

COPD Part II: Advanced COPD Therapy

Case related questions.

Scenario:

Ms. H is a 65-year-old woman with Chronic Obstructive Pulmonary Disease (COPD) and a forced expiratory volume in 1 second (FEV₁) of 45% of predicted. You have been following her for several years and have treated her with fluticasone/salmeterol 250/50 mcg 1 puff twice daily, tiotropium 18 mcg (1 capsule) inhaled daily, and albuterol 2 puffs or a nebulizer treatment every 6 hours as needed. Despite using her inhalers regularly, she feels that her symptoms have gotten progressively worse over the last year. She has been admitted to the hospital twice in the last year for COPD exacerbations but has never been intubated or required BiPAP. Since her last hospitalization, she feels like she hasn't recovered to her previous baseline and is using an albuterol rescue inhaler 5-6 times daily. She has a chronic cough and brings up a moderate amount of pale-yellow mucus daily. Some days, she has trouble getting the mucus up but breathes a bit better once she does. She quit smoking 16 years ago and had a 30-pack-year history. In the office, she is comfortable appearing. Her resting saturation is 93% breathing ambient air. Her other vitals are within normal limits. Her pulmonary exam is notable for decreased breath sounds bilaterally with a prolonged expiratory phase but no wheezes or rhonchi. She has no clubbing or peripheral edema. The rest of the exam is normal. Review of her laboratory data reveals absolute serum eosinophil values consistently ranging 300 – 400 cells/ul. She has no history of asthma or atopy.

Question 1a: Is her current inhaler therapy appropriate?

Question 1b: What other pharmacologic treatment options are available to help Ms. H given that she is already on maximal bronchodilator therapy, long-acting muscarinic antagonist/long-acting beta-agonist/inhaled corticosteroid with albuterol rescue (LAMA/LABA/ICS)? What evidence supports their use?

Question 1c: What non-pharmacologic treatment options are available to help Ms. H?

Question 1d: What additional considerations apply when caring for women with COPD?

Scenario cont.:

You confirm that Ms. H's oxygen saturations remain 90% or greater on room air with exertion. She begins therapy with roflumilast. She has had some diarrhea for the first couple of weeks on the medication, but this has improved, and she denies significant side effects. After further discussion, she decides to enroll in pulmonary rehab.

Question 2: What is pulmonary rehabilitation, and in what ways is it beneficial for COPD patients?

Scenario cont.:

Ms. H had strong participation in pulmonary rehabilitation and increased her 6-minute walk distance. Unfortunately, she still struggles with severe dyspnea and limited exertional capacity. A friend suggested she ask you about lung volume reduction and she wonders if she is a candidate.

Question 3a: What is lung volume reduction and how can it be performed?

Question 3b: What patient characteristics are favorable (and unfavorable) for lung volume reduction?

Question 3c: What evaluation is necessary prior to consideration for lung volume reduction?

Scenario cont.:

On evaluation, Ms. H has an FEV₁ of 42% pred, TLC 110% pred, RV 145% predicted, and DLCO 32% pred. Her CT shows severe, relatively homogeneous emphysema. Her ABG on room air shows 7.32/65/54. Echocardiogram shows normal RV and LV size/function and an estimated pulmonary artery systolic pressure of 44 mmHg. You explain that she is not a candidate for either LVRS or BLVR due to homogeneous emphysema, insufficient air-trapping, and significant hypercapnia.

Question 4a: Would Ms. H benefit from nocturnal non-invasive positive pressure ventilation?

Question 4b: How would you obtain approval for NIPPV?

