Antibiotics, Expectorants, and Cough Suppressants



Lifespan Cardiovascular Institute

Rhode Island Hospital • The Miriam Hospital Newport Hospital

Delivering health with care.®

Center For Cardiac Fitness
Pulmonary Rehab
The Miriam Hospital

Objectives

- Review the mechanism of action (MOA), dosing, benefits, and various options for:
 - Expectorants
 - Cough suppressants
 - Antibiotics for moderate to severe COPD exacerbations
 - Macrolides
 - Respiratory fluoroquinolones
 - Pseudomonas aeruginaosa coverage



- Limited data to suggest improvements to lung to the limit or overall feelings of well-being
- Limited data to suggest improvements to lung
 MOA:
 - Wakes up the nerve in the stomach and causes an increase in airway secretions
 - Ex: Guaifenesin, ipecac, bromhexine, ammonium salts
 - Emetics
- Other MOAs:
 - Decrease in mucous thickness or an enhancement of the mucociliary escalator
 - Mucociliary escalator
 - 2 parts:
 - Mucous-producing goblet cells
 - Ciliated epithelium
 - Bacteria become trapped in the mucous
 - Cilia, which are constantly beating, push bacteria up and out of the throat

Expectorants

Guaifenesin

- Dose
 - Extended release tabs 600 to 1200 mg every 12 hours
 - Immediate release tabs/syrup 200 to 400 mg every 4 to 6 hours
 - Max = 2400 mg/24 hours
- MOA
 - Increases hydration of mucous and facilitates clearance of mucous from cilia
- Side effects
 - Dizziness, drowsiness, headache, nausea/vomiting, stomach upset, hypouricemia, skin rash
- Water
 - Helps thin and clear mucous

Cough Suppressants

- Centrally-acting MOA:
 - Suppress cough via an action on the central cough center
 - Ex: Dextromethorphan, codeine, long-acting morphine, gabapentin (off-label)

- Peripherally-acting MOA:
 - Depending upon the agent, acts locally in the lung/pleura
 - Ex: Benzonatate

Cough Suppressants: Centrally-Acting

Dextromethorphan

- Dosing
 - Immediate release 10 to 20 mg every 4 hours or 30 mg every 6 hours
 - Extended release 60 mg every 12 hours
 - Max = 120 mg/24 hours
- MOA
 - Decreases sensitivity of cough receptors and interrupts cough impulse transmission by depressing the medullary cough center through sigma receptor stimulation (UpToDate)
- Side effects
 - Confusion, excitement, irritability, serotonin syndrome
- Serotonin syndrome
 - Agitation, confusion, hallucinations, hyper-reflexia, myoclonus, shivering, and tachycardia
 - More likely to occur with higher doses, concomitant use of SSRIs/SNRIs

Cough Suppressants: Centrally-Acting

Codeine

- Not routinely recommended for use by CHEST physicians
- Dose
 - 30 mg every 4 to 6 hours; may increase to 60 mg every 4 to 6 hours
 - Max = 360 mg/24 hours
- MOA
 - Suppresses cough via direct central action in the medulla (UpToDate)
- Side effects
 - CNS/respiratory depression, constipation, hypotension
- Morphine
 - Similar to codeine
 - Not much data to support use of efficacy
 - Extended release: 5 mg twice daily; can increase to 10 mg twice daily

Cough Suppressants: Centrally-Acting

- Gabapentin
 - Dose
 - Immediate-release 300 mg daily
 - Max = 1800 mg/24 hours (in 2 divided doses)
 - MOA
 - GABA (gamma aminobutyric acid) agonist
 - Unclear, but thought to affect the cough center in the brain
 - Side effects
 - Diarrhea, nausea, emotional lability, somnolence, nystagmus, tremor, weakness, & peripheral edema
- Pregabalin
 - Limited data for use
 - Dose
 - Immediate-release 300 mg daily plus SPT (speech pathology therapy)
 - Side effects & MOA
 - Same as gabapentin

Cough Suppressants: Peripherally-Acting

Benzonatate

- Dosing:
 - 100 to 200 mg 3x/day as needed for cough
 - Max per single dose: 200 mg
 - Max: 600 mg/24 hours
- MOA:
 - Tetracaine congener
 - Suppresses cough by anesthetizing the respiratory stretch receptors in the lungs and pleura
- Side effects:
 - Chest numbness, chills, confusion, dizziness, hallucination, headache,

ANTIBIOTICS AND COPD EXACERBATIONS

Exacerbations

Mild

- At least **one** of the following:
 - Increased dyspnea
 - Increased sputum volume
 - Increased sputum purulence
- No antibiotics required

Moderate/Severe

- At least two of the following:
 - Increased dyspnea
 - Increased sputum volume
 - Increased sputum purulence

Antibiotics required

Differentiate between uncomplicated and complicated COPD exacerbation

Moderate to Severe Exacerbations

Uncomplicated COPD

- Must have all four of the following:
 - <65 years of age</p>
 - FEV1 >50% predicted
 - <2 exacerbations per year</p>
 - No cardiac disease

Complicated COPD

- One or more of the following risk factors:
 - >65 years of age
 - FEV1 <50% predicted</p>
 - >2 exacerbations per year
 - Cardiac disease

