formoterol, 9/4.8 mcg
- **Duaklir® Pressair®** — aclidinium and formoterol, 400/12 mcg
- **Stiolto® Respimat®** — olodaterol and tiotropium bromide, 2.5/2.5 mcg

Add-On Medicines

Monoclonal Antibody (biologics, injection)

- **Cinqair®** — reslizumab, 100 mg — A
- **Dupixent®** — dupilumab, 100/200/300 mg — A C
- **Fasenra™** — benralizumab, 30 mg — A
- **Nucala®** — mepolizumab, 100 mg — A
- **Tezspire™** — tezepelumab-ekko, 210 mg — A
- **Xolair®** — omalizumab, 75/150 mg — A

PDE Inhibitors

- **PDE4 Daliresp®** — roflumilast, 250/500 mcg — C
- **PDE3/4 Ohtuvayre™** — ensifentrine, 3mg/2.5mL — C

Leukotriene Receptor Antagonists (LTRA)

- **Singulair®** — montelukast sodium, 4/5/10 mg
- **Zyflo®** — zileuton ER, 600 mg

Use a valved holding chamber/spacer

All HFA inhalers should be used with a compatible valved holding chamber/spacer.

You can also connect with a lung health navigator for one-on-one, free support from the American Lung Association's Lung HelpLine at 1-800-LUNGUSA.

How-To Videos

STEP 6 SCHEDULED HIGH DOSE ICS FORMOTEROL / LAMA / BIOLOGICS

Quick Reliever Medicines

Short-Acting Beta$_2$-Agonists (SABA)

- **Albuterol Sulfate HFA** — albuterol sulfate, 90 mcg — G
- **Albuterol Sulfate Neb** — 0.64 mg/3 ml; 1.25 mg/3 ml; 2.5 mg/3 ml
- **ProAir® RespiClick** — albuterol sulfate, 117 mcg
- **Proventil® HFA** — albuterol sulfate, 120 mcg — G
- **Ventolin® HFA** — albuterol sulfate, 90 mcg
- **Xopenex HFA®** — levalbuterol tartrate, 50 mcg — G
- **Xopenex® Neb** — levalbuterol hydrochloride, 0.31 mg/3 ml; 0.63 mg/3 ml; 1.25 mg/3 ml — G

Short-Acting Muscarinic Antagonists (SAMA)

- **Atrovent® HFA** — ipratropium bromide, 17 mcg — C
- **Atrovent® Neb** — ipratropium bromide, 250/500 mcg — G

AIR

- **Short-Acting Combinations (SABA-ICS)**
- **AirSupra®** — (albuterol and budesonide), 80, 90 mcg — AIR

Short-Acting Combinations (SABA-SAMA)

- **Combivent® Respimat®** — ipratropium bromide and albuterol, 20/100 mcg — C
- **DuoNeb®** — ipratropium bromide and albuterol sulfate, 0.5 mg-3 mg/3 ml — G

Maintenance/Controller Medicines

Inhaled Corticosteroids (ICS) asthma only

- **Alvesco® HFA** — ciclesonide, 80/160 mcg
- **ArmonAir™ RespiClick®** — fluticasone propionate, 55/113/232 mcg
- **Arnuity® Ellipta®** — fluticasone furoate, 100/200 mcg
- **Asmanex® HFA** — mometasone furoate, 100/200 mcg
- **Asmanex® Twisthaler®** — mometasone furoate, 110/220 mcg
- **Budesonide Inhalation Suspension** — 0.25 mg/2 ml/.5 mg/2 ml/1 mg/2 ml
- **Fluticasone Propionate Diskus®** — fluticasone propionate, 50/100/250 mcg
- **Fluticasone Propionate HFA** — fluticasone propionate, 44/110/220 mcg
- **Pulmicort® Flexhaler®** — budesonide, 90/180 mcg
- **Pulmicort Respules®** — budesonide inhalation suspension, 0.25 mg/2 ml, 0.5 mg/2 ml, 1 mg/2 ml
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- **Striverdi® Respimat®** — olodaterol hydrochloride, 2.5 mcg

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- **Anoro® Ellipta** — umeclidinium and vilanterol, 55/22, 62.5/25 mcg
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How-To Videos

Asthma Exacerbations

OUTPATIENT: short course pred. 40-50mg x5-7d + controller/reliever regimen, consider 4x controller ICS if mild (NEJM 2018;278:902)

INPATIENT: assess severity of exacerbation (VS, mental status, SpO_2, WOB, PEF < 50% severe), consider VBG/ABG, CXR

Severe: ↑resp drive→↑RR→↓pCO_2, nl/↓pH suggest resp. failure. If sig hypoxemia, consider resp. failure vs PTX, PNA, PE, plug, etc.

Floor Patient	ICU Patient (Thorax 2003;58:81)

- **Bronchodilators**: albuterol (2.5-5g) ± ipratropium (0.5-1.5mg) q20m x3
  - DuoNebs in ED a/w ↓admit (Cochrane Rev 2017)
  - SABA mono-tx unless severe/worsening (GINA 2023, NAEPP 2020)
- **Steroids**: **pred 40-60mg** total **x5-7d** (Cochrane Rev 2016)
- **O_2** >92% (93-95% in severe; >95% increases pCO_2; Thorax 2011;66:937)
	- **Bronchodilators**: albuterol + ipratropium**, Methylpred 125mg IV q6h**
	- **NIV**: BIPAP -> BIPAP w/ sedation -> HFNC
	- **Rescue therapies**: Mg IV 2g, continuous albuterol nebs (CAB). Less data: IV epi, ketamine, inhaled anesthetic, Heliox. *ECMO=last resort*
	- **Mechanical ventilation:** large ETT (8+), ↑insp flow rate (80-100L/min), ↓V_T (6-8cc/kg), ↓RR (10-14), ↓PEEP, paralysis; **Goal:** max exp. phase, minimize hyperinflation, permissive hypercapnia

- **If impending respiratory failure**: stacked DuoNebs (x3/h), methylpred IV 60-125mg q6h, Mg IV 2g/20min, transfer to ICU	

Evidence behind the update in GINA 2019 Strategy

- The SMART strategy (meta-analysis of 16 RCTs) in JAMA 2018
  - showed pts showed fewer asthma exacerbations, hospitalizations, ED visits with ICS-LABA vs SABA.
  - The ICS-LABA had 23% fewer exacerbations than those with higher dose ICS-LABA as maintenance. In NEJM 2018, a pair of trials SYGMA 1 and SYGMA 2 (Symbicort Given as needed in Mild Asthma).
- SYGMA 1 showed prn budesonide-formoterol as superior to prn terbutaline and similar to maintenance budesonide but with lower cumulative ICS dose.
- SYGMA 2 showed that budesonide-formoterol prn was noninferior to BID budesonide for rate of severe asthma exacerbations but inferior to symptom control (but 1/4th the amount of inhaled glucocorticoid exposure!).

A 58-year-old man comes to the office due to increased dyspnea on exertion and wheezing over the last 2 months. He has never had these symptoms before and says they "make it harder to sleep." There is no family history of asthma.

On physical examination, the lungs have good air movement with scattered wheezes and no crackles. No edema is present at the ankles.

The results of pulmonary function testing are as follows:

FVC	85% of predicted
FEV1	67% of predicted
FEV1/FVC ratio	65% of predicted

Which of the following additional findings would most strongly support the diagnosis of asthma as opposed to chronic obstructive lung disease in this patient?

Decreased lung residual volume (1%)

Near-complete reversibility of airway obstruction (82%)

No history of smoking (3%)

Normal carbon monoxide diffusion capacity (12%)

Persistent productive cough (0%)

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On physical examination, the lungs have at the ankles.

The results of pulmonary function testing

Which of the following additional findings obstructive lung disease in this patient?

Asthma vs COPD			
	Asthma	**COPD**	**Late-stage COPD**
FVC	Normal/↓	Normal/↓	↓/↓↓
FEV_1	↓	↓	↓↓
FEV_1/FVC	↓	↓	↓↓
Bronchodilator response	Reversible	Partially reversible/ nonreversible	Usually nonreversible
Chest x-ray	Normal	Normal	Hyperinflation, loss of lung markings
DLCO	Normal/↑	Normal/↓	↓

COPD = chronic obstructive pulmonary disease; **DLCO** = diffusion capacity of the lung for carbon monoxide.

- A. Decreased lung residual volume (1%)
- ✓ B. Near-complete reversibility of airway obstruction (82%)
- C. No history of smoking (3%)
- D. Normal carbon monoxide diffusion
- E. Persistent productive cough (0%)

The most effective way of **differentiating** asthma and chronic obstructive pulmonary disease (COPD) is **spirometry** before and after **administration of a bronchodilator** (usually albuterol). In patients with asthma, there is a significant **reversal in airway obstruction** (**≥12% increase in FEV1**, absolute increase in FEV1 of ≥200 mL) in response to bronchodilator therapy. Patients with COPD may have partial reversibility, but near-complete restoration of normal airflow after bronchodilator administration effectively rules out COPD.

Question 17

A 40-year-old man is evaluated 10 days after an emergency department visit for a cough, chest tightness, wheezing, and shortness of breath. He was treated with nebulized albuterol and sent home with a 5-day course of prednisone and an albuterol metered-dose inhaler. Since completing the prednisone, he has felt well, with no further symptoms and no need to use the albuterol. He reports a similar episode requiring an emergency department visit 1 year ago.

On physical examination, vital signs are normal. Oxygen saturation is 97% with the patient breathing ambient air. Cardiopulmonary examination is normal.

Spirometry is normal.

Which of the following is the most appropriate management?

A Budesonide-salmeterol

B Fluticasone

C Measurement of exhaled nitric oxide

D Methacholine challenge testing

Submit Your Answer

Question 17

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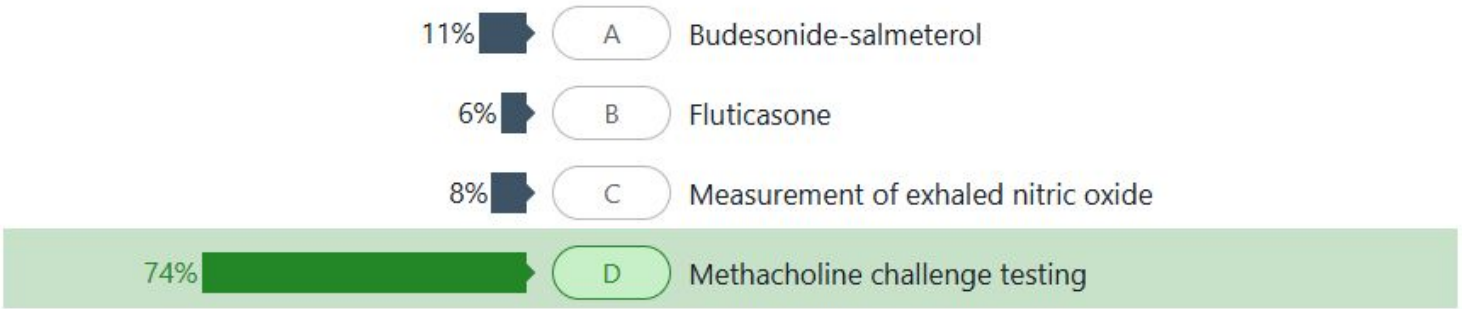
Which of the following is the most appropriate management?