COPD Part II: Advanced COPD Therapy

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Educational Objectives:

1. Summarize current evidence for triple inhaler therapy
2. Describe pharmacologic and nonpharmacologic adjunctive therapies
3. Identify which patients should be prescribed supplemental O2 therapy
4. Outline the benefits of pulmonary rehabilitation
5. Identify patients who may benefit from lung volume reduction
6. Determine which patients in whom to consider nocturnal non-invasive nocturnal ventilation

Scenario:

Ms. H is a 65-year-old woman with Chronic Obstructive Pulmonary Disease (COPD) and a forced expiratory volume in 1 second (FEV₁) of 45% of predicted. You have been following her for several years and have treated her with fluticasone/salmeterol 250/50 mcg 1 puff twice daily, tiotropium 18 mcg (1 capsule) inhaled daily, and albuterol 2 puffs or a nebulizer treatment every 6 hours as needed. Despite using her inhalers regularly, she feels that her symptoms have gotten progressively worse over the last year. She has been admitted to the hospital twice in the last year for COPD exacerbations but has never been intubated or required BiPAP. Since her last hospitalization, she feels like she hasn't recovered to her previous baseline and is using an albuterol rescue inhaler 5-6 times daily. She has a chronic cough and brings up a moderate amount of pale-yellow mucus daily. Some days, she has trouble getting the mucus up but breathes a bit better once she does. She quit smoking 16 years ago and had a 30-pack-year history. In the office, she is comfortable appearing. Her resting saturation is 93% breathing ambient air. Her other vitals are within normal limits. Her pulmonary exam is notable for decreased breath sounds bilaterally with a prolonged expiratory phase but no wheezes or rhonchi. She has no clubbing or peripheral edema. The rest of the exam is normal. Review of her laboratory data reveals absolute serum eosinophil values consistently ranging 300 – 400 cells/ul. She has no history of asthma or atopy.

Question 1a: Is her current inhaler therapy appropriate?

Yes. An extensive evidence base supports the use of long-acting bronchodilators (LABAs and LAMAs) and inhaled corticosteroids (ICS) in patients with COPD. Robust data confirms that these medications decrease exacerbation rates, reduce symptom burden, and increase exercise tolerance. While they historically have not shown a mortality benefit compared to placebo in randomized trials, these studies mainly focused on reduction in symptoms, exacerbation rates, and improvement in quality of life. Regardless, these medications form the foundation of pharmacologic treatment for COPD.

Several trials have now demonstrated the benefit of so-called “triple therapy,” consisting of an ICS, LABA, and LAMA, in patients with COPD *and* a history of exacerbations.¹⁻³ Specifically, triple therapy consistently reduces the rate of moderate to severe exacerbations and increases health status compared to either dual therapy with LABA/LAMA or LABA/ICS. In addition to proving the benefit of triple therapy over dual therapy, secondary analyses of the original randomized controlled trials (RCTs) have shown triple therapy reduces mortality in patients with a history of exacerbations. Whether the convincing benefit of triple therapy extends to patients without a history of exacerbations is not known, as the trials comparing triple therapy to dual therapy included only patients with a recent history of exacerbation.

ICS-containing regimens may not benefit all patients, particularly those with consistently low serum eosinophils (<100 cells/uL).⁴ Given the increased risk of pneumonia in patients on an ICS, it is important to consider which patients are likely to benefit from an ICS.⁵ This patient has values consistently ≥ 300 which add further data to support a benefit with the use of ICS. GOLD guidelines now recommend routine measurement of blood eosinophil counts to guide decisions about ICS use.⁶

In summary, symptomatic patients with severe COPD and a history of recent exacerbations benefit from triple therapy, as is the case with our patient. This is also consistent with the GOLD guidelines, most recently updated in 2025.⁶ Whenever possible, achieving triple therapy via a single inhaler may improve adherence and other important clinical outcomes when compared to multiple inhalers.⁷ In the case of Ms. H, one could consider transitioning her from her multiple inhalers to a single-inhaler triple therapy regimen if not cost prohibitive.

Question 1b: What other pharmacologic treatment options are available to help Ms. H given that she is already on maximal bronchodilator therapy (LAMA/LABA/ICS with albuterol rescue)? What evidence supports their use?

