

بِسْمِ اللّٰهِ الرَّحْمٰنِ الرَّحِیْمِ

COPD & ASTHMA CASES

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Case 1

- A 24-year-old woman is seen for a complaint of shortness of breath and wheezing.
- She notes the symptoms to be worse when she has exercised outdoors and is around cats. She has had allergic rhinitis in the spring and summer for many years and suffered from eczema as a child.
- On physical examination, she is noted to have expiratory wheezing.
- Her pulmonary function tests demonstrate an FEV1 of 2.67 (79% predicted), FVC of 3.81 L (97% predicted), and an FEV1/FVC ratio of 70% (86% predicted). After administration of albuterol, the FEV1 increases to 3.0 L (12.4%). Which of the following statements regarding the patient's disease process is true?

- **A.** Confirmation of the diagnosis will require methacholine challenge testing.
- **B.** Mortality due to the disease has been increasing over the past decade.
- **C.** The most common risk factor in individuals with the disorder is genetic predisposition.
- **D.** The prevalence of the disorder has not changed in the past several decades.
- **E.** The severity of the disease does not vary significantly within a given patient with the disease.

- **The answer is E**
- The patient in this clinical scenario presents with symptoms typical of asthma, including shortness of breath and wheezing. She also manifests evidence of atopy, the most common risk factor for developing asthma, with sensitivity to outdoor allergens and cats.
- In addition, the patient has a history of allergic rhinitis and eczema, both of which are commonly seen in individuals with asthma. Indeed, over 80% of asthma patients have a concomitant diagnosis of allergic rhinitis.
- Atopy is present in 40%–50% of the population of affluent countries, but only a small proportion of these individuals develop asthma. Many studies have shown a genetic predisposition via family history and recent genome-wide screens, but no single genetic profile has shown high positive predictive value.

- Overall, the prevalence of asthma in developed countries has increased over the past 30 years, but recently has leveled off, with a prevalence of about 15% in children and 10%–12% in adults.
- Asthma deaths remain rare and have decreased in recent decades. In the 1960s, asthma deaths did increase with an overuse of short-acting β -agonist medications. However, since the introduction of inhaled corticosteroids as maintenance therapy, deaths have declined. Risk factors for fatal asthma include frequent use of rescue inhalers, lack of therapy with inhaled corticosteroids, and prior hospitalizations for asthma.
- Interestingly, the overall disease severity does not vary significantly within a given patient over the course of the disease. Individuals who have mild asthma typically continue to have mild asthma, whereas those with severe disease present with severe disease.

Case 2

- Which of the following patients is appropriately diagnosed with asthma?
- **A.** A 24-year-old woman treated with inhaled corticosteroids for cough and wheezing that has persisted for 6 weeks following a viral upper respiratory infection
- **B.** A 26-year-old man who coughs and occasionally wheezes following exercise in cold weather
- **C.** A 34-year-old woman evaluated for chronic cough with an FEV1/FVC ratio of 68% with an FEV1 that increases from 1.68 L (52% predicted) to 1.98 L (61% predicted) after albuterol (18% change in FEV1)
- **D.** A 44-year-old man who works as a technician caring for the mice in a medical research laboratory and complains of wheezing, shortness of breath, and cough that are most severe at the end of the week
- **E.** A 60-year-old man who has smoked two packs of cigarettes per day for 40 years who has dyspnea and cough and who has airway hyperreactivity in response to methacholine

- **The answer is C.**
- The preferred method for diagnosing asthma is demonstration of airflow obstruction on spirometry that is at least partially reversible. This is demonstrated in option C, with a decreased FEV1/FVC ratio, decreased FEV1, and a significant increase in FEV1 following administration of albuterol.
- For an individual to be considered responsive to a bronchodilator, the individual should experience an increase in either FEV1 or FVC of at least 200 mL and 12%.
- Option A describes someone with post viral cough syndrome, which can persist for several weeks following a viral upper respiratory infection.
- Option B describes someone with exercise-induced bronchoconstriction (EIB), which, in absence of other symptoms to suggest asthma, should not be diagnosed as asthma. Isolated EIB lacks the characteristic airway inflammation of asthma and does not progress to asthma

- Although it is estimated that 80%–90% of individuals with asthma experience EIB, many individuals who have EIB do not also have asthma. EIB is caused by hyperventilation with inhalation of cool dry air that leads to bronchospasm.
- Option D describes someone with occupational asthma that has occurred after working with animals in the medical laboratory for many years. Symptoms that are characteristic of occupational asthma are symptoms only while at work that improve on the weekends and during holidays.
- Option D describes someone with COPD. In COPD, 25%–48% of individuals can demonstrate bronchial hyperresponsive in response to methacholine.