Educational Objective: Diagnose asthma with bronchial challenge testing.

The most appropriate management for this patient is methacholine challenge testing (**Option D**). Confirmation of reversible airflow obstruction is a cornerstone of asthma diagnosis, and spirometry should be performed on all patients with suspected asthma. For some patients, however, airflow obstruction is not present during the initial spirometry, and a bronchial challenge test is indicated to evaluate for bronchial hyperreactivity, which supports an asthma diagnosis. The test is usually performed with inhaled methacholine, although other stimuli (exercise, mannitol) also have been validated. Bronchial challenge tests measure spirometry following a controlled inhaled stimulus; a positive test is indicated by a drop in the measured FEV_1. If the result is negative, it is unlikely that the patient has asthma, but a positive result in isolation is not specific enough to diagnose asthma. Therefore, to confirm the diagnosis, patients with a positive methacholine challenge test and suggestive asthma symptoms must also respond clinically to treatment with asthma therapies. This patient's typical symptoms and improvement with standard asthma therapy would indicate asthma if the methacholine challenge test result were positive.

Key Points

- For patients with asthma symptoms and a normal spirometry, a positive bronchial challenge test followed by relief of symptoms with standard asthma therapy confirms the diagnosis of asthma.
- A negative bronchial challenge test excludes the diagnosis of asthma in most patients.

Although initiating a trial of asthma treatment with budesonide-salmeterol or fluticasone (**Options A, B**) could be considered, guidelines indicate that it is preferable to first establish a diagnosis to avoid prescribing unnecessary or incorrect treatment. It is more difficult to establish the diagnosis of asthma once the patient is taking controller medications.

Does a positive methacholine test alone diagnosis asthma?

No +Methacholine test + Symptoms

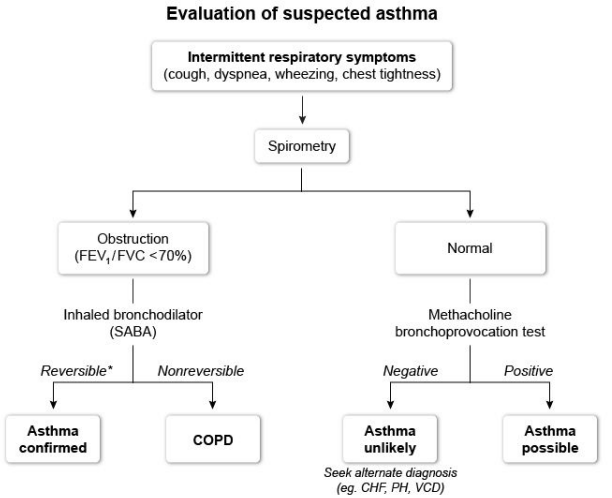
Is FeNO used in diagnosis of asthma?
No. however, it can be characteristic of Type 2 airway inflammation

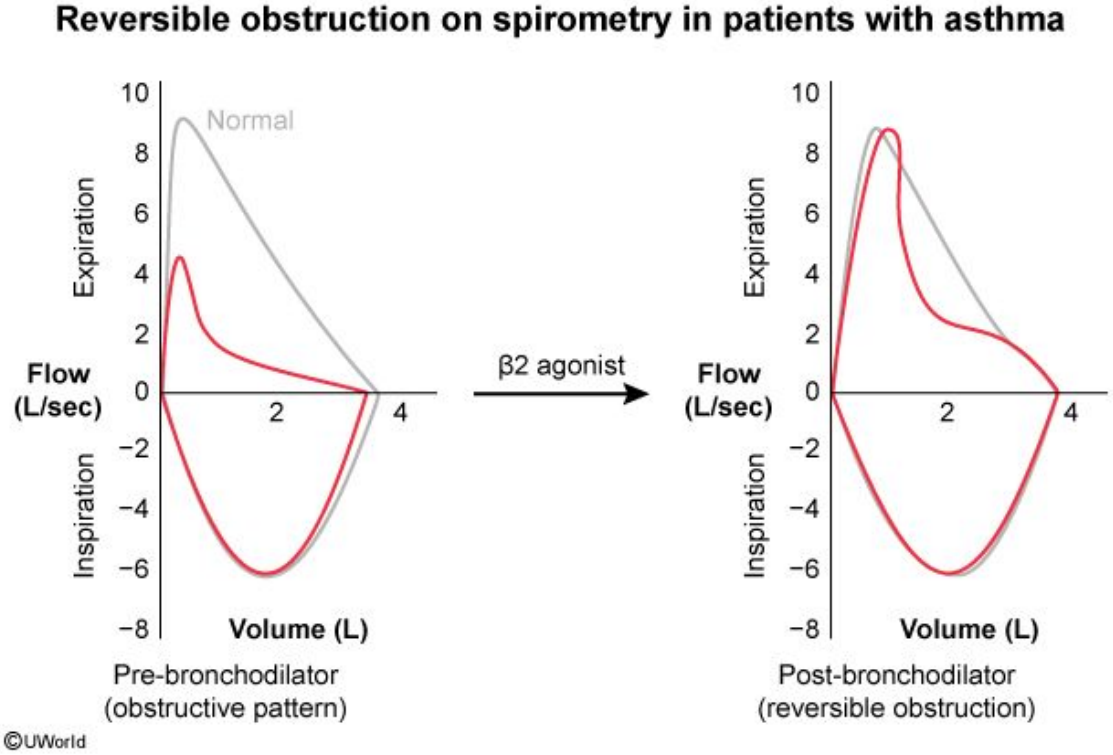
Measurement of the fractional exhaled nitric oxide (FeNO) (**Option C**) in an exhaled breath sample provides a noninvasive way to quantify eosinophilic airway inflammation and serves as a complementary tool in the management of lung diseases, in particular, asthma. However, the role of FeNO in the diagnosis of asthma has not been established. Although an elevated FeNO is characteristic of type 2 airway inflammation, FeNO is also elevated in disorders such as eosinophilic bronchitis, atopy, and allergic rhinitis and is not elevated in some asthma phenotypes. Spirometry remains the first test of choice to diagnose asthma.

Bronchodilator response: FEV1 / FVC < 70%, 12% and after bronchodilation -> 200ml increase FEV1 or FVC, w/ FEV1/ FVC > 70% after bronchodilator

Methacholine Challenge - >20% fall in FEV1 at a methacholine Concentration of < 8mg/ml

High Sensitivity, low specificity





A 57-year-old man comes to the physician with mild dyspnea on exertion and wheezing for the past 6 months. He experiences dyspnea when walking 4-5 blocks or when climbing stairs. The patient sleeps poorly and often has wheezing at night when lying down, especially when lying on his back. He has an occasional cough but attributes this to allergic rhinitis. The patient has a history of childhood asthma for which he used albuterol as needed until he was 25 years old, but says that he "grew out of it." He does not use tobacco, alcohol, or illicit drugs.

Vital signs and physical examination are within normal limits. His BMI is 30 kg/m^2.

Electrocardiogram (ECG) is unremarkable.

What is the best next step in management of this patient?

Albuterol and inhaled corticosteroid (8%)

Exercise stress test (9%)

Non-contrast CT scan of the chest (2%)

Sleep study (12%)

Spirometry (65%)

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- B. Exercise stress test (9%)
- C. Non-contrast CT scan of the chest (2%)
- D. Sleep study (12%)
- ✓ E. Spirometry (65%)

A clinical history of intermittent respiratory symptoms of varying intensity, often worse at night, should raise suspicion for asthma or other obstructive lung diseases such as chronic obstructive pulmonary disease (COPD). Wheezing is a coarse whistling sound caused by airflow through a narrowed airway. However, "all that wheezes is not asthma." Conditions other than bronchospasm can result in wheezing. Congestive heart failure (ie, cardiac asthma) can elicit wheezing due to bronchial narrowing from pulmonary edema. Vocal cord dysfunction, postnasal drip, and both intra- and extrathoracic obstruction can also cause wheezing.

Initial evaluation of stable patients with wheezing should include pulmonary function testing (spirometry) to confirm the diagnosis of asthma and assess the severity. Conventional chest x-ray may be obtained in patients with focal or persistent wheezing. Additional imaging studies, such as chest CT, can be considered based on results of initial tests **(Choice C)**.

(Choice A) Once the diagnosis of asthma is confirmed, treatment with inhaled bronchodilators and corticosteroids can be initiated. A trial of therapy can be used to diagnose asthma only if spirometric evaluation is not available.

Don't Be Tricked

- Normal spirometry does not rule out asthma.
- A normal bronchoprovocation test rules out asthma; a positive test confirms airway hyperresponsiveness, of which asthma is but one cause; clinical correlation of this finding with symptoms and other testing is needed.
- Wheezing does not equal asthma; consider HF, COPD, vocal cord dysfunction, and upper airway obstruction.

Question 24

A 50-year-old man is referred for poorly controlled asthma. Triggers include exercise and exposure to dust, pollen, and fumes. He has allergic rhinitis. He has been treated with several courses of glucocorticoids, but symptoms recurred after he stopped treatment despite regular use of his fluticasone-salmeterol and tiotropium inhalers. His only other medication is albuterol. He has good inhaler technique.

On physical examination, vital signs are normal. BMI is 23. Pulmonary examination reveals few expiratory wheezes. The remainder of the examination is unremarkable.

Laboratory studies reveal a normal total IgE level and complete blood count.

Chest radiograph is normal. Spirometry demonstrates moderate airflow obstruction that improves with bronchodilators.

Which of the following is the most appropriate diagnostic test to perform next?

A Absolute blood eosinophil count

B α_1-Antitrypsin level

C *Aspergillus*-specific IgE level

D Measurement of common allergen-specific IgE levels

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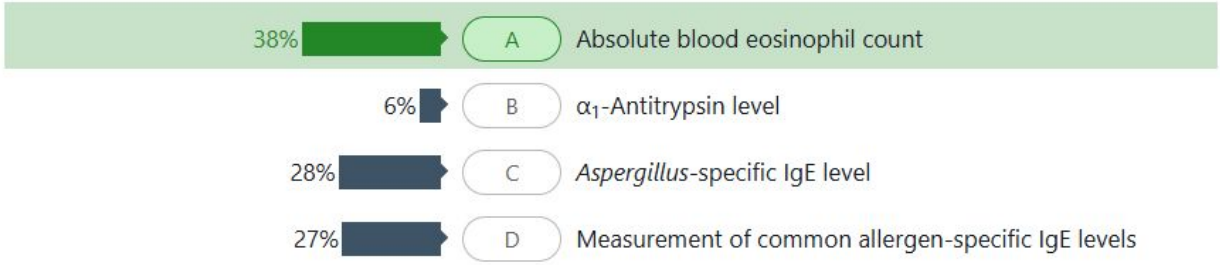


Educational Objective: **Diagnose allergic asthma phenotype.**

The most appropriate diagnostic test for this patient is measurement of the absolute blood eosinophil count (**Option A**). The patient presents with symptoms suggestive of allergic asthma; establishing this asthma phenotype can help direct therapy. Clinical characteristics suggesting a type 2 asthma phenotype include atopy, seasonal exacerbations, hay fever, and allergen sensitization. Biomarker evaluation in these patients often demonstrates serum or sputum eosinophilia and/or high IgE levels. This patient has a normal IgE level, but this does not preclude type 2 asthma. Obtaining a blood absolute eosinophil count will help establish the phenotype. In patients with severe disease, elevated levels of IgE and eosinophils are therapeutic targets for biologic therapies. Several types of biologic therapies are available that are directed against type 2 inflammation, targeting pathways involved in activation of eosinophils and IgE production. Use of antibody therapies in eligible patients with severe persistent allergic asthma despite standard therapy reduces symptoms, exacerbations, and need for oral glucocorticoids.