Recent studies have begun to expand the options available for treatment of COPD beyond the traditional bronchodilators and inhaled steroids that have been the mainstay for decades. Until recently, only roflumilast (Daliresp) and chronic azithromycin had shown benefit for selected patients with exacerbations that persisted despite triple therapy.

In 2023, the injectable biologic dupilumab (Dupixent), a monoclonal antibody directed against IL-4 and IL-13, demonstrated a significant reduction in exacerbations and decrease in symptoms when added to patients already on triple therapy with a serum eosinophil count ≥ 300 at the time of enrollment.⁸ The benefit of dupilumab at reducing exacerbations

was replicated in a second trial in 2024, but this trial did not demonstrate a reduction in symptoms.⁹ Dupilumab is now recommended for patients with exacerbations despite triple therapy who have serum eosinophil counts ≥ 300 . Dupilumab was well tolerated and had no major adverse events. Other biologic agents targeting eosinophilic inflammation have yet to show benefit in COPD without a significant asthma overlap.

Ensifentrine (Ohtuvayre), a nebulized inhibitor of phosphodiesterases 3 & 4, was FDA approved for treatment of COPD in 2024 based on data from the ENHANCE I & II trials, which were published together.¹⁰ These randomized trials compared nebulized ensifentrine 3mg twice daily to placebo in patients who were either not on maintenance inhalers or *only* on a LABA or LAMA, not both. Some patients were also on ICS. Compared to placebo, ensifentrine improved lung function and decreased exacerbation rates but had only a modest impact on respiratory symptoms. There were no major adverse side effects, especially gastrointestinal distress which is a major issue with the oral PDE inhibitor, roflumilast. Given that ensifentrine was not studied in patients on either dual long-acting bronchodilators or triple therapy, it's unclear whether it would have added benefit in these patients. As of this update in December of 2024, the estimated cost of ensifentrine is roughly \$30,000 per year.

Table 1: Additional Pharmacologic Agents for COPD Beyond LAMA, LABA, and ICS

Agent (dosing)	Mechanism	Evidence	Key Considerations
Azithromycin (250mg orally once daily or 3x weekly)	Macrolide antibiotic with anti- inflammatory and immunomodulatory properties	Albert et al ¹¹ : patients with moderate to severe COPD and either continuous oxygen therapy or ≥ 1 exacerbation in the last year: - Decreased time to first exacerbation was (266 days vs 174 days) - Decreased Exacerbation rate by 27% in 1 year	<u>Side effects</u> : hearing loss, nausea, diarrhea, development of bacterial resistance Benefit may be attenuated in patients who are actively smoking ¹²
Roflumilast (500mcg orally once daily)	PDE-4 inhibitor	REACT TRIAL ¹³ : patients with severe COPD, chronic bronchitis and at ≥ 2 exacerbations in the previous year: Fewer moderate-severe exacerbations (13%)	<u>Side effects</u> : Diarrhea (10%), nausea, reduced appetite, abdominal pain, sleep problems, and weight loss
Dupilumab (300mg subcutaneous every 2 weeks)	Monoclonal antibody against IL-4 & IL-13	BOREAS ⁸ & NOTUS ⁹ trials: patients with COPD on triple tx, GOLD E, serum eos ≥ 300 & chronic bronchitis. Excluded asthma. - BOREAS: 30% reduction in exacerbations and decreased resp sx. - NOTUS: 34% reduction in exacerbations, no change in resp sx.	No significant difference in adverse events compared to placebo SubQ injection given at home Benefit of dupilumab even greater in patients with higher serum eos or FeNO
Enfisentrine (3mg nebulized twice daily)	PDE-3 & PDE-4 inhibitor	ENHANCE I & II trials ¹⁰ : COPD with sx. Not on maintenance or either LABA or LAMA +/- ICS. Asthma excluded. - ENHANCE I: 44% reduction in annualized exacerbation rate and slight improvement in resp sx. - ENHANCE II: 43% reduction in annualized exacerbation rate. No change in sx.	No significant difference in adverse events compared to placebo No patients on LABA/LAMA or triple tx in trial, so not clear whether benefit would extend to these patients

There is no comparative efficacy data to help guide the choice between the above agents. In most cases, the choice is made based on consideration of side effect profile, insurance coverage, and the patient's out-of-pocket cost.

