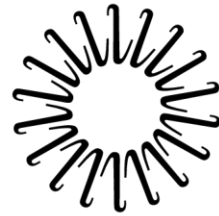


# Antibiotics, Expectorants, and Cough Suppressants



**Lifespan Cardiovascular Institute**

**Rhode Island Hospital • The Miriam Hospital  
Newport Hospital**

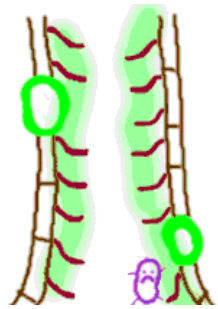
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# Objectives

- 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 aeruginosa* coverage

# expectorants



- Limited data to suggest improvements to lung function or overall feelings of well-being
- 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, sedation, pruritic skin rash, constipation, gastrointestinal distress, nausea

# **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
  - FEV1 >50% predicted
  - <2 exacerbations per year
  - No cardiac disease

## Complicated COPD

- **One or more** of the following risk factors:
  - >65 years of age
  - FEV1 <50% predicted
  - >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)
  - Recent hospitalization
    - $\geq 2$  days' duration during last 90 days
  - Frequent administration of antibiotics
    - $\geq 4$  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

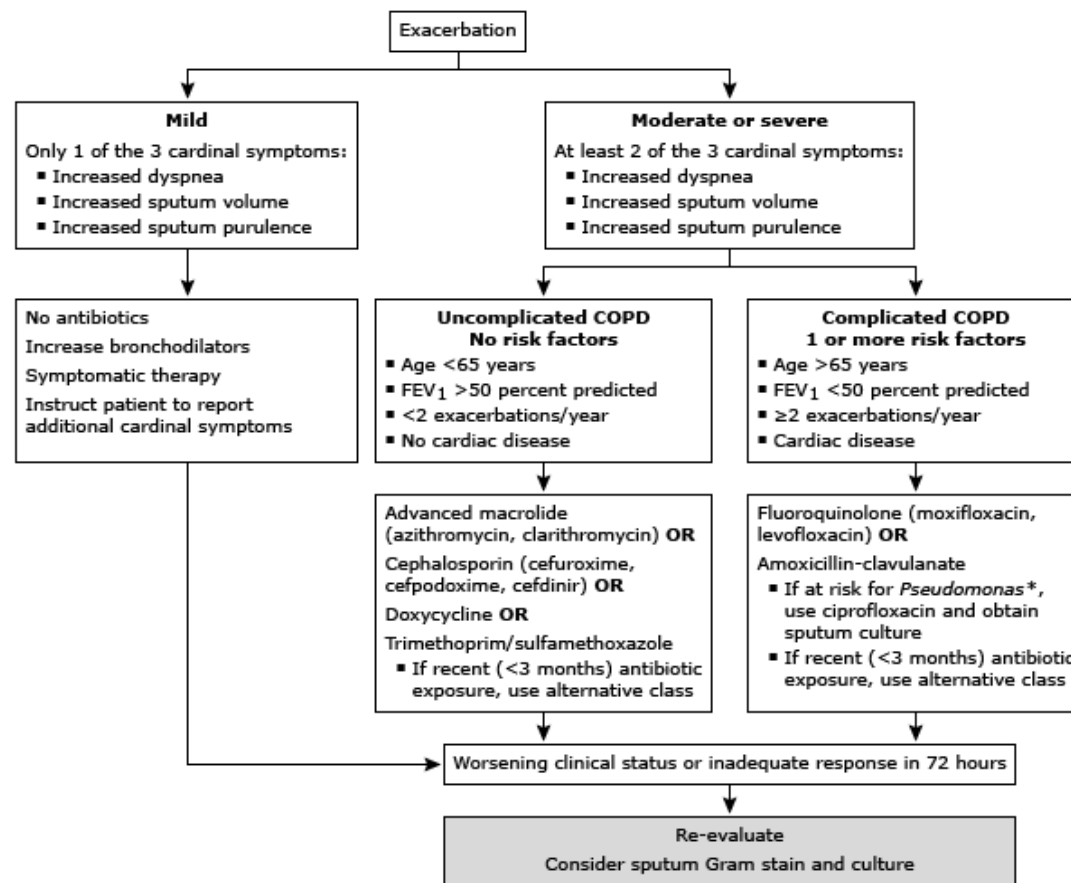
- Macrolides
  - Dosing
    - Azithromycin 500 mg by mouth daily for 3 days
    - Clarithromycin 500 mg every 12 hours for 5 days
  - Duration
    - Typically 5 to 7 days
      - Azithromycin is shorter due to long half-life
      - Data suggests a 5-day duration is equally effective while decreasing 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 pneumoniae*
    - *Pseudomonas aeruginosa* (Levofloxacin ONLY)