Key Points

- Clinical characteristics suggesting a type 2 asthma phenotype include atopy, seasonal exacerbations, hay fever, and allergen sensitization.
- For patients with symptoms suggestive of type 2 asthma phenotype, measurement of IgE levels and total eosinophil count can be used to confirm this asthma phenotype and direct therapy.

An α_1-antitrypsin level (**Option B**) should be obtained once in all patients with chronic obstructive pulmonary disease. A pattern of basilar emphysema, associated liver disease or panniculitis, or a strong family history of emphysema in patients with COPD suggests possible α-1 antitrypsin deficiency, but none of these features is sufficiently sensitive for the condition. Routine testing is not indicated in patients with asthma.

Patients with allergic bronchopulmonary aspergillosis (ABPA) present with difficult-to-control asthma, productive cough, and expectoration of mucus plugs. Commonly accepted diagnostic criteria include elevated IgE levels, positive skin tests to *Aspergillus* antigens, increased *Aspergillus*-specific IgE and IgG levels, and either central bronchiectasis or infiltrates. This patient does not have the clinical phenotype of ABPA, radiographic findings, or elevated IgE level suggesting ABPA. Measuring *Aspergillus*-specific IgE level (**Option C**) is not indicated.

Identifying the presence of atopy can identify an allergic asthma phenotype in a patient with respiratory symptoms. Atopic status can be measured by skin prick testing or measurement of allergen-specific IgE testing (**Option D**). Skin prick testing is rapid, simple, and relatively inexpensive. Measurement of immunoglobulin-specific IgE is more expensive but not more accurate. However, the first management step for this patient is to measure the total blood eosinophil count to determine his asthma phenotype.

Question 40

A 27-year-old woman is evaluated for a cough and chest tightness that occur during and after exercise. She has been training for her first marathon, but she has been unable to increase her training intensity because of these symptoms. She denies cough or chest tightness at any other time. She reports no stridor, throat tightness, or noisy inspiration during the episodes.

On physical examination, vital signs and pulmonary examination are normal.

Baseline spirometry is normal. Exercise testing demonstrates a significant decrease in FEV_1 from baseline.

Which of the following inhaled medications is the most appropriate next step in treatment?

A Salmeterol daily

B Budesonide twice daily

C Budesonide-formoterol before exercise

D Ipratropium before exercise

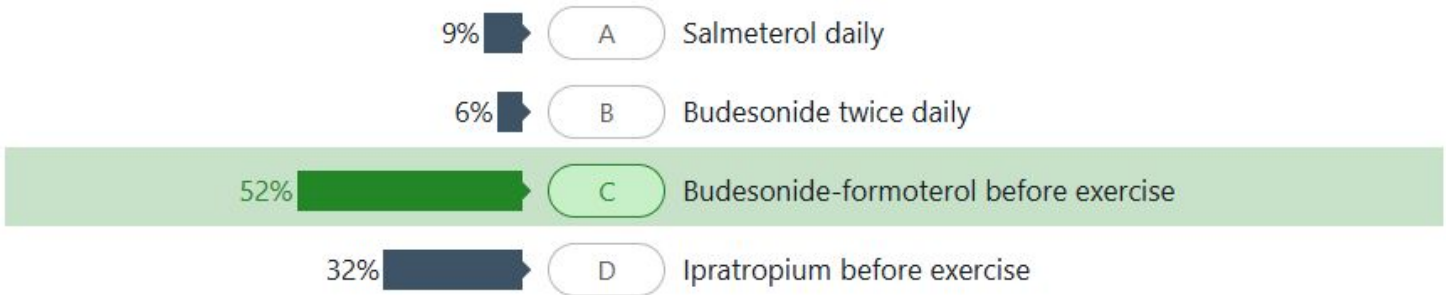
Question 40

A 27-year-old woman is evaluated for a cough and chest tightness that occur during and after exercise. She has been training for her first marathon, but she has been unable to increase her training intensity because of these symptoms. She denies cough or chest tightness at any other time. She reports no stridor, throat tightness, or noisy inspiration during the episodes.

On physical examination, vital signs and pulmonary examination are normal.

Baseline spirometry is normal. Exercise testing demonstrates a significant decrease in FEV_1 from baseline.

Which of the following inhaled medications is the most appropriate next step in treatment?



Educational Objective: Manage exercise-induced bronchoconstriction.

The most appropriate management is to begin budesonide-formoterol 5 to 20 minutes before exercise (**Option C**). Exercise-induced bronchoconstriction (EIB) is acute, measurable airway obstruction that occurs in response to exercise. It is one of the most common triggers of symptoms in patients with known asthma. It also occurs in patients without asthma (typically, elite athletes) during periods of high-intensity exercise. Environmental factors such as cold, dry air, exposure to high levels of trichloramines in swimming pools, and inhalation of airborne particulates and ozone can play a key role in precipitating symptoms. For safety, current Global Initiative for Asthma (GINA) guidelines no longer recommend treatment of intermittent asthma, including EIB, with a short-acting β_2-agonist (SABA) alone. All adults should receive a glucocorticoid-containing controller treatment to reduce their risk of serious exacerbations and to control symptoms. The glucocorticoid controller medication can be administered either as regular daily treatment or, in milder asthma, as the combination glucocorticoid-formoterol taken whenever needed for asthma relief. Accordingly, GINA guidelines recommend a daily inhaled glucocorticoid plus a SABA before exercise or low-dose budesonide-formoterol before exercise. Nonpharmacologic measures, including pre-exercise warm-up and warming cold air before inhalation (e.g., with a mask or scarf), are also recommended. In contrast, the 2020 Asthma Guideline Update from the National Asthma Education and Prevention Program has continued the previous recommendation of as-needed SABA-only use for this group of patients.

Key Points

- Exercise-induced bronchoconstriction is an acute, measurable airway obstruction that occurs in response to exercise.
- Global Initiative for Asthma guidelines recommend that initial pharmacologic therapy for exercise-induced bronchoconstriction should consist of a daily inhaled glucocorticoid plus a short-acting β_2-agonist or low-dose budesonide-formoterol before exercise, whereas the National Asthma Education and Prevention Program recommends a short-acting β_2-agonist.

Use of single-agent long-acting β_2-agonists (LABAs) such as salmeterol (**Option A**) is not recommended because of a demonstrated increased risk of asthma-related death when used without a simultaneous controller medication. Clinical trial results show that LABAs used with inhaled glucocorticoids do not significantly increase the risk of asthma-related hospitalization, intubation, or death compared with inhaled glucocorticoids alone, and they result in significantly fewer asthma exacerbations.

Daily use of low-dose inhaled glucocorticoids (**Option B**) would expose this patient to a significantly higher total dose of inhaled glucocorticoids compared with as-needed use. In addition, if daily inhaled controller medication with a glucocorticoid is prescribed, it should usually be accompanied by a SABA before exercise and as needed for quick relief.

In patients with asthma, inhaled ipratropium (**Option D**) is generally not used for quick relief because of its delayed onset and peak action of 15 minutes and 1 to 2 hours, respectively. A SABA is preferred to ipratropium, either with a daily inhaled glucocorticoid or administered with an inhaled glucocorticoid.

Question 43

A 23-year-old man is evaluated for cough, rhinorrhea, and wheezing of 3 weeks' duration. He has no fevers, chills, or chest pain and no history of asthma or allergies. He is a pastry chef and notes that his symptoms improve on nonworking weekends.

On physical examination, vital signs are normal. Oxygen saturation is 94% with the patient breathing ambient air. Expiratory wheezing is noted.

Laboratory studies show a normal *Aspergillus*-specific IgE level.

Spirometry reveals moderate airflow obstruction that improves after inhaled albuterol.

Chest radiograph is normal.

Which of the following is the most likely diagnosis?

A Acute bronchitis

B Acute hypersensitivity pneumonitis

C Allergic bronchopulmonary aspergillosis

D Occupational asthma

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Spirometry reveals moderate airflow obstruction that improves after inhaled albuterol.

Chest radiograph is normal.

Which of the following is the most likely diagnosis?

2%	A	Acute bronchitis
11%	B	Acute hypersensitivity pneumonitis
2%	C	Allergic bronchopulmonary aspergillosis
85%	D	Occupational asthma

Answer & Critique

Correct Answer: D

You answered D.

Educational Objective: **Diagnose occupational asthma.**

The most likely diagnosis is occupational asthma (**Option D**). This patient presents with one of the most common types of occupational asthma, bakers' asthma. Occupational asthma includes both asthma caused by exposure to sensitizing or irritant substances in the workplace and preexisting asthma that is exacerbated by these same factors. Typical sensitizing agents are high-molecular-weight substances, such as proteins, that induce an IgE-mediated immunologic response. In bakers' asthma, exposure to proteins in wheat and rye flour is a likely cause. Once sensitized, patients may react to very low levels of exposure. A key clinical indicator is the relationship of symptoms to work exposure; patients often improve on weekends and during time away from work. Spirometry before and after workplace exposures is a cost-effective way to confirm a suspected diagnosis of occupational asthma. Alternatively, serial peak flow measurements can be used. In addition to pharmacologic therapy, treatment consists of reducing exposure to the offending agent through workplace modifications or removing patients from the workplace entirely.

Key Points

- Occupational asthma includes asthma caused by exposure to sensitizing or irritant substances in the workplace, including high-molecular-weight substances, such as proteins, that induce an IgE-mediated immunologic response.
- Occupational asthma is characterized by an improvement in symptoms when the patient is away from work.

Acute bronchitis (**Option A**) is a lower respiratory tract infection of the large airways, often caused by viral pathogens. It is often preceded by symptoms of upper respiratory tract infection such as headache, sore throat, and rhinitis. Most cases of acute bronchitis are self-limiting and resolve within 1 to 3 weeks. Although this patient's symptoms are similar to those of bronchitis, the symptom duration and improvement away from the workplace suggest a different cause.

Acute hypersensitivity pneumonitis (**Option B**) is also caused by inhalation of sensitizing antigens, but it leads to a markedly different clinical syndrome than occupational asthma. It is characterized by fever, cough, and fatigue within 12 hours of a major exposure to an inciting antigen. Inspiratory crackles are heard during physical examination.