Question 1c: What non-pharmacologic treatment options are available to help Ms. H?

In addition to pharmacologic management, it is also important to discuss the following:

- Smoking cessation in patients with active tobacco use, consider pharmacotherapy to increase success at quitting
 - Oxygen therapy for patients with resting hypoxemia
 - Pulmonary rehabilitation
 - Vaccinations against influenza, pneumococcus, SARS-CoV-2, and RSV
 - Mucus clearance education, if pertinent
 - Pursed lip breathing techniques
1. Regarding supplemental oxygen: All patients, regardless of stage of disease, should be evaluated for evidence of oxygen desaturation with ambulation/exercise. For those with resting hypoxemia ($\text{SpO}_2 \leq 88\%$ or $\text{paO}_2 \leq 55$), continuous oxygen therapy reduces mortality if used for $>15\text{h}$ per day and should be initiated in all patients who meet these criteria.¹⁴⁻¹⁵ The LOTT trial found no decrease in time-to-death or time-to-first hospitalization in patients with stable COPD and moderate desaturation at rest (SpO_2 89-93%) or with exercise (SpO_2 80-90%).¹⁶ Citing evidence that exertional supplemental oxygen improves exercise capacity in the laboratory setting, the ATS guideline for home oxygen therapy for adults with chronic lung disease provides a conditional recommendation to prescribe supplemental oxygen in patients with exertional hypoxemia (low quality evidence).¹⁷ Given the inherent burdens associated with ambulatory supplemental oxygen, deciding whether to initiate oxygen therapy should be individualized in this group.

Question 1d: What additional considerations apply when caring for women with COPD?

Since 2000, the age-adjusted rate for COPD-related deaths has improved in men.¹⁸ However, it is unchanged in white women and has increased in black women. Women are often underdiagnosed, and spirometry testing and pulmonary referrals are less common. This is an important consideration as female patients could be more likely to present with more advanced disease at the time of initial consultation.¹⁹

Scenario cont.:

You confirm that Ms. H's oxygen saturations remain 90% or greater on room air with exertion. She begins therapy with roflumilast. She has had some diarrhea for the first couple of weeks on the medication, but this has improved, and she denies significant side effects. After further discussion, she decides to enroll in pulmonary rehab.

Question 2: What is pulmonary rehabilitation, and in what ways is it beneficial for COPD patients?

The American Thoracic Society's document on pulmonary rehabilitation defines it as:
a comprehensive intervention based on a thorough patient assessment followed by patient-tailored therapies that include, but are not limited to, exercise training,

education, and behavior change, designed to improve the physical and psychological condition of people with chronic respiratory disease and to promote the long-term adherence to health-enhancing behaviors.²⁰

Health behavior change is vital to any intervention in chronic disease care. Pulmonary rehabilitation provides a framework for patients to cultivate self-efficacy, learn positive adaptive behaviors, and reduce the impact of the disease on their daily lives.

Regular aerobic exercise is essential for patients with COPD of any severity. Pulmonary rehabilitation should be offered to all COPD patients with severe obstruction ($FEV_1 < 50\%$) and considered for patients with $FEV_1 \geq 50\%$ if symptomatic and/or exercise limited. Multiple studies have shown that pulmonary rehabilitation improves exercise capacity, health-related quality of life, and recovery after acute exacerbation. It also reduces dyspnea, hospitalizations, depression, and anxiety associated with COPD. It may also reduce mortality in patients with a recent history of hospitalization for COPD exacerbation. (see GOLD guidelines, 2025 update, for a summary of primary studies).⁶

In patients with more severe exercise impairment, optimizing medical treatment of their COPD and other comorbid conditions may maximize the effectiveness of pulmonary rehabilitation. Prior to referral for pulmonary rehabilitation, assessing for non-pulmonary sources of dyspnea (such as coronary artery disease) is also important.