Moderate to severe Exacerbations

- Three most common bacterial pathogens:
 - Haemophilus influenzae
 - Moraxella catarrhalis
 - Streptococcus pneumoniae
 - Plus local patterns of antibiotic resistance

Moderate to severe Exacerbations: Inpatient

- Risk of pseudomonas when:
 - Severe COPD (FEV1 <50% predicted)</p>
 - Recent hospitalization
 - ≥ 2 days' duration during last 90 days
 - Frequent administration of antibiotics
 - ≥ 4 courses within the last year
 - Isolation of pseudomonas during previous exacerbation
 - Pseudomonas colonization during stable period
 - Systemic glucocorticoid use

moderate to Severe Exacerbations: Antibiotics

Uncomplicated COPD

- Advanced macrolide
 - Azithromycin, clarithromycin
- Cephalosporin
 - Cefuroxime, cefpodoxime, cefdinir
- Doxycycline
- Bactrim (sulfamethoxazole-trimethoprim)
- If recent (<3 months) use, switch to alternative agent

Complicated COPD

- Fluoroquinolone
 - Levofloxacin, moxifloxacin
- Amoxicillin-clavulanate
 - If at risk for pseudomonas, switch to ciprofloxacin

 If recent (<3 months) use, switch to alternative agent

Uncomplicated COPD: Moderate/severe exacerbation

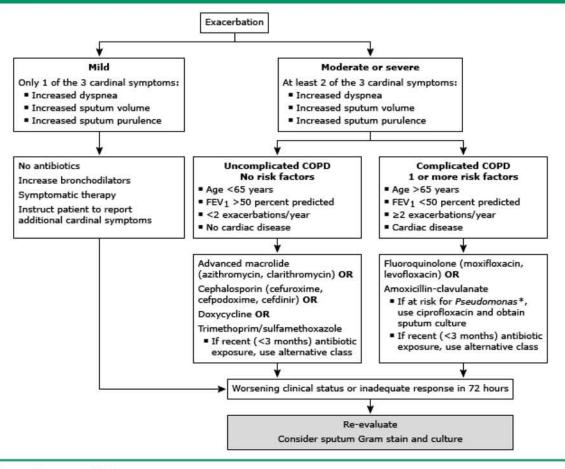
Macrolides

- Dosing
 - Azithromycin 500 mg by mouth daily for 3 days
 - Clarithromycin 500 mg every 12 hours for 5 days
- Duration
 - Typically 5 to 7 days
 - Azithromycin is shorter due to long half-life
 - Data suggests a 5-day duration is equally effective while decreasing incidence of side effects
- Side effects
 - Upset stomach, N/V, diarrhea
 - QTc prolongation (risk increased with meds, co-morbidities)
- Bugs it targets
 - Haemophilus influenzae
 - Moraxella catarrhalis
 - Streptococcus pneumoniae

Complicated COPD: Moderate/severe Exacerbation

- Respiratory Fluoroquinolones (FQ)
 - Dosing
 - Levofloxacin 750 mg daily
 - Moxifloxacin 400 mg daily
 - Duration
 - Typically 5 to 7 days
 - Side effects
 - Upset stomach, N/V, diarrhea
 - QTc prolongation (risk increased with meds, co-morbidities)
 - *Clostridium difficile* colitis
 - Bugs to target
 - Haemophilus influenzae
 - Moraxella catarrhalis
 - Streptococcus pneumonia
 - Pseudomonas aeruginosa (Levofloxacin ONLY)

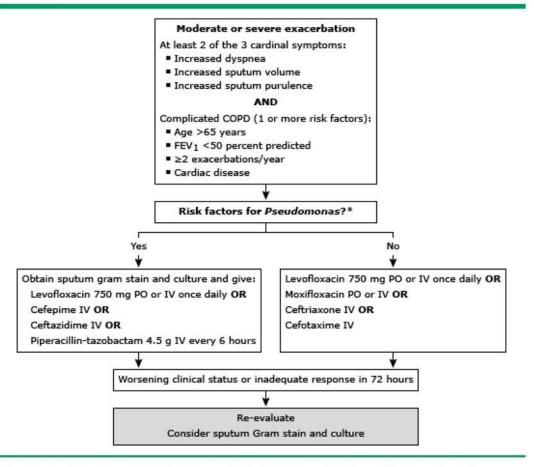
Outpatient management of exacerbations of COPD



- * Pseudomonas risk factors:
 - Frequent administration of antibiotics (4 or more courses over the past year)
 - Recent hospitalization (2 or more days' duration in the past 90 days)
 - Isolation of Pseudomonas during a previous hospitalization
 - Severe underlying COPD (FEV₁ <50 percent predicted)

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Antibiotic treatment of exacerbations of COPD in hospitalized patients



The doses recommended above are intended for patients with normal renal function; the doses must be adjusted in patients with renal insufficiency.

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Conclusion

 Various cough suppressants and expectorants are available to relieve mucous production

- Depending upon the severity of the exacerbation, you may require antibiotics
 - Not every COPD exacerbation requires antibiotics
 - Judicious use means antibiotics are available when they are truly needed

Check with the doctor and/or pharmacist to make sure your