Chronic Obstructive Pulmonary Disease (COPD)

Exacerbations



Diagnosis

- A COPD exacerbation should be considered in a resident with a known history of COPD and increased cough, shortness of breath, or sputum production from baseline.¹⁻³
- COPD exacerbations are commonly triggered by respiratory virus infections (e.g., rhinovirus, influenza, COVID-19) and testing for these should be considered.⁴
 - Even if it's not influenza season, test residents who are symptomatic for influenza, especially if two or more develop symptoms within 72 hours of each other.⁵
- Distinguishing COPD exacerbations and community-acquired pneumonia in a resident with a known history of COPD can be challenging. 1,6,7
 - If a chest x-ray does not show a new infiltrate, a COPD exacerbation is more likely.
- When bacteria are involved with COPD exacerbation, the most common are *Haemophilus influenzae*, *Moraxella catarrhalis*, and *Streptococcus pneumoniae*.^{8,9}
- Pseudomonas aeruginosa, Klebsiella pneumoniae, and other Gram-negative bacteria are less commonly associated with COPD exacerbations and are usually limited to residents with COPD who have had extensive antibiotic exposure. Sputum culture should be obtained for residents with this risk factor.^{1,8,9}

Treatment

- In additional to standard treatment modalities (e.g., bronchodilators, anti-inflammatory agents, anti-cholinergics), antibiotics are generally recommended in patients with new sputum purulence plus either worsened shortness of breath or increased sputum production.¹⁻³
- Known adverse events associated with antibiotics should be carefully weighed against the potentially
 marginal benefits that antibiotics provide prior to prescribing antibiotics to residents with mild COPD
 exacerbations.²
- Empiric treatment^{1,2}
 - Azithromycin 500 mg orally once daily for 3 days or doxycycline 100 mg orally twice a day for 5 days¹⁰⁻¹⁷
 - Azithromycin has a long half-life; 3 days provides coverage for ~ 1 week.¹⁸
 - Azithromycin and doxycycline are less likely to cause Clostridioides difficile infection compared to alternate options¹⁹⁻²¹
 - If a resident recently received azithromycin or doxycycline, or is taking azithromycin prophylaxis, alternate options include amoxicillin/clavulanate or oral second and third generation cephalosporins²²
 - Fluoroquinolones are discouraged unless the resident has a known history of infection due to organisms resistant to standard therapy.²²
- Prophylactic antibiotics for individuals with recurrent COPD exacerbations (at least two per year) may result in a modest decrease in the frequency of future exacerbations.^{1,23}
 - Prophylaxis should only be considered for residents who are already receiving maximized nonantimicrobial treatment
 - The decision to initiate prophylaxis should be made on a case-by-case basis taking into account frequency of exacerbations, resident preferences, potential risk factors, financial constraints, and input from the resident's pulmonologist and/or primary care practitioner.
- Recommended prophylactic regimens are azithromycin 250 mg orally daily or 500 mg three times a week.^{1,23,24}
 - Azithromycin use has been associated with QTc prolongation
 - If Azithromycin prophylaxis is being considered, a baseline electrocardiogram should be obtained and additional QTc prolonging agents should be avoided whenever possible.