Scenario cont.:

Ms. H had strong participation in pulmonary rehabilitation and increased her 6-minute walk distance. Unfortunately, she still struggles with severe dyspnea and limited exertional capacity. A friend suggested she ask you about lung volume reduction and she wonders if she is a candidate.

Question 3a: What is lung volume reduction and how can it be performed?

Lung volume reduction is a consideration in patients with severe COPD ($FEV_1 < 45\%$ predicted), significant air trapping, defined as a residual volume (RV) $> 150\%$ predicted, and exercise limitation despite maximal pharmacologic therapy and regular aerobic exercise.²¹ Historically it was only performed via lung volume reduction surgery (LVRS), a surgical procedure involving resection of up to a third of severely emphysematous lung tissue from one or both upper lung zones. More recently, bronchoscopic approaches to lung volume reduction have emerged (called BLVR for bronchoscopic lung volume reduction).²²⁻²⁴ This is performed via insertion of one-way valves into the airways to collapse regions of emphysematous lung tissue. The decision as to whether a patient is a candidate for surgical versus bronchoscopic lung volume reduction is complex and involves a multidisciplinary discussion involving interventional pulmonologists and thoracic surgeons.

Several possible mechanisms explain the benefits of lung volume reduction. First, expansion of remaining lung may increase elastic recoil, which holds small airways open to reduce airway resistance and dynamic hyperinflation. Second, reducing overall volume of the chest returns the diaphragm and chest wall closer to normal resting position, restoring mechanical advantage during breathing. Third, removal or collapse of excess dead space may improve ventilation/perfusion (V/Q) matching and gas exchange despite the decrease in overall alveolar surface area.

Question 3b: What patient characteristics are favorable (and unfavorable) for lung volume reduction?

Table 2. Favorable and Unfavorable Characteristics When Considering Either LVRS or BLVR

	Favorable characteristics	Unfavorable characteristics
LVRS	• Severe, apical predominant emphysema • Severe obstruction ($FEV_1 \leq 45\%$ pred) • Severe air trapping ($RV > 150\%$ pred) • Apical hypoperfusion on V/Q ($< 10\%$ perfusion to upper lung thirds) • Apical air trapping on V/Q (long tracer half-life in upper lung thirds) • Low exercise capacity after pulmonary rehab (< 25 W on cycle ergometry for women, < 40 W for men) • Single organ disease • No tobacco in the last 6 months	• Airways disease phenotype (i.e. severe obstruction but only mild emphysema) • Homogenous or basilar predominant emphysema • Insufficient obstruction ($FEV_1 > 45\%$ pred) • Insufficient air trapping ($RV < 150\%$) • Preserved apical perfusion on V/Q ($\geq 20\%$ perfusion to upper lung thirds) • FEV_1 and DLCO <u>both</u> $< 20\%$ predicted • Severe comorbid illness • Active smoking • $P_aCO_2 > 60$ • Pulmonary hypertension or systolic heart failure • Prior thoracic surgery
BLVR	• Severe, heterogenous emphysema • Severe obstruction ($FEV_1 \leq 45\%$ pred) • Hyperinflation ($TLC > 100\%$ pred) • Severe air trapping ($RV > 150\%$ pred) • Completed or enrolled in pulmonary rehab • mMRC ≥ 2 • BMI < 33 • Optimized on maximal inhaler therapy • 6MWD < 500m • Lack of collateral lobar ventilation	• $FEV_1 < 15\%$ predicted • DLCO $< 20\%$ predicted • Homogenous emphysema • Presence of large bullae ($> 30\%$ hemithorax) • 6MWD < 100m or > 500m • Pulmonary hypertension (PASP > 45mmHg) • Concerning nodule in target lobe • Hypercapnia ($P_aCO_2 > 60$ mmHg) • Systolic heart failure (LVEF $< 45\%$) or unstable arrhythmia, CAD • BMI > 35 • Active smoking • Daily prednisone > 20mg • Prior chest surgery (e.g. transplant, LVRS, lobectomy, sternotomy)

