

# Don't Cover Your Cough!

Antibiotics for Acute Bronchitis?

Tamara Link, DNP, FNP-BC,  
Family Nurse Practitioner

Illinois Summit on Antimicrobial Stewardship  
July 12, 2016

# Disclosure

- I have no actual or potential conflict of interest in relation to this program or presentation.

# Pretest Question 1

You should consider treating a healthy adult patient with acute bronchitis with an antibiotic when their cough exceeds 10 days.

A. True

B. False

# Pretest Question 2

Acute bronchitis in healthy adults is caused by a viral etiology in more than 90% of the cases.

- A. True
- B. False

# Pretest Question 3

Discolored or purulent sputum alone in a patient with acute bronchitis is a good predictor of a bacterial etiology.

- A. True
- B. False

# Pretest Question 4

Studies show that patient's are usually dissatisfied with their visit if they expect an antibiotic prescription but don't get one.

A. True

B. False

# Why do we prescribe antibiotics for acute respiratory tract infections?

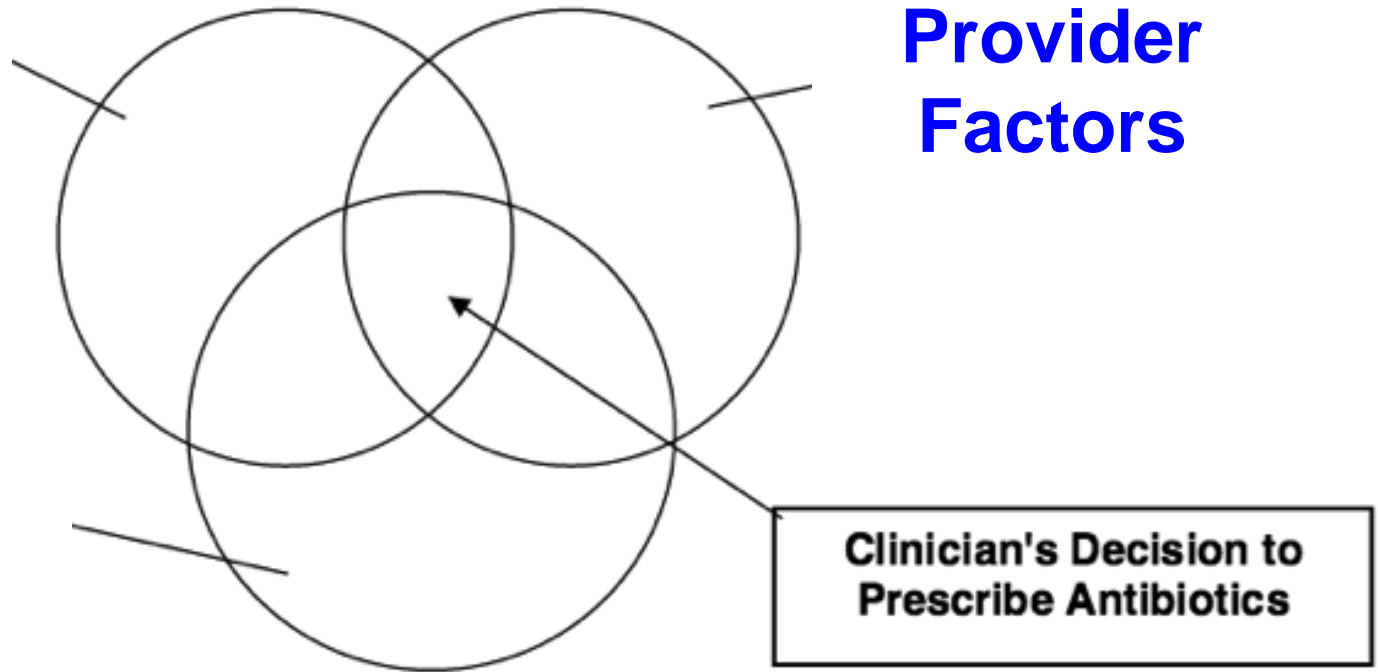


# Factors Associated with Antibiotic Prescribing

**Patient  
Factors**

**Provider  
Factors**

**System  
Factors**



Adapted from Agency for Healthcare Research and Quality. (2006). Technical Review No. 9: Closing the Quality Gap: A Critical Analysis of Quality Improvement Strategies. Volume 4-Antibiotic Prescribing Behavior (AHRQ Publication No. 04[06]-0051-4).



# Patient Factors

## Influencing Antibiotic Prescribing



- Expectation or demand
- Previous experience with past treatment
- Misunderstanding of antibiotics for viral illness
- Physical symptoms or complaints



# True or False

Studies show that providers can almost always correctly identify patients who expect antibiotics.





**FALSE!**

Providers have only a "fair"  
accuracy in predicting which patients want Rx  
1 out of 4



# True or False

Patients who do not receive an antibiotic prescription are on average more dissatisfied with their office visit





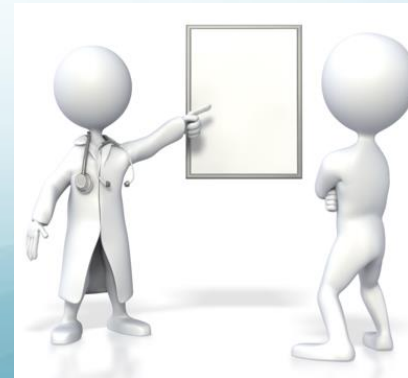
**FALSE!**

Numerous studies show that patient satisfaction is not adversely affected when they do NOT receive an antibiotic!

Gonzales et al., *Ann Intern Med* 2001; 134: 521-529  
Linder, et al. *Clin Ther*, 2003; 25: 2419-2430.  
Metlay et al., *Ann Emer Med*, 2007; 50(3), 22-230  
Ong et al., *Ann of Emer Med*, 2007; 50 (3), 213-220  
Ranji et al., *Med Care*, 2006; 46(8), 847–862  
Snow et al., *Ann Intern Med*, 2001; 134(6), 134:518  
Thoolen et al., *Health Psych Review*, 2012; 6(1), 92-112

# Believe it or not!

Patient's report greater satisfaction  
when they believe they have  
a good understanding of their illness.



# Provider Factors

## Influencing Antibiotic Prescribing

- Longer duration of practice
- Non-teaching practice setting
- Clinicians over 30 years old
- NPs/ PAs?
- Urgent care setting



Agency for Healthcare Research and Quality. 2006; AHRQ Publication No. 04[06]-0051-4

Dosh et al., *JFP*, 2000; , 49(5): 407-414

Gonzales et al., *JAMA Int Med*. 2013; 174 (4): 267-274

Roth et. al., *Am J Man Care*. 2012; 18 (6): 217-224

# Other Provider Factors

- Uncertainty about diagnosis
- Abundance of caution
- Lack of knowledge
- Past experience with ARTI treatment
- Concern about not harming patient
- Busy! Wanting to expedite office visit
- Desire to avoid follow up visits





Are we harming our patients by not giving an antibiotic?

How many patients do you have to treat with an antibiotic to prevent ONE Hospitalization for pneumonia?





Number needed to treat to prevent  
1 hospitalization for pneumonia:  
**12,255**



# Take a Guess

If you do NOT give an antibiotic prescription for ARTI visit, how much longer is the office visit?





**ONE minute!**

NOT giving an antibiotic prescription does not significantly increase the duration of an office visit

# What is