Allergic bronchopulmonary aspergillosis (ABPA) (**Option C**) is an ongoing immunologic response to inhaled *Aspergillus*. The reaction leads to persistent eosinophilic airway inflammation, increased IgE levels, and eventually tissue damage with airway remodeling. Diagnostic criteria include the presence of asthma, elevated IgE levels, positive skin tests to *Aspergillus* antigens, increased pulmonary *Aspergillus*-specific IgE and IgG levels, and either central bronchiectasis or infiltrates. The patient's normal *Aspergillus*-specific IgE level and chest radiograph do not support a diagnosis of ABPA.

Treatment of asthma syndromes:

- Allergic asthma: treat as asthma; may require monoclonal antibody treatment if severe and associated with type 2 asthma phenotype
- Aspirin-exacerbated respiratory disease: aspirin and NSAID avoidance; stepped asthma care, including leukotriene-receptor antagonist
- Cough-variant: treat as asthma if reversible bronchoconstriction demonstrated
- Exercise-induced bronchospasm: SABA or low-dose budesonide-formoterol 15 minutes before exercise
- Occupational: avoid exposure through respiratory protection or removal from workplace
- Vocal cord dysfunction: speech therapy

Question 80

A 54-year-old man is evaluated during a follow-up visit for asthma. He has a 5-year history of persistent asthma. He has had one exacerbation within the last year, which was treated with glucocorticoids. He reports no wheezing but notes an intermittent nonproductive cough. His Asthma Control Test score is 24, indicating well-controlled asthma. He reports adherence to his maintenance inhaler and demonstrates good inhaler technique. He describes symptoms of epigastric burning following meals. He has no other gastrointestinal symptoms. He does not smoke, and he exercises daily without limitation. Medications are fluticasone-salmeterol 100/50 µg and an albuterol inhaler.

On physical examination, vital signs are normal, and no wheezing is noted. Spirometry is normal. Fractional exhaled nitric oxide level is normal.

Which of the following is the most appropriate management?

A. Begin omeprazole

B. Discontinue fluticasone-salmeterol; begin fluticasone 250 µg

C. Increase fluticasone-salmeterol strength to 500/50 µg

D. Perform upper endoscopy

Submit Your Answer

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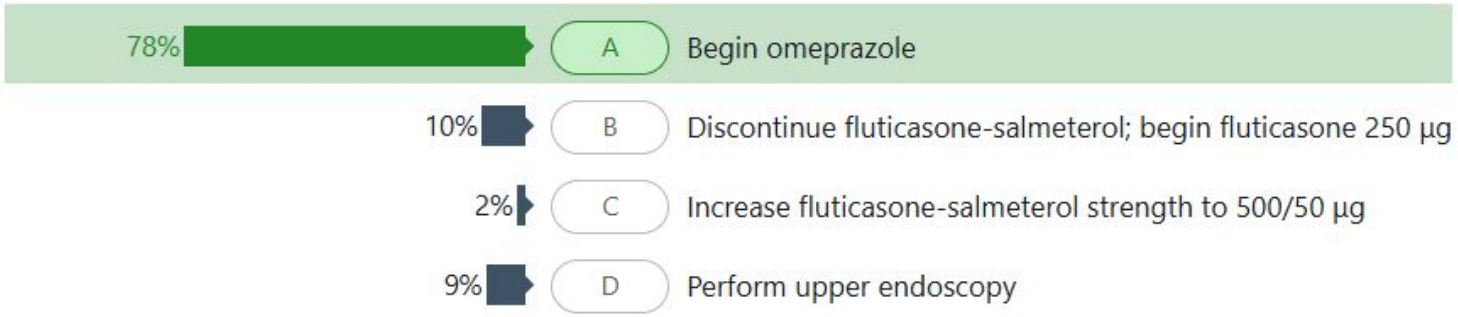
Which of the following is the most appropriate management?



Answer & Critique

Correct Answer: A

You answered A.

Educational Objective: **Treat gastroesophageal reflux disease in a patient with asthma.**

The most appropriate management for this patient is to begin omeprazole (**Option A**). The patient has a normal Asthma Control Test score, normal spirometry, and normal fractional exhaled nitric oxide, which all confirm that his asthma is well controlled. Measurement of the fraction of nitric oxide in an exhaled breath sample provides a noninvasive way to quantify eosinophilic airway inflammation and serves as a complementary tool in the diagnosis and management of asthma. However, his cough and other symptoms suggest gastroesophageal reflux disease (GERD), a common asthma comorbidity. At each asthma visit, clinicians should assess patient symptom control, inhaler technique and adherence, and comorbidities such as rhinosinusitis, obesity, and GERD. GERD is more common in patients with asthma than the general population and may contribute to respiratory symptoms such as cough, wheezing, and dyspnea. Potential mechanisms by which GERD may cause cough or worsened asthma control include increased vagal tone, bronchial hyperreactivity, and microaspiration of gastric contents into the upper airways. Empiric treatment of GERD in patients without worrisome symptoms such as weight loss, dysphagia, or hematemesis consists of a proton pump inhibitor such as omeprazole.

Key Points

- Gastrointestinal reflux disease is more common in patients with asthma than the general population and may contribute to respiratory symptoms such as cough, wheezing, and dyspnea.
- Patients with respiratory symptoms and gastroesophageal reflux disease should be treated with an empiric trial of a proton pump inhibitor.

Switching to a medium-dose inhaled glucocorticoid (**Option B**) is not needed because the patient is tolerating the current therapy and it is controlling his asthma symptoms.

Stepping up this patient's therapy by increasing the strength of his inhaled glucocorticoid (**Option C**) maintenance inhaler is not necessary without signs of worsening asthma.

Performing upper endoscopy (**Option D**) is unnecessary in patients with uncomplicated GERD without suspicion for malignancy, erosive esophagitis, or mechanical issues causing dysphagia, such as webs, rings, or strictures. Patients whose reflux symptoms do not improve should be considered for further testing such as endoscopy and 24-hour esophageal pH monitoring.

A 33-year-old man with a history of asthma and chronic rhinosinusitis comes to the emergency department complaining of shortness of breath. He developed an upper respiratory infection 3 days earlier and woke today with increased sinus headache and mild dyspnea. He started diphenhydramine, albuterol, and ibuprofen. He also took his normal dose of fluticasone/salmeterol 250/50 and nasal fluticasone but became increasingly dyspneic over the next 3 hours. He has had sinus surgery twice (most recently last year) and removal of nasal polyps 2 years ago.

The patient is in mild respiratory distress. His pulse is 115/min, respirations are 23/min, and pulse oximetry is 98% on 2L oxygen by nasal canula. Examination reveals significant rhinorrhea, diffuse bilateral wheezes, conjunctival injection, and facial erythema. He is given methylprednisolone and albuterol nebulizer treatments, with improvement of his symptoms over the next 24 hours.

In addition to tapering doses of prednisone, which of the following would most likely benefit this patient?

Discontinuation of salmeterol (3%)

Macrolide antibiotic (10%)

Montelukast (46%)

Referral for anti-IgE therapy (31%)

Tiotropium (7%)

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- B. Macrolide antibiotic (10%)
- ✓ C. Montelukast (46%)
- ✗ D. Referral for anti-IgE therapy (31%)
- E. Tiotropium (7%)

Aspirin-exacerbated respiratory disease	

Clinical features	• Samter's triad
	  ○ Chronic rhinosinusitis with nasal polyposis
	  ○ Asthma
	  ○ Aspirin (or NSAID) sensitivity
	• Ingestion can result in acute asthma exacerbation, profuse rhinorrhea, conjunctival injection, and erythematous flushing of the face
	• Symptoms begin within 30 minutes to 3 hours after ingestion

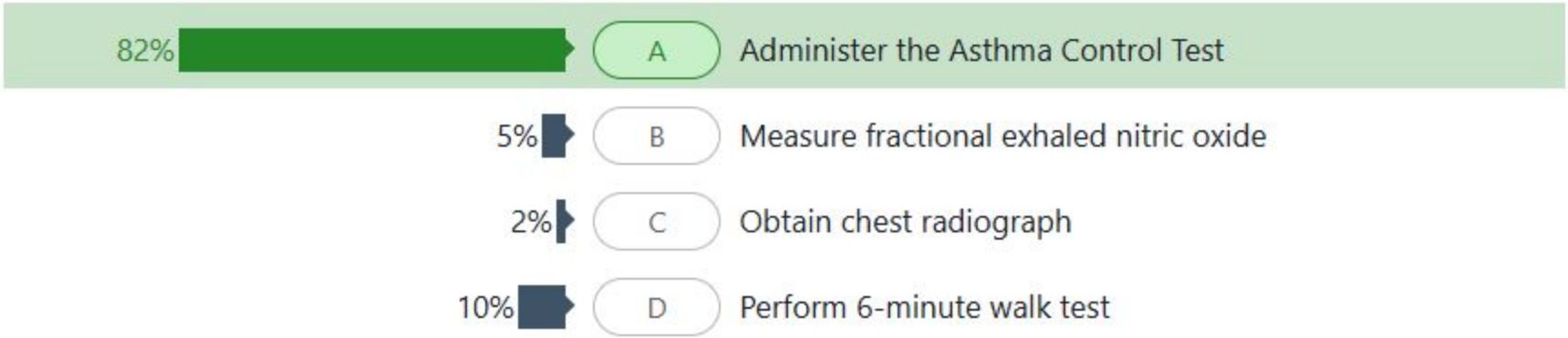
Treatment	• Avoid NSAIDs, if possible • Add leukotriene receptor antagonist (eg, montelukast, zafirlukast) • Consider aspirin desensitization if aspirin use is required for other medical conditions

Question 85

A 34-year-old man is evaluated at a routine follow-up examination. He has a history of spirometry-confirmed asthma. He reports feeling well and denies sinus symptoms, gastroesophageal reflux disease, and tobacco use. He demonstrates excellent inhaler technique. Medications are inhaled budesonide and albuterol.

On physical examination, vital signs are normal, and the remainder of the examination is unremarkable.

Which of the following is the most appropriate next step in evaluation?



Educational Objective: **Assess asthma symptom control using a standardized, validated questionnaire.**

The most appropriate next step in management is to administer a standardized, validated questionnaire such as the Asthma Control Test (**Option A**) to assess symptom control. Assessment of symptom control and risk is an essential component in the management of asthma and should be performed at each medical touchpoint. The Asthma Control Test and the Asthma Control Questionnaire are standardized, validated questionnaires that can discriminate between well-controlled and inadequately controlled asthma based on patient symptoms. These symptom control tools provide scores and cut points to distinguish different levels of control and to assess the patient's progress. When different systems are used to assess asthma control, the results broadly correlate but are not identical and using the same tool for each patient is most reasonable. Numerical asthma control tools are more sensitive to change in symptom control than categorical tools. In the Asthma Control Test, scores range from 5 to 25, with a higher score indicating better asthma control. Scores that correspond to other than well-controlled asthma suggest the need to review asthma risk factors, exposures, adherence, and inhaler technique, and the need for step-up therapy.

Key Points

- Assessment of symptom control is an essential component in the management of asthma and should be performed using a standardized, validated questionnaire.
- At present, fractional exhaled nitric oxide measurement (FeNO) is not recommended to guide asthma treatment in the general population.