Case 3

- A 28-year-old woman with longstanding mild persistent asthma comes to see you because she just found out that she is pregnant. Her only medications are inhaled beclomethasone twice a day and albuterol as needed. She typically uses her albuterol less than twice per week. She wants to know what to expect regarding her asthma severity and whether any medication changes should be made at this time. Which of the following statements is correct?

- **A.** She should continue her current therapy and follow symptoms.
- **B.** She should switch from inhaled albuterol as needed to inhaled tiotropium as needed.
- **C.** She should switch from inhaled beclomethasone to a inhaled salmeterol.
- **D.** There is a greater than 70% chance that her asthma symptoms will become less severe during pregnancy.
- **E.** There is a greater than 70% chance that her asthma symptoms will become more severe during pregnancy.

- **The answer is A.**
- Approximately one-third of asthmatic patients who are pregnant improve during the course of a pregnancy, one-third deteriorate, and one-third are unchanged.
- It is important to maintain good control of asthma because poor control may have adverse effects on fetal development. Compliance may be a problem because there is often concern about the effects of antiasthma medications on fetal development.
- The drugs that have been used for many years in asthma therapy have now been shown to be safe and without teratogenic potential. These drugs include short-acting β -agonists (e.g., albuterol), inhaled corticosteroids (e.g., beclomethasone), and theophylline; there is less safety information about newer classes of drugs such as LABAs (e.g., salmeterol), antileukotrienes, and anti-immunoglobulin (Ig) E.

- If an oral corticosteroid is needed, it is better to use prednisone rather than prednisolone because it cannot be converted to the active prednisolone by the fetal liver, thus protecting the fetus from systemic effects of the corticosteroid. There is no contraindication to breast-feeding when patients are using these drugs.

Case 4

- A 24-year-old woman was diagnosed with asthma 4 months ago and was treated with inhaled albuterol as needed. Since her last visit, she feels generally well and typically requires using her inhaler approximately four to seven times a week when around pollen or cats or when exercising in cold air. The inhaled albuterol generally helps, and she only requires a repeat round of inhalations approximately two times a week. She is on no other medications and is a nonsmoker, and her only pet is a goldfish named Puffer. Based on this information, you advise which of the following?
- **A.** Add inhaled beclomethasone
- **B.** Add inhaled salmeterol twice a day
- **C.** Add inhaled tiotropium
- **D.** Continue present therapy
- **E.** Think of a new name for the goldfish

- **The answer is A.**
- For patients with mild, intermittent asthma, a short-acting β 2-agonist is all that is required. However, use of a reliever medication more than twice a week indicates the need for regular controller therapy.
- This patient is using her reliever medication frequently; therefore, a controller should be added to her regimen.
- The treatment of choice for all patients is an inhaled corticosteroid given twice daily.
- If symptoms are not controlled, a long-acting β -agonist (LABA) should be added.
- Anticholinergics, including tiotropium, may be used as additional bronchodilators in patients with asthma that is not controlled by inhaled corticosteroid and LABA combinations.
- Low doses of theophylline or an antileukotriene may also be considered as an add-on therapy, but these are less effective than LABA.

				OCS
			LABA	LABA
		LABA	ICS High dose	ICS High dose
	ICS Low dose	ICS Low dose		
Short-acting β_2 -agonist as required for symptom relief				
Mild intermittent	Mild persistent	Moderate persistent	Severe persistent	Very severe persistent

Case 5

- A 69-year-old man with COPD has been admitted to the hospital three times over the past year for COPD exacerbations. He has daily cough with sputum production and an FEV1 of 45% predicted. He previously smoked a pack of cigarettes daily for 50 years, quitting 1 year ago. His oxygen saturation on room air is 91%. Which of the following treatments is most likely to decrease the frequency of his exacerbations?
- **A.** Azithromycin 250 mg three times weekly
- **B.** Continuous oxygen at 2 L/min
- **C.** Nocturnal bilevel positive airway pressure with an inspiratory pressure of 18 cm H₂O and expiratory pressure of 12 cm H₂O
- **D.** Roflumilast 500 µg daily
- **E.** Theophylline 300 mg daily

- **The answer is D.**
- Acute exacerbations of COPD are a frequent cause of morbidity and mortality in COPD. Risk factors for development of acute exacerbation include severity of airflow obstruction (FEV1 <50% predicted), history of prior exacerbations, and elevated ratio of pulmonary artery to aorta on chest CT.
- Most acute exacerbations are associated with airway inflammation or infection, including acquiring a new strain of bacteria or a viral respiratory infection.
- Therefore, strategies for prevention have been primarily focused on decreasing inflammatory responses and preventing infections.
- The selective phosphodiesterase-4 inhibitor roflumilast has been demonstrated to decrease exacerbation frequency in individuals with COPD who have symptoms of chronic bronchitis and frequent exacerbations.