- 2020 Gold Reports: 2020 Global Strategy for Prevention, Diagnosis and Management of COPD. Global Initiative for Chronic Obstructive Lung Disease. 2020. https://goldcopd.org/gold-reports/. Accessed April 23, 2021.
- VA/DoD Clinical Practice Guidelines: Management of Chronic Obstructive Pulmonary Disease (COPD) (2014). U.S. Department of Veterans Affairs. 2014. https://www.healthquality.va.gov/guidelines/CD/copd/. Accessed April 23, 2021.
- Criner GJ, Bourbeau J, Diekemper RL, et al. Prevention of acute exacerbations of COPD: American College of Chest Physicians and Canadian Thoracic Society Guideline. Chest. 2015 Apr;147(4):894-942. PMID: 25321320.
- Interim Guidance for Influenza Outbreak Management in Long-Term Care and Post-Acute Care Facilities. Feb 2, 2017 https://www.cdc.gov/flu/professionals/infectioncontrol/ltc-facility-guidance.htm. Accessed February 18, 2020.
- Uyeki TM, Bernstein HH, Bradley JS, et al. Clinical practice guidelines by the Infectious Diseases Society of America: 2018 update on diagnosis, treatment, chemoprophylaxis, and institutional outbreak management of seasonal influenza. Clin Infect Dis. 2019 Mar 5;68(6):e1-e47. PMID: 30566567.
- Hurst JR. Consolidation and exacerbation of COPD. Med Sci (Basel). 2018 Jun; 6(2): 44. PMID: 29865214.
- Saleh A, Lopez-Campos JL, Hartl S, et al. The effect of incidental consolidation on management and outcomes in COPD exacerbations: data from the European COPD Audit. PLoS One. 2015 Jul 27;10(7):e0134004. PMID: 26214175.
- Sapey E, Bafadhel M, Bolton CE, et al. Building toolkits for COPD exacerbations: lessons from the past and present. Thorax. 2019 Sep;74(9):898-905. PMID: 31273049.
- Beasley V, Joshi PV, Singanayagam A, et al. Lung microbiology and exacerbations in COPD. Int J Chron Obstruct Pulmon Dis. 2012;7:555-69. PMID: 22969296.
- Milstone AP. Use of azithromycin in the treatment of acute exacerbations of COPD. Int J Chron Obstruct Pulmon Dis. 2008 Dec; 3(4): 515–20. PMID: 19281070.
- Albertson TE, Louie S, Chan AL. The diagnosis and treatment of elderly patients with acute exacerbation of chronic obstructive pulmonary disease and chronic bronchitis. J Am Geriatr Soc. 2010 Mar;58(3):570-9. PMID: 20398122.
- Zervos M, Martinez FJ, Amsden GW, et al. Efficacy and safety of 3-day azithromycin versus 5-day moxifloxacin for the treatment of acute bacterial exacerbations of chronic bronchitis. Int J Antimicrob Agents. 2007 Jan;29(1):56-61. PMID: 17189096.

- Wang Y, Bos JH, Boezen HM, et al. Influence of age on real-life effects of doxycycline for acute exacerbations among COPD outpatients: a population-based cohort study. BMJ Open Respir Res. 2020. Feb;7(1):e000535. PMID: 32075781.
- Zhang HL, Tan M, Qiu AM, et al. Antibiotics for treatment of acute exacerbation of chronic obstructive pulmonary disease: a network meta-analysis. BMC Pulm Med. 2017 Dec 12;17(1):196. PMID: 29233130.
- Hunter MH, King DE. COPD: Management of acute exacerbations and chronic stable disease. Am Fam Physician. 2001 Aug 15;64(4):603-12. PMID: 11529259.
- Doxycycline Drug Summary. Prescribers' Digital Reference. 2021. https://www.pdr.net/drug-summary/Doxy-100-doxycycline-3447. Accessed June 2, 2021.
- Doxycycline: Drug information. UpToDate. 2021. https://www.uptodate.com/contents/doxycycline-drug-information?search=doxycycline%20COPD&source=search_result&selectedTitle=3~150&usage. Accessed June 2, 2021.
- Blasi F, Cazzola M, Tarsia P, et al. Azithromycin and lower respiratory tract infections. Expert Opin Pharmacother. 2005 Oct;6(13):2335-51. PMID: 16218893.
- Doernberg SB, Winston LG, Deck DH, et al. Does doxycycline protect against development of *Clostridium difficile* infection? Clin Infect Dis. 2012 Sep 1; 55(5): 615–20. PMID: 22563022.
- Tariq R, Cho J, Kapoor S, et al. Low risk of primary Clostridium difficile infection with tetracyclines: a systematic review and metaanalysis. Clin Infect Dis. 2018 Feb 1;66(4):514-22. PMID: 29401273.
- Brown KA, Langford B, Schwartz KL, et al. Antibiotic prescribing choices and their comparative *C. difficile* infection risks: a longitudinal case-cohort study. Clin Infect Dis. 2021 Mar 1;72(5):836-44. PMID: 32069358.
- Joyner KR, Walkerly A Seidel K, et al. Comparison of narrow-versus broad-spectrum antibiotics in elderly patients with acute exacerbations of chronic obstructive pulmonary disease. J Pharm Pract. 2020 Jul 10;;897190020938190. PMID: 32648514.
- Hearth SC, Normansell R, Maisey S, et al. Prophylactic antibiotic therapy for chronic obstructive pulmonary disease (COPD). Cochrane Database Syst Rev. 2018 Oct 30;10(10):CD009764. PMID: 30376188.
- FDA Drug Safety Communication: Azithromycin (Zithromax or Zmax) and the risk of potentially fatal heart rhythms. U.S. Food & Drug Administration. February 2018. https://www.fda.gov/drugs/drug-safety-and-availability/fda-drug-safety-communication-azithromycin-zithromax-or-zmax-and-risk-potentially-fatal-heart. Accessed April 23, 2021.

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