At present, fractional exhaled nitric oxide measurement (FeNO) (**Option B**) is not recommended to guide asthma treatment in the general population. Studies have demonstrated that FeNO-guided treatment reduces exacerbation rates compared with guideline-based treatment, but further studies are needed to identify the populations of patients most likely to benefit from FeNO-guided care and the optimal frequency of FeNO monitoring. For example, the 2020 Asthma Guideline Update from the National Asthma Education and Prevention Program conditionally recommends FeNO monitoring in patients with persistent allergic asthma, for whom there is uncertainty in choosing, monitoring, or adjusting anti-inflammatory therapies based on history, clinical findings, and spirometry as part of an ongoing asthma monitoring and management strategy. Similarly, the 2021 American Thoracic Society guideline offers a conditional recommendation that measurement of FeNO be completed in patients with asthma in whom treatment is being considered. Although such testing may reduce asthma exacerbations, other important outcomes such as overall asthma control and acute care visits and hospitalizations for asthma, did not reach statistical significance. This patient does not need FeNO measurement.

Although a chest radiograph (**Option C**) is helpful in the initial evaluation of significant respiratory symptoms, it would not be indicated as routine care in a patient with controlled asthma symptoms.

The 6-minute walk test (**Option D**) provides a valid and reliable measure of exercise capacity in patients with lung disease. Patients walk at their own pace along a course for 6 minutes, and the total distance walked is recorded. The test can be used to assess response to therapy in patients with chronic respiratory disorders, especially pulmonary arterial hypertension, but there is no indication for this test in routine asthma care.

A 24-year-old man comes to the physician complaining of poor asthma control. He previously had not required therapy, but 3 months ago he developed an upper respiratory infection and has had difficulty controlling his symptoms since then. He was treated in the emergency department and discharged with tapering prednisone, fluticasone/salmeterol 100/50 µg, and albuterol metered-dose inhaler. The patient improved initially but his breathing did not return to normal. He has also been to an urgent care center twice in the last 2 months for breathing difficulty and has required nebulizer therapy. He tried to use his albuterol inhaler on each of these occasions but did not find relief. The patient is compliant with his medications and does not use tobacco, alcohol, or illicit drugs.

His temperature is 36.7 C (98 F), blood pressure is 118/78 mm Hg, pulse is 64/min, and respirations are 12/min. His pulse oximetry is 97% on room air. Physical examination shows a healthy young man in no acute distress. Lung examination shows mild end-expiratory wheezes but no crackles. He coughs during deep inspiration. Cardiac examination is normal.

Which of the following is the most appropriate next step in management of this patient?

Assess inhaler technique and provide education (91%)

Increase fluticasone/salmeterol to 250/50 µg (3%)

Order a nebulizer for home use (1%)

Prescribe an antibiotic (0%)

Start montelukast (2%)

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A 28-year-old primigravid woman at 20 weeks gestation comes to the office for asthma follow-up. Her asthma has been managed with combination mometasone-formoterol for relief as needed. She has never been hospitalized for asthma. Prior to pregnancy, the patient used a reliever inhaler no more than 1 or 2 times per month. However, over the past 2 months, she has used her inhaler several days per week. The patient also reports occasionally awakening at night with cough and wheezing. She denies any specific asthma triggers and does not own any pets.

Temperature is 36.7 C (98 F), blood pressure is 110/70 mm Hg, pulse is 84/min, and respirations are 16/min. Pulse oximetry is 96% on room air. The patient is not in acute distress and is breathing comfortably. Lung examination demonstrates good air entry with scattered expiratory wheezing bilaterally.

Results of spirometry are as follows:

Forced vital capacity (FVC)	80% of predicted
Forced expiratory volume in 1 second (FEV_1)	67% of predicted
FEV_1/FVC ratio	64% of predicted

Which of the following is the most appropriate pharmacotherapy?

Add daily tiotropium to the current regimen (10%)

Continue the current regimen without changes (3%)

Give a 7-day oral prednisone taper (6%)

Schedule mometasone-formoterol twice daily (75%)

Switch to fluticasone-salmeterol as needed (3%)

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A 36-year-old woman comes to the office due to episodic shortness of breath and cough productive of a trace amount of whitish sputum, occurring once or twice a week for the last 6 months. Symptoms seem worse when it is hot and humid and at night, but they do not disturb her sleep. Medical history is significant for allergic rhinitis, gastroesophageal reflux disease, and obesity. Medications include cetirizine, intranasal fluticasone, and pantoprazole. The patient smoked a pack of cigarettes daily at age 18-25. She feels well today and has no respiratory complaints.

Vital signs are within normal limits. BMI is 32 kg/m^2. Examination of the nasal passages shows boggy, edematous turbinates and no polyps. Pulmonary auscultation demonstrates clear breath sounds bilaterally with no wheezing. The remainder of the examination is normal.

The patient returns to the clinic for pulmonary function tests several days later, reporting that "my allergies and breathing are acting up again." Spirometry data are as follows:

Prebronchodilator	
FVC	90%
FEV_1	57%
FEV_1/FVC ratio	60%
Postbronchodilator	
FVC	96%
FEV_1	78%
FEV_1/FVC ratio	80%

Which of the following inhaled medication regimens would be most appropriate for initial management of this patient's condition?

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- Budesonide as needed (15%)
- Budesonide-formoterol as needed (69%)
- Ipratropium as needed (6%)
- Tiotropium daily (6%)
- Umeclidinium-vilanterol as needed (2%)

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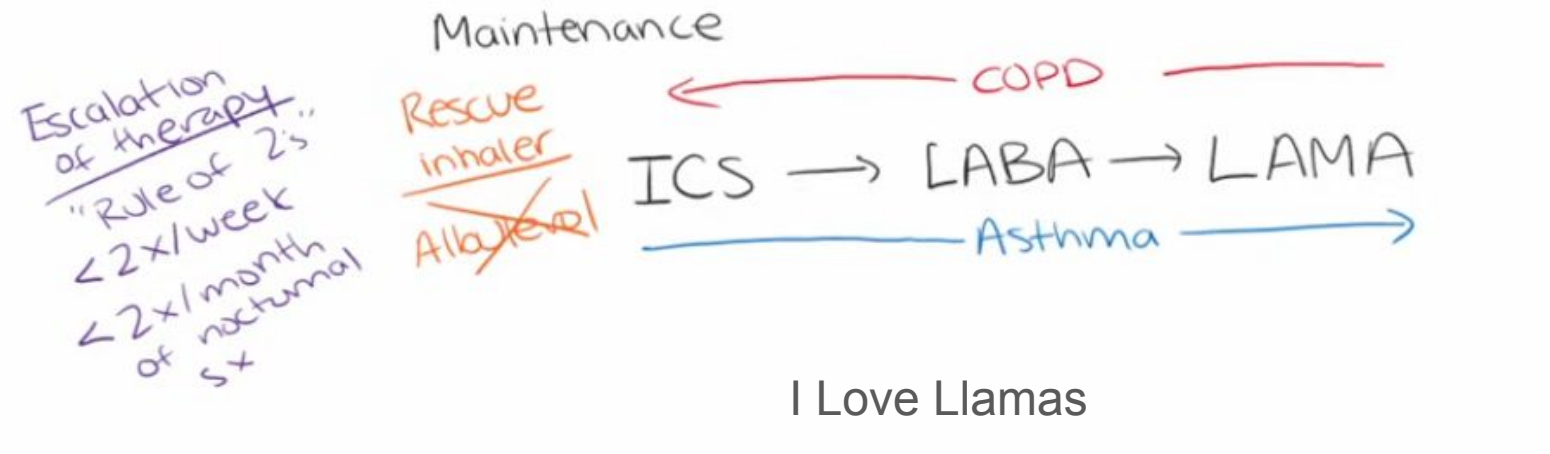
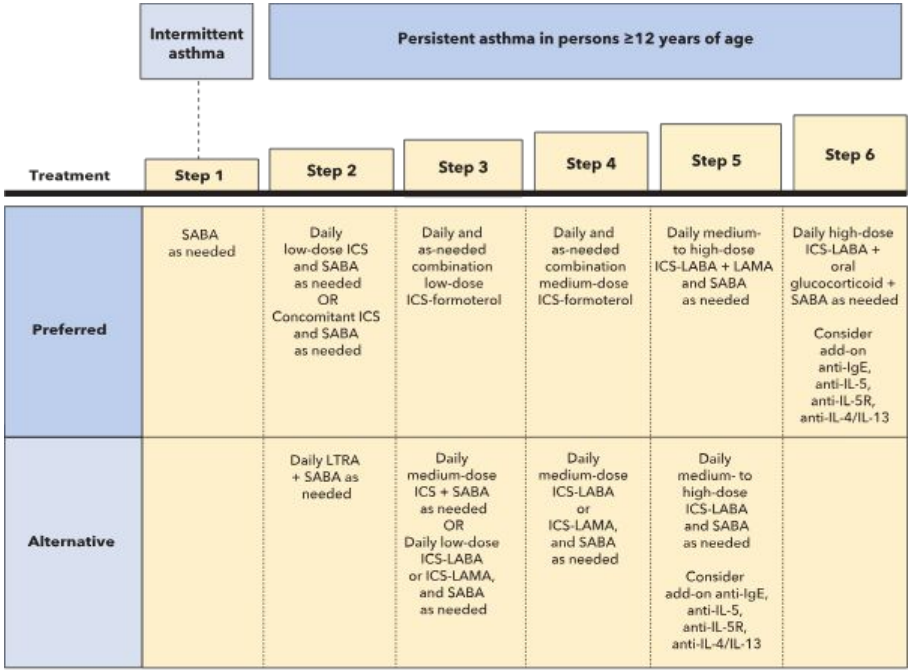
Asthma severity for patients not on controller medication			
Asthma severity	**Symptom frequency/ SABA use**	**Nighttime awakenings**	**Indicated therapy initiation**
Intermittent	≤2 days a week	≤2 times a month	Step 1
Mild persistent	>2 days a week but not daily	3-4 times a month	Step 2
Moderate persistent	Daily	>1 time a week but not nightly	Step 3
Severe persistent	Throughout the day	4-7 times a week	Step 4 or 5
SABA = short-acting beta-2 agonist.			



I Love Llamas



Assess control
Use of objective measures, self-report, and health care utilization

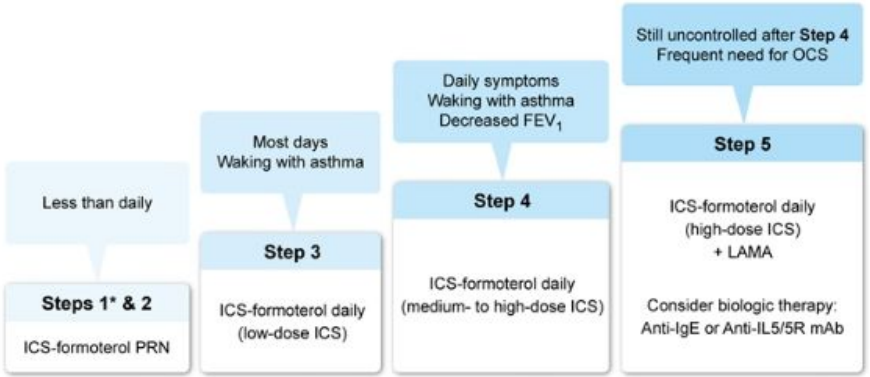
Step up if needed (first check adherence, inhaler technique, environmental factors, and comorbidities)
Step down if possible (and asthma is well controlled x 3 months)

- At each step, include patient education, environmental control, and management of comorbidities.
- For steps 2-4: Consider subcutaneous allergen immunotherapy for patients whose asthma is controlled at initiation, buildup, and maintenance phases.
- If step 4 care or higher is needed, consult with an asthma specialist.

