

IMPACT OF COPD EXACERBATION

- Hospital mortality of patients admitted for a COPD exacerbation is approximately 10%, and the long-term outcome is poor. Mortality reaches 40% in 1 year¹
- Patients with COPD incurred much higher inpatient expenditures than their counterparts, a finding supported by longer average hospital stays in patients with COPD²
- In a healthcare utilization study (2000-2001), COPD patients were hospitalized more often from respiratory illnesses than those without COPD (11.8% vs 0.5%). They were also more likely to be hospitalized for any reason (42.1% vs 12.6%)³
- Antibiotics should be considered for patients with purulent acute COPD exacerbation¹
- Outpatient management of COPD should include
 - Educating patients to understand the symptoms of an acute exacerbation and lower respiratory tract infection¹
 - Providing educational strategies that improve patient adherence to medication and management regimens including taking medication appropriately, maintaining an exercise program after pulmonary rehabilitation, undertaking and sustaining smoking cessation, and using devices such as nebulizers, spacers, and oxygen concentrators properly¹

CONSIDERATIONS FOR CHOICE OF ANTIBIOTIC(S)

- Patients with exacerbations of COPD present with three cardinal symptoms: increased dyspnea, increased sputum volume, and increased sputum purulence¹
- Patients with exacerbations of COPD with two of the cardinal symptoms, if increased purulence of sputum is one of the two symptoms¹
- Patients with a severe exacerbation of COPD that requires mechanical ventilation have shown that other microorganisms, such as enteric gram-negative bacilli and *P. aeruginosa*, may be more frequent¹
- If *Pseudomonas* spp and/or other Enterobacteriaceae are suspected, consider combination therapy⁴

References: 1. Global Initiative for Chronic Obstructive Lung Disease (GOLD). *Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease* (Updated 2006). www.goldcopd.org. Accessed March 7, 2007. 2. Yu-Ishenberg KS, Vanderplas K, Chang EY, Shah H. Utilization and medical care expenditures in patients with chronic obstructive pulmonary disease: a managed care claims data analysis. *Dis Manage Health Outcomes*. 2005;13:405-412. 3. Tinkelman DG, George D, Halbert RJ. Chronic obstructive pulmonary disease in patients under age 65: utilization and costs from a managed care sample. *J Occup Environ Med*. 2005;47:1125-1130. 4. Celli BR, MacNee W, and ATS/ERS Task Force committee members. Standards for the diagnosis and treatment of patients with COPD: a summary of the ATS/ERS position paper. *Eur Respir J*. 2004;23:932-946.

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Managing Chronic Obstructive Pulmonary Disease (COPD)

Antibiotics for Acute Exacerbation Management

An approach for determining if antibiotics should be initiated for patients with an acute exacerbation of chronic obstructive pulmonary disease



ACUTE COPD EXACERBATION

- COPD is often associated with worsening of symptoms or exacerbations¹
- According to the 2006 Global Initiative for Chronic Obstructive Lung Disease (GOLD) Guidelines, patients with *Stage I: Mild COPD to Stage II: Moderate COPD* often experience an exacerbation that may be associated with worsening airflow limitation with shortness of breath due to exertion, and cough sputum production that is sometimes also present. Patients typically seek medical attention because of chronic respiratory symptoms or an exacerbation of their disease¹
- In *Stage III: Severe COPD*, an exacerbation is characterized by further worsening of airflow limitation, greater shortness of breath, reduced exercise capacity, and fatigue¹
- An exacerbation in *Stage IV: Very Severe COPD* is commonly associated with severe airflow limitation and chronic respiratory failure. At this stage, these exacerbations may be life-threatening¹
- Increased breathlessness, the most common symptom of exacerbation, may be accompanied by wheezing and chest tightness, increased cough and sputum, change of the color and/or tenacity of sputum, and fever¹