## Outpatient management of exacerbations of COPD

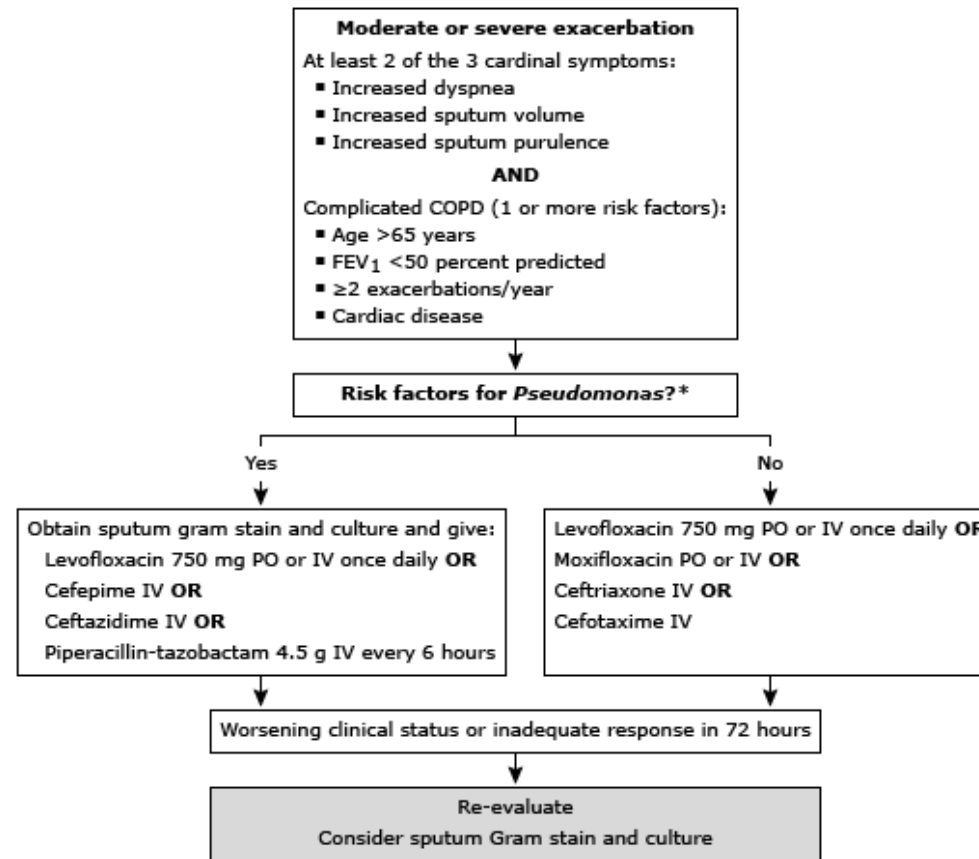


\* *Pseudomonas* risk factors:

- 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 (FEV<sub>1</sub> <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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- 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 (FEV<sub>1</sub> <50 percent predicted)

# 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