- The macrolide antibiotic azithromycin has both anti-inflammatory and antibiotic properties. In a randomized controlled trial, it has been shown to decrease exacerbation frequency and increase time to first exacerbation when administered at a dose of **500 mg daily**

Case 6

- A 56-year-old woman is admitted to the ICU with a 4-day history of increasing shortness of breath and cough with copious sputum production. She has known **severe COPD** with an **FEV1 of 42%** predicted. On presentation, she has a room air blood gas with a **pH of 7.26**, **PaCO₂ of 78 mmHg**, and **PaO₂ of 50 mmHg**. She is in obvious respiratory distress with use of accessory muscles and retractions. Breath sounds are quiet with diffuse expiratory wheezing and rhonchi. No infiltrates are present on chest radiograph. Which of the following therapies has been demonstrated to have the greatest reduction in mortality rate for this patient?
- **A.** Administration of inhaled bronchodilators
- **B.** Administration of IV glucocorticoids
- **C.** Early administration of broad-spectrum antibiotics with coverage of *P aeruginosa*
- **D.** Early intubation with mechanical ventilation
- **E.** Use of noninvasive positive-pressure ventilation

- **The answer is E.**
- Acute exacerbations of COPD are marked by an increase in dyspnea, an increase in sputum, and a change in sputum color. Prompt treatment can improve symptoms and decrease hospitalizations and mortality in this setting. In patients presenting with hypercarbic respiratory failure in the setting of an acute exacerbation, the treatment that has demonstrated the strongest reduction in mortality, when compared to traditional mechanical ventilation, is non invasive positive-pressure ventilation (NIPPV).
- NIPPV also decreases the need for endotracheal intubation, complications, and length of stay in the hospital.
- Antibiotics, bronchodilators, and glucocorticoids are all cornerstones of therapy in the treatment of acute exacerbations in COPD but have not been demonstrated in clinical trials to have similar mortality benefits in the situation of acute hypercarbic respiratory failure.

- Specifically, no benefit is demonstrated for intravenous versus oral corticosteroids.
- Likewise, the choice of antibiotic should be made based on local susceptibility patterns, and need for broadspectrum antibiotics that cover for *Pseudomonas* is not typically indicated.
- Recent studies have demonstrated that high-flow nasal oxygen may be an effective alternative to NIPPV, with improved outcomes (need for mechanical ventilation) and improved patient comfort.

Case 7

- A 63-year-old man with a long history of cigarette smoking comes to see you for a 4-month history of progressive shortness of breath and dyspnea on exertion. The symptoms have been indolent, with no recent worsening. He denies fever, chest pain, or hemoptysis. He has a daily cough of 3 to 6 tablespoons of yellow phlegm. The patient says he has not seen a physician for over 10 years. Physical examination is notable for normal vital signs, a prolonged expiratory phase, scattered rhonchi, elevated jugular venous pulsation, and moderate pedal edema. Hematocrit is 49%. Which of the following therapies is most likely to prolong his survival?
- A. Atenolol
- B. Enalapril
- C. Oxygen
- D. Prednisone
- E. Theophylline

- **The answer is C.**
- The only therapies that have been proven to improve survival in patients with COPD are **smoking cessation, oxygen in patients with resting hypoxemia, and lung volume reduction surgery** in a very small subset of highly selected patients.
- This patient probably has resting hypoxemia resulting from the presence of an elevated jugular venous pulse, pedal edema, and elevated hematocrit.
- Theophylline has been shown to increase exercise tolerance in patients with COPD through a mechanism other than bronchodilation.
- Oral glucocorticoids are not indicated in the absence of an acute exacerbation and may lead to complications if they are used indiscriminately.
- Atenolol and enalapril have no specific role in therapy for COPD but are often used when there is concomitant hypertension or cardiovascular disease.