Quick relief for all patients:

- SABA as needed for symptoms: up to 3 treatments at 20-minute intervals as needed
- In steps 3 and 4, ICS-formoterol 1-2 puffs as needed up to a maximum total daily dosage of 12 puffs (54 µg)
- Use of SABA >2 days a week (not prevention of EIB) indicates inadequate control and the need to step up therapy

Step-up strategy for asthma treatment (adults)



***Step 1:** Alternatively, ICS + SABA may be used PRN.

ICS = inhaled corticosteroid; **LAMA** = long-acting muscarinic antagonist; **LTRA** = leukotriene receptor antagonist; **mAb** = monoclonal antibody; **OCS** = oral corticosteroid; **PRN** = as needed; **SABA** = short-acting beta-2 agonist.

All patients should receive one of these three combination treatments:

For mild asthma, an inhaled glucocorticoid–formoterol combination as needed or low-dose inhaled glucocorticoid whenever a SABA is taken.

Regular inhaled glucocorticoid or inhaled glucocorticoid + LABA daily plus SABA when needed.

Maintenance and rescue treatment with inhaled glucocorticoid–formoterol.

A 28-year-old woman comes to the emergency department due to worsening shortness of breath and wheezing for the last 2 days. She has not had any fever, chills, or chest pain. The patient has a history of asthma, and symptoms occur mainly during winter. She does not have nocturnal asthma episodes. The patient uses budesonide-formoterol intermittently as needed, which usually controls her symptoms. However, over the last few hours, she has taken several puffs of her inhaler with no improvement. She has no other medical conditions and takes no other medications. The patient does not use tobacco or recreational drugs.

Temperature is 36.7 C (98.1 F), blood pressure is 128/76 mm Hg, pulse is 108/min, and respirations are 32/min. The patient is in marked respiratory distress. Lung examination shows bilateral wheezing and prolonged expiration with the use of accessory muscles. Peak expiratory flow rate is 120 L/min, which is 30% of her baseline.

Nebulized bronchodilators and systemic corticosteroids are administered, and the patient is admitted to the hospital. Two days later, symptoms are markedly improved, and the lungs are clear on auscultation, with excellent air movement. The patient wishes to return home. Her asthma action plan is reviewed at the bedside. An outpatient follow-up appointment is arranged for 2 weeks following discharge.

Which of the following medication regimens is most appropriate for this patient until that time?

Continuation of inhaled budesonide-formoterol as needed (1%)

Scheduled inhaled budesonide-formoterol twice daily (10%)

Short course (5-10 days) of oral prednisone, and continuation of inhaled budesonide-formoterol as needed (14%)

Short course (5-10 days) of oral prednisone, and scheduled inhaled budesonide-formoterol twice daily (70%)

Short course (5-10 days) of oral prednisone, and scheduled inhaled tiotropium daily (2%)

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- ✓ D. Short course (5-10 days) of oral prednisone, and scheduled inhaled budesonide-formoterol twice daily (70%)
- E. Short course (5-10 days) of oral prednisone, and scheduled inhaled tiotropium daily (2%)

ACUTE EXACERBATIONS

An asthma exacerbation (attack) is an acute worsening of baseline symptoms, usually with a large decline in expiratory airflow. Most exacerbations are triggered by aeroallergen exposure or viral upper respiratory infection. Other precipitants include NSAIDs (ie, AERD) and beta blockers. Exacerbations can evolve over days, hours, or minutes.

Less severe exacerbations

A slower buildup has a more favorable prognosis (when treated early) and lends itself to outpatient management. Patients without signs of impending respiratory failure (eg, wheezing but good air movement, ability to hold breath and use inhalers) and stable social situations are good candidates for outpatient treatment. This usually involves:

- A short course of oral corticosteroids (eg, **prednisone** 40-60 mg/day for 5-7 days).
- A step up in existing therapy (eg, increase dose or frequency of ICS bronchodilator).

Educational objective:

Heightened bronchial inflammation persists for several days after symptomatic resolution of an acute asthma exacerbation, accounting for a high risk for relapse. After discharge from the hospital, patients should complete a short course of oral corticosteroids. In addition, the existing controller regimen should be temporarily stepped up for 2-4 weeks pending clinical reassessment of asthma control.

Question 13

A 35-year-old woman is evaluated for a cough and wheezing occurring several times during the week, unrelated to exercise. She has a history of asthma that was previously well controlled with a budesonide inhaler. She is also taking albuterol five times weekly with good response. Her symptoms have woken her once in the past month. She reports no additional symptoms and no environmental triggers. She is a nonsmoker. Inhaler technique is good.

On physical examination, vital signs are normal. Oxygen saturation is 96% with the patient breathing ambient air. Expiratory wheezing is noted.

Which of the following treatments should be started?

A Add formoterol

B Azithromycin

C Prednisone

D Tiotropium

Submit Your Answer

Question 13

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On physical examination, vital signs are normal. Oxygen saturation is 96% with the patient breathing ambient air. Expiratory wheezing is noted.

Which of the following treatments should be started?

75%	A	Add formoterol
0%	B	Azithromycin
15%	C	Prednisone
10%	D	Tiotropium

Answer & Critique

Correct Answer: A

You answered A.

Educational Objective: **Treat mild persistent asthma by stepping up therapy.**

The most appropriate treatment is to step up therapy by adding a long-acting β_2-agonist (LABA) to the current inhaled glucocorticoid (**Option A**); the preferred method would be by starting a combined budesonide-formoterol inhaler. This patient has mild persistent asthma with low-dose inhaled glucocorticoid maintenance therapy and now has increasing symptoms requiring frequent use of her short-acting β_2-agonist (SABA) inhaler. A step up in therapy is indicated for inadequate asthma control, including either use of a SABA more than twice weekly (not related to prevention of exercise-induced bronchospasm) or need for a SABA two or more times monthly for nocturnal symptoms. Guidelines indicate that the preferred next step is combined therapy with a low-dose inhaled glucocorticoid and LABA in a single inhaler. When LABAs

Key Points

- The preferred next step for patients with inadequately controlled mild persistent asthma on an inhaled glucocorticoid is combined therapy with a low-dose inhaled glucocorticoid and long-acting β_2-agonist in a single inhaler.
- Administration of a glucocorticoid and long-acting β_2-agonist in a single inhaler is preferred because it improves adherence and may reduce cost compared with administration of each drug in a separate inhaler.

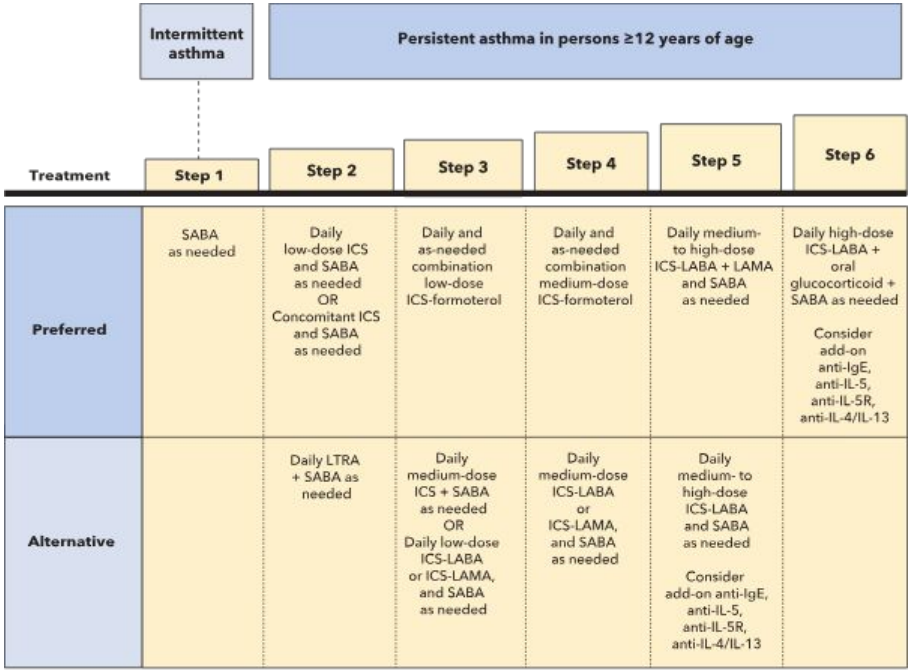
two or more times monthly for nocturnal symptoms. Guidelines indicate that the preferred next step is combined therapy with a low-dose inhaled glucocorticoid and LABA in a single inhaler. When LABAs are added to inhaled glucocorticoids, they provide improved control and decrease the risk of exacerbations. Administration in a single inhaler is preferred because it improves adherence and may reduce cost compared with administration of each drug in a separate inhaler. Other treatment options would include increasing the patient's regimen to a medium-dose inhaled glucocorticoid or adding a leukotriene receptor antagonist to her current dose of an inhaled glucocorticoid.

administration of each drug in a separate inhaler.

Azithromycin (**Option B**) can be used to treat upper and lower respiratory tract infections and is also recommended as add-on therapy given three times weekly for persistent asthma not controlled by combined moderate- to high-dose inhaled glucocorticoids with LABA. However, this patient does not have symptoms that suggest infection and has not yet had a trial of combined inhaled glucocorticoid–LABA therapy, making this choice incorrect.

Use of prednisone (**Option C**) could be considered if the patient does not improve with a step up in her maintenance therapy or if her clinical symptoms become more severe. However, this would not be recommended as the initial choice.

Long-acting muscarinic antagonists (LAMAs) such as tiotropium (**Option D**) provide sustained airway dilation. When added to therapy for asthma not controlled with inhaled glucocorticoid–LABA combination therapy, tiotropium has been shown to improve lung function and reduce exacerbations. However, no substantial evidence shows that LAMAs should be the first choice for long-acting airway dilation, and National Asthma Education and Prevention Program guidelines specifically advise against using a LAMA as the initial agent to step up from inhaled glucocorticoid controller therapy.