Abbreviations: W = Watts, TLC = Total Lung Capacity, mMRC = Modified Medical Research Council Dyspnea Scale, BMI = Body Mass Index, 6MWD = 6-Minute Walk Distance, DLCO = Diffusing Capacity for Carbon Monoxide, P_aCO_2 = Arterial Partial Pressure of Carbon Dioxide, PASP = Pulmonary Artery Systolic Pressure, LVEF = Left Ventricular Ejection Fraction, CAD = Coronary Artery Disease

Compiled from references 21 – 24.

Question 3c: What evaluation is necessary prior to consideration for lung volume reduction?

Patient selection: The main indication for lung volume reduction assessment referral is severe dyspnea despite aggressive treatment with bronchodilators, oxygen as necessary, and exercise (preferably pulmonary rehabilitation).

Testing should include:

- Full pulmonary function tests with plethysmography to evaluate lung volumes (gas dilution methods may significantly underestimate volumes)
- High-resolution chest CT without contrast to assess severity and distribution of emphysema as well as software analysis of emphysema and lobar integrity if BLVR is being considered
- Arterial blood gas to exclude significant hypercapnia
- Echocardiogram to exclude significant pulmonary hypertension or LV dysfunction
- Quantitative perfusion analysis by ventilation/perfusion nuclear scan or SPECT scan if surgical approaches are being considered.

Scenario cont.:

On evaluation, Ms. H has an FEV₁ of 42% pred, TLC 110% pred, RV 145% predicted, and DLCO 32% pred. Her CT shows severe, relatively homogeneous emphysema. Her ABG on room air shows 7.32/65/54. Echocardiogram shows normal RV and LV size/function and an estimated pulmonary artery systolic pressure of 44 mmHg. You explain that she is not a candidate for either LVRS or BLVR due to homogeneous emphysema, insufficient air-trapping, and significant hypercapnia.

Question 4a: Would Ms. H benefit from nocturnal non-invasive positive pressure ventilation?

While robust data support the use of non-invasive positive pressure ventilation (NIPPV) such as bilevel positive airway pressure (BiPAP) during acute exacerbations of COPD, the use of NIPPV in chronic stable COPD remains somewhat controversial. Studies evaluating nocturnal NIPPV have produced mixed results, probably due to significant differences in study design. Despite this conflicting data, more recent reviews of multiple trials suggest a benefit in mortality, risk of hospitalization, and dyspnea^{25,26}; however, data is conflicting on whether this therapy improves the quality of life.²⁷ A patient like Ms. H with stable COPD and documented hypercapnia might benefit from nocturnal NIPPV. As such, the ATS guideline on nocturnal NIV in stable hypercapnic COPD suggests NIPPV after excluding OSA as the cause of sleep-related hypoxemia.²⁸ In this patient with chronic retention, NIPPV should be discussed with her after ruling out obstructive sleep apnea.

Question 4b: How would you obtain approval for NIPPV?

To qualify a stable COPD patient for home NIPPV, insurance criteria generally require that the patient have:

- Chronic hypercapnia ($p\text{CO}_2 \geq 52$)
- Nocturnal hypoxemia ($\text{SpO}_2 \leq 88\%$ for ≥ 5 min of nocturnal recording time on 2 L/min or patients baseline O_2 dose, whichever is higher)
- Documentation that sleep apnea (OSA or central sleep apnea) has been considered and ruled out (formal sleep study is not necessarily required, but documentation must indicate it is not clinically likely).