Rationale and Patient Assessment for Antibiotic Therapy in COPD

According to GOLD¹

- Randomized placebo-controlled studies of antibiotic treatment in exacerbations of COPD have demonstrated a beneficial effect of antibiotics on lung function
- Antibiotics are recommended only when patients with worsening dyspnea and cough also have increased sputum volume and purulence
- Prophylactic and continuous use of antibiotics have no effect on the frequency of COPD exacerbations. Thus, the use of antibiotics, other than for treating infectious exacerbations of COPD and other bacterial infections, is not recommended¹

Figure 1. Stratification of patients with COPD exacerbated for antibiotic treatment and potential microorganisms involved in each group.¹

GROUP	DEFINITION ^a	MICROORGANISMS
GROUP A	Mild exacerbation: No risk factors for poor outcome	<i>H. influenzae</i> <i>S. pneumoniae</i> <i>M. catarrhalis</i> <i>Chlamydia pneumoniae</i> Viruses
GROUP B	Moderate exacerbation with risk factor(s) for poor outcome	Group A plus presence of resistant organisms (β-lactamase producing, penicillin-resistant <i>S. pneumoniae</i>), Enterobacteriaceae (<i>K. pneumoniae</i> , <i>E. coli</i> , <i>Proteus</i> , <i>Enterobacter</i> , etc)
GROUP C	Severe exacerbation with risk factor(s) for <i>P. aeruginosa</i> infection	Group B plus: <i>P. aeruginosa</i>

a. Risk factors for poor outcome in patients with COPD exacerbation: presence of comorbid diseases, severe COPD, frequent exacerbations (>3/yr), and antimicrobial use within last 3 months.

Figure 2. Antibiotic treatment in exacerbations of COPD.^{a,b,1}

GROUP	ORAL TREATMENT (No particular order)	ALTERNATIVE ORAL TREATMENT (No particular order)	PARENTERAL TREATMENT (No particular order)
GROUP A	Patients with only one cardinal symptom ^c should not receive antibiotics If indication then: • β-lactam (Penicillin, Ampicillin/Amoxicillin ^d) • Tetracycline • Trimethoprim/Sulfamethoxazole	• β-lactam/β-lactamase inhibitor (Co-amoxiclav) • Macrolides (Azithromycin, Clarithromycin, Roxithromycin ^e) • Cephalosporins -2nd or 3rd generation • Ketolides (Telithromycin)	
GROUP B	• β-lactam/β-lactamase inhibitor (Co-amoxiclav)	• Fluoroquinolones ^e (Gemifloxacin, Levofloxacin, Moxifloxacin)	• β-lactam/β-lactamase inhibitor (Co-amoxiclav, ampicillin/sulbactam) • Cephalosporins -2nd or 3rd generation • Fluoroquinolones ^e (Levofloxacin, Moxifloxacin)
GROUP C	In patients at risk for <i>Pseudomonas</i> infections: • Fluoroquinolones ^e (Ciprofloxacin, Levofloxacin – high dose ^f)		• Fluoroquinolones ^e (Ciprofloxacin, Levofloxacin – high dose ^f) or • β-lactam with <i>P. aeruginosa</i> activity

a. All patients with symptoms of a COPD exacerbation should be treated with additional bronchodilators ± glucocorticosteroids.
b. Classes of antibiotics are provided (with specific agents in parentheses). In countries with high incidence of *S. pneumoniae* resistant to penicillin, high dosages of Amoxicillin or Co-amoxiclav are recommended. (See Figure 1 for definition of Groups A, B, and C.)

c. Cardinal symptoms are increased dyspnea, sputum volume, and sputum purulence.

d. This antibiotic is not appropriate in areas where there is increased prevalence of β-lactamase producing *H. influenzae* and *M. catarrhalis* and/or of *S. pneumoniae* resistant to penicillin.

e. Not available in all areas of the world.

f. Dose 750 mg effective against *P. aeruginosa*.