Assess control
Use of objective measures, self-report, and health care utilization

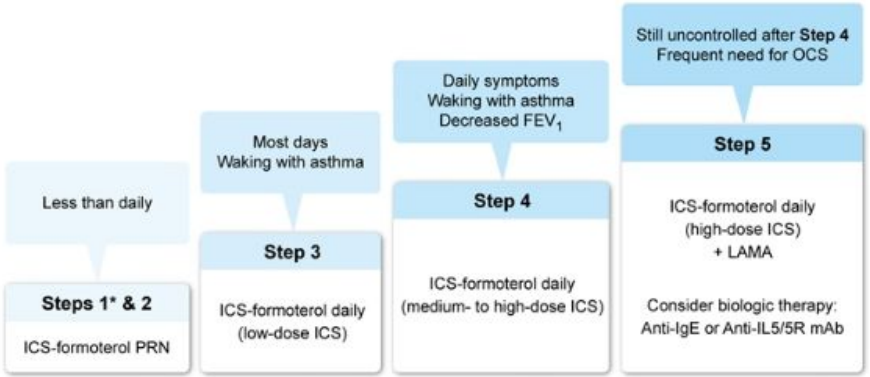
Step up if needed (first check adherence, inhaler technique, environmental factors, and comorbidities)
Step down if possible (and asthma is well controlled x 3 months)

- At each step, include patient education, environmental control, and management of comorbidities.
- For steps 2-4: Consider subcutaneous allergen immunotherapy for patients whose asthma is controlled at initiation, buildup, and maintenance phases.
- If step 4 care or higher is needed, consult with an asthma specialist.

Quick relief for all patients:

- SABA as needed for symptoms: up to 3 treatments at 20-minute intervals as needed
- In steps 3 and 4, ICS-formoterol 1-2 puffs as needed up to a maximum total daily dosage of 12 puffs (54 µg)
- Use of SABA >2 days a week (not prevention of EIB) indicates inadequate control and the need to step up therapy

Step-up strategy for asthma treatment (adults)



***Step 1:** Alternatively, ICS + SABA may be used PRN.

ICS = inhaled corticosteroid; **LAMA** = long-acting muscarinic antagonist; **LTRA** = leukotriene receptor antagonist; **mAb** = monoclonal antibody; **OCS** = oral corticosteroid; **PRN** = as needed; **SABA** = short-acting beta-2 agonist.

ICS-LABA > doubling ICS dose	Cochrane meta-analysis (48 RCTs, 15,155 participants): ICS-LABA reduced exacerbations requiring oral corticosteroids (RR 0.88) vs higher-dose ICS; NNT=73 over 12 weeks
SMART Budesonide-formoterol reduces exacerbation: ICS alone or ICS-LABA+SABA	NOVEL START trial 62% reduction in severe exacerbations versus albuterol alone
LABA monotherapy CI - increased asthma related deaths	SMART trial salmeterol 4 FDA mandated trial led to removal of black box for ICS-LABA
Tiotropium (LAMA) improves lung function and may reduce exacerbations in uncontrolled asthma	TRIMARAN/TRIGGER trial - triple therapy reduced severe exacerbations

A 36-year-old woman comes to the office due to episodic shortness of breath and cough productive of a trace amount of whitish sputum, occurring once or twice a week for the last 6 months. Symptoms seem worse when it is hot and humid and at night, but they do not disturb her sleep. Medical history is significant for allergic rhinitis, gastroesophageal reflux disease, and obesity. Medications include cetirizine, intranasal fluticasone, and pantoprazole. The patient smoked a pack of cigarettes daily at age 18-25. She feels well today and has no respiratory complaints.

Vital signs are within normal limits. BMI is 32 kg/m^2. Examination of the nasal passages shows boggy, edematous turbinates and no polyps. Pulmonary auscultation demonstrates clear breath sounds bilaterally with no wheezing. The remainder of the examination is normal.

The patient returns to the clinic for pulmonary function tests several days later, reporting that "my allergies and breathing are acting up again." Spirometry data are as follows:

Prebronchodilator	
FVC	90%
FEV_1	57%
FEV_1/FVC ratio	60%
Postbronchodilator	
FVC	96%
FEV_1	78%
FEV_1/FVC ratio	80%

Which of the following inhaled medication regimens would be most appropriate for initial management of this patient's condition?

- Budesonide as needed (15%)
- Budesonide-formoterol as needed (69%)
- Ipratropium as needed (6%)
- Tiotropium daily (6%)
- Umeclidinium-vilanterol as needed (2%)

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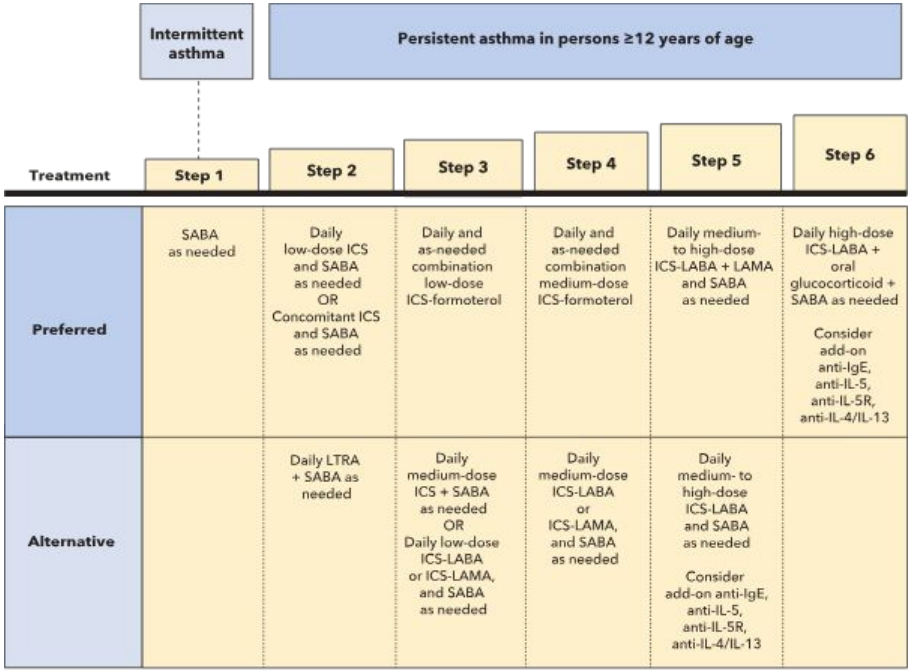

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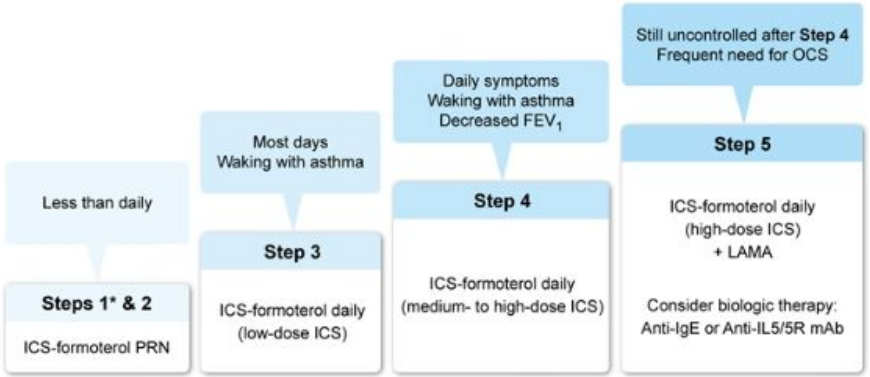

***Step 1:** Alternatively, ICS + SABA may be used PRN.

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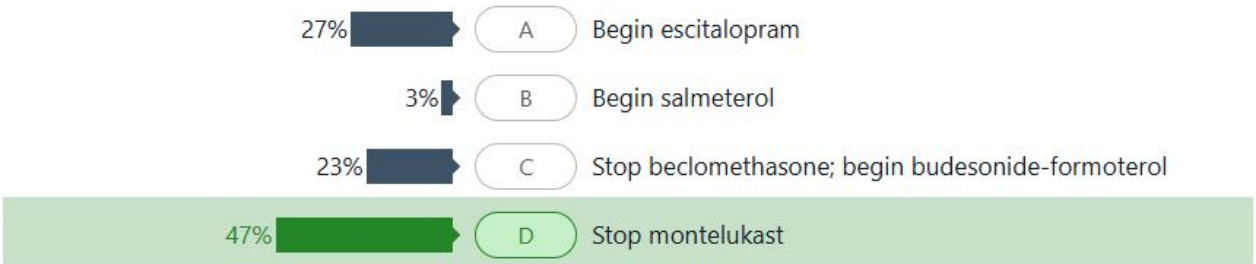
Question 58

A 25-year-old man is seen in follow-up examination for asthma diagnosed 2 months ago. He reports that his symptoms are now well controlled without use of his rescue inhaler, and results of the Asthma Control Test confirm well-controlled asthma. During the visit, he describes feeling down on many days, with difficulty falling asleep and early morning awakening. Depression screening with the Patient Health Questionnaire-2 is positive. Medications are beclomethasone, montelukast, and albuterol.

On physical examination, vital signs and pulmonary examination are normal.

Which of the following is the most appropriate treatment?



Answer & Critique

Correct Answer: D

You answered D.

The most appropriate treatment is to stop montelukast (**Option D**). After initiation of asthma therapies, patients should be reassessed for symptom control and medication tolerance. Montelukast has been associated with significant adverse mental health effects and may be the cause of the patient's depression. Depressive symptoms can occur in patients with and without a previous history of depression or other neuropsychiatric disorders. In March 2020 the FDA added a boxed warning to montelukast, strengthening previous warnings about behavior and mood-related changes, including suicides, associated with this medication. The FDA also advised against using montelukast for allergic rhinitis because other first-line medications, such as intranasal glucocorticoids, are widely available and more efficacious and because many physicians are unaware of montelukast's potential adverse mental health effects. This patient's asthma symptoms are well controlled, and he has new symptoms and a positive Patient Health Questionnaire-2 result suggesting depression; therefore, montelukast should be discontinued, and the patient should be monitored for improvement in his depressive symptoms, which typically resolve if medication related. Other adverse effects include anaphylaxis, angioedema, dizziness, dyspepsia, muscle weakness, and elevated transaminases occurring in less than 2% of all patients. The occurrence of eosinophilic granulomatosis with polyangiitis has been described in patients taking antileukotriene agents, but most cases occur following discontinuation of glucocorticoids for severe asthma and may simply represent an uncovering of a previously undiagnosed condition. It remains unclear if this adverse event is caused by the drug.

Key Points

- After initiation of asthma therapies, patients should be reassessed for symptom control and medication tolerance.
- Montelukast should be discontinued in patients with symptoms suggestive of depression.

Escitalopram (**Option A**) is a selective serotonin reuptake inhibitor used to treat depression and anxiety in adults. Adding an antidepressant to this patient's regimen is not necessary because the montelukast may be the cause of the patient's depression and discontinuation of the medication may resolve his symptoms.

Controller medications such as salmeterol or budesonide-formoterol (**Options B, C**) can be stepped up or down with the goal of maintaining symptom control and minimizing medication exposure. Stepping up this patient's treatment regimen with additional controller medications is not indicated because his asthma symptoms are well controlled. Instead, his therapy should be stepped down, and the first drug to be discontinued is montelukast.

A 49-year-old woman is evaluated in the office following a recent hospitalization for an asthma exacerbation. Her symptoms have improved but she continues to have dyspnea and intermittent wheezing. She has had two other hospitalizations within the past year for asthma exacerbations despite the chronic use of oral glucocorticoids. Other than a 3-year history of asthma, her medical history is unremarkable. Medications are mometasone/formoterol, montelukast, albuterol, tiotropium, and prednisone.