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Post-Test Related Questions

1. A 56-year-old male presents to your office for ongoing management of severe COPD (FEV1 25%). He is on inhaled fluticasone-salmeterol at the maximum dose as well as tiotropium once daily and PRN albuterol. He is maintained on 2L NC continuous supplemental oxygen. He has had several COPD exacerbations in the last year and thus you are contemplating starting him on either chronic azithromycin therapy or roflumilast. Which of the following is a reported side effect of azithromycin but NOT roflumilast?
 - a. Visual changes
 - b. Hearing loss
 - c. Gastrointestinal upset
 - d. Weight loss
2. A 75-year-old female with severe COPD presents to your office for ongoing management. Her most recent PFTs reveal an FEV1 is 18% predicted, and her DLCO is 20% predicted. Her CT scan shows significant emphysema, most prominent at the apices. A VQ scan is pending. She has no other significant comorbidities but continues to have poor exercise tolerance despite pulmonary rehab. Additional testing includes a normal echocardiogram, and her last ABG was 7.37/58/90 on her baseline 2L NC. You are considering her candidacy for lung volume reduction surgery as she is not a transplant candidate due to her age. Which of the following would make her an unfavorable candidate for this procedure?
 - a. Significant exercise limitations/decreased exercise capacity
 - b. Apical predominance of her emphysema
 - c. Elevated baseline PCO₂
 - d. Baseline oxygen requirement
 - e. Reduced FEV1 of 18% and reduced DLCO of 20%
 - f. None of the above. She is a good candidate for this procedure.
3. A 60-year-old male with COPD presents to your office for ongoing management. You are considering his candidacy for nocturnal non-invasive ventilatory (NIV) support via BiPAP. He has had a prior sleep study that excluded obstructive sleep apnea (OSA). His ABG on room air is 7.35/66/80. Which of the following is true regarding his ability to qualify for nocturnal NIV from an insurance standpoint?
 - a. He would likely currently qualify based on his documented hypercapnia alone
 - b. He would qualify if he also has documented nocturnal hypoxemia
 - c. He would not qualify because he does not have a co-existent OSA
 - d. None of the above

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Post-Test Related Questions with Answer Key

1. A 56-year-old male presents to your office for ongoing management of severe COPD (FEV1 25%). He is on inhaled fluticasone-salmeterol at the maximum dose as well as tiotropium once daily and PRN albuterol. He is maintained on 2L NC continuous supplemental oxygen. He has had several COPD exacerbations in the last year and thus you are contemplating starting him on either chronic azithromycin therapy or roflumilast. Which of the following is a reported side effect of azithromycin but NOT roflumilast?
 - a. Visual changes
 - b. Hearing loss**
 - c. Gastrointestinal upset
 - d. Weight loss
2. A 75-year-old female with severe COPD presents to your office for ongoing management. Her most recent PFTs reveal an FEV1 is 18% predicted, and her DLCO is 20% predicted. Her CT scan shows significant emphysema, most prominent at the apices. A VQ scan is pending. She has no other significant comorbidities but continues to have poor exercise tolerance despite pulmonary rehab. Additional testing includes a normal echocardiogram, and her last ABG was 7.37/58/90 on her baseline 2L NC. You are considering her candidacy for lung volume reduction surgery as she is not a transplant candidate due to her age. Which of the following would make her an unfavorable candidate for this procedure?
 - a. Significant exercise limitations/decreased exercise capacity
 - b. Apical predominance of her emphysema
 - c. Elevated baseline PCO2
 - d. Baseline oxygen requirement
 - e. Reduced FEV1 of 18% and reduced DLCO of 20%**
 - f. None of the above. She is a good candidate for this procedure.
3. A 60-year-old male with COPD presents to your office for ongoing management. You are considering his candidacy for nocturnal non-invasive ventilatory (NIV) support via BiPAP. He has had a prior sleep study that excluded obstructive sleep apnea (OSA). His ABG on room air is 7.35/66/80. Which of the following is true regarding his ability to qualify for nocturnal NIV from an insurance standpoint?
 - a. He would likely currently qualify based on his documented hypercapnia alone
 - b. He would qualify if he also has documented nocturnal hypoxemia**
 - c. He would not qualify because he does not have a co-existent OSA
 - d. None of the above