On physical examination, vital signs are normal. Oxygen saturation is 95% on ambient air. Pulmonary examination reveals expiratory wheezes with good air movement. The remainder of the physical examination is unremarkable.

Laboratory studies reveal leukocyte count of 10,000/μL (10×10^9/L) with 650 eosinophils/μL (0.65×10^9/L). Serum IgE level is 12 U/mL (12 kU/L) (normal range, 0-90 U/mL [0-90 kU/L]).

FEV_1 is 56% of predicted. Chest radiograph is normal

Which of the following is the most appropriate treatment?

A. Begin Doxycycline
B. Change mometasone/formoterol to fluticasone/salmeterol
C. Initiate a trial of mepolizumab
D. Initiate a rial of omalizumab therapy

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Asthma Medications

Drug	Formulations	Adverse Effects
Short-Acting β_2-Agonists		
Albuterol	HFA-MDI, nebulizer solution	Tachycardia and hypokalemia
Levalbuterol	HFA-MDI, nebulizer solution	Should not be used as monotherapy
Short-acting Anticholinergics (Muscarinic Antagonists)		
Ipratropium bromide	HFA-MDI, nebulizer solution	Dry mouth, tachycardia, acute narrow-angle glaucoma (rare)
Albuterol/ipratropium bromide	HFA-MDI, nebulizer solution	Same and combined effects of both drug classes

Long-Acting β_2-Agonists		
Formoterol[a]	DPI	Tremor, tachycardia; black box warning for use of long-acting β_2-agonist monotherapy in asthma
Salmeterol	DPI	
Arformoterol[a]	Nebulizer solution	
Formoterol fumarate[a]	Nebulizer solution	
Olodaterol[a]	SMI	
Indacaterol maleate[a]	DPI	

Long-acting Muscarinic Antagonists (Anticholinergics)		
Tiotropium	DPI, SMI	Dry mouth, tachycardia, urinary retention, acute narrow-angle glaucoma (rare)
Aclidinium bromide	DPI	
Umeclidinium	DPI	
Glycopyrrolate	DPI	
Inhaled Glucocorticoids		
Beclomethasone	HFA-MDI	Dysphonia, xerostomia, oral candidiasis, bruising, pneumonia; low incidence of oral glucocorticoid adverse effects
Budesonide	DPI, nebulizer solution	
Fluticasone propionate	HFA, DPI	
Fluticasone furoate	DPI	
Mometasone	DPI	
Ciclesonide	HFA-MDI	
Flunisolide	HFA-MDI	

Inhaled Glucocorticoids and Long-Acting β_2-Agonists		
Budesonide and formoterol[a]	HFA	Same as combined effects of both drug classes
Fluticasone and salmeterol	HFA, DPI	
Mometasone furoate and formoterol fumarate[a]	HFA	
Fluticasone furoate and vilanterol[a]	DPI	
Oral Glucocorticoids		
Prednisone	Tablet, liquid	Bruising, adrenal suppression, osteoporosis, glaucoma, diabetes mellitus, opportunistic infection, insomnia, cataracts, hypertension, weight gain, myopathy, acne
Prednisolone	Tablet, liquid	
Methylprednisolone	IV infusion, tablet	
Leukotriene-Modifying Agents		
Montelukast	Tablet	Headache; rarely liver disease; neuropsychiatric events, including suicidal thoughts and actions
Zafirlukast	Tablet	
Zileuton (5-lipoxygenase inhibitor)	Tablet	

Biologic Agents		
Omalizumab (anti-IgE)	Subcutaneous injection	Anaphylaxis, increased risk for malignancy
Mepolizumab (anti-IL-5)	Subcutaneous injection	
Reslizumab (anti-IL-5) Benralizumab (anti-IL-5) Dupilumab (anti-IL-4 and IL-13)	IV infusion Subcutaneous injection Subcutaneous injection	
Other		
Theophylline	Tablet, capsule, liquid	Tachycardia, nausea, overdose can be fatal

Don't Be Tricked

- Do not administer theophylline with fluoroquinolones or macrolides (may result in theophylline toxicity).
- Do not use LABAs as single agents in asthma (increased mortality rate).

Biologic Treatments Available for Asthma

	OMALIZUMAB (XOLAIR)	MEPOLIZUMAB (NUCALA)	BENRALIZUMAB (FASENRA)	RESLIZUMAB (CINQAIR)	DUPILUMAB (DUPIXENT)	TEZEPELUMAB-EKKO (TEZSPIRE)
Asthma Indication	Moderate-to-severe asthma and positive allergy test to perennial aeroallergen (allergic asthma)	Severe eosinophilic asthma	Severe eosinophilic asthma	Severe eosinophilic asthma	Moderate-to-severe eosinophilic asthma or OCS-dependent asthma	Severe asthma
Approved Ages	6+	6+	6+	18+	6+	12+
Mode of Administration	Subcutaneous injection (shot)	Subcutaneous injection (shot)	Subcutaneous injection (shot)	Intravenous infusion (IV)	Subcutaneous injection (shot)	Subcutaneous injection (shot)
Setting of Administration	Clinic or home	Clinic or home	Clinic or home	Clinic	Clinic or home	Clinic or home
Dosing Interval	Every 2-4 weeks	Every 4 weeks	Every 4 weeks for the first 3 doses, then every 8 weeks	Every 4 weeks	Every 2 weeks or every 4 weeks	Every 4 weeks
Molecule/ Target	IgE /Anti-IgE monoclonal antibody	IL-5/Anti-IL-5 monoclonal antibody	IL-5 receptor/ Anti-IL-5 receptor monoclonal antibody	IIL-5/Anti-IL-5 monoclonal antibody	IL-4 and IL-13/ Anti-IL-4R alpha monoclonal antibody	TSLP/Anti-TLSP monoclonal antibody

Abbreviations used: immunoglobulin-E (IgE), interleukin (IL), oral corticosteroids (OCS), thymic stromal lymphopoietin (TSLP)

Updated: October 2025 • aafa.org

What is the target and mechanism of omalizumab (Xolair)?
Target: Anti-IgE
Mechanism: Prevents circulating IgE from binding to high-affinity receptors on mast cells and basophils
Key biomarker: Positive skin test or in vitro reactivity to perennial aeroallergenHow is omalizumab (Xolair) dosed and administered?
Route: Subcutaneous
Frequency: Every 2-4 weeks (based on weight and pretreatment IgE levels)
Dose range: 75-375 mg
Age: ≥6 years
What are the key safety concerns with omalizumab (Xolair)?
Black box warning: Anaphylaxis (~0.1-0.2% risk)
Must be administered in healthcare setting with observation period
Serum sickness-like reactions reported
Risk of eosinophilic granulomatosis with polyangiitis (EGPA)

Mepolizumab (Nucala) What is the target and mechanism of mepolizumab (Nucala)? **Target:** Anti-IL-5 **Mechanism:** Binds to circulating IL-5, preventing it from binding to IL-5 receptor on eosinophils **Key biomarker:** Blood eosinophils ≥150/μL

Mepolizumab Dosing How is mepolizumab (Nucala) dosed and administered? **Route:** Subcutaneous **Adults/adolescents:** 100 mg every 4 weeks **Children 6-11 years:** 40 mg every 4 weeks **Age:** ≥6 years

Mepolizumab Safety What are the key adverse effects of mepolizumab (Nucala)? Herpes zoster reactivation, Hypersensitivity reactions (rare), Helminthic infections, Abrupt discontinuation of oral corticosteroids can cause withdrawal symptoms

Benralizumab (Fasenra) What is the target and mechanism of benralizumab (Fasenra)? **Target:** Anti-IL-5Rα **Mechanism:** Binds to IL-5 receptor alpha on eosinophils and basophils, causing antibody-dependent cell-mediated cytotoxicity and depletion **Key biomarker:** Blood eosinophils ≥150/μL (≥300/μL suggested)

Benralizumab Dosing How is benralizumab (Fasenra) dosed and administered? **Route:** Subcutaneous **Dose:** 30 mg every 4 weeks for first 3 doses, then every 8 weeks **Age:** ≥6 years (FDA updated from ≥12 years)

Reslizumab (Cinqair)

What is the target and mechanism of reslizumab (Cinqair)? **Target:** Anti-IL-5 **Mechanism:** Binds to circulating IL-5, preventing it from binding to IL-5 receptor on eosinophils **Key biomarker:** Blood eosinophils ≥400/μL

Reslizumab Dosing How is reslizumab (Cinqair) dosed and administered? **Route:** Intravenous infusion (only IV biologic for asthma) **Dose:** 3 mg/kg every 4 weeks **Age:** ≥18 years

Reslizumab Safety What is the key safety concern with reslizumab (Cinqair)? **Black box warning:** Anaphylaxis (~0.3% risk in clinical trials) Must be observed by healthcare professional after administration Helminthic infections

Dupilumab (Dupixent) What is the target and mechanism of dupilumab (Dupixent)? **Target:** Anti-IL-4Rα **Mechanism:** Binds to IL-4 receptor alpha, blocking both IL-4 and IL-13 signaling in hematopoietic cells, epithelial cells, and airway smooth muscle **Key biomarker:** Blood eosinophils ≥150/μL and/or FeNO ≥25 ppb

D**upilumab Dosing** How is dupilumab (Dupixent) dosed and administered? **Route:** Subcutaneous **Adults/adolescents:** Initial 400 mg, then 200 mg every 2 weeks (or 600 mg initial, then 300 mg every 2 weeks for OCS-dependent or concomitant atopic dermatitis) **Children 6-11 years:** Weight-based dosing **Age:** ≥6 years

Dupilumab Safety What are the key adverse effects of dupilumab (Dupixent)? Conjunctivitis, Transient blood eosinophilia, Risk of EGPA and eosinophilic pneumonia,Injection site reactions (up to 18%), Live vaccines should be avoided

Tezepelumab (Tezspire) What is the target and mechanism of tezepelumab (Tezspire)? **Target:** Anti-TSLP (thymic stromal lymphopoietin) **Mechanism:** Prevents TSLP from binding to its receptor on dendritic cells, mast cells, type 2 innate lymphoid cells, and T helper 2 cells **Unique feature:** Effective across broad range of eosinophil counts; no specific biomarker required

Tezepelumab Dosing How is tezepelumab (Tezspire) dosed and administered? **Route:** Subcutaneous **Dose:** 210 mg every 4 weeks **Age:** ≥12 years

Tezepelumab Safety What are the common adverse effects of tezepelumab (Tezspire)? Pharyngitis, Arthralgia, Back pain, Live vaccines should be avoided

Biologics - General Efficacy What is the general efficacy of biologics for severe asthma? **30-70% reduction** in relative risk of severe asthma exacerbations compared to placebo, Reduced symptoms and improved quality of life, Oral corticosteroid-sparing effect demonstrated for benralizumab, mepolizumab, dupilumab, and reslizumab, Trial of at least 4 months needed to assess initial response

Biologics - When to Consider When should biologics be considered for asthma management? Uncontrolled severe asthma despite **optimized maximal therapy** (high-dose ICS-LABA ± LAMA), Persistent exacerbations or poor symptom control, To avoid or minimize high-dose inhaled or oral corticosteroids, Refer to pulmonologist or allergist before initiating, Continue other controller medications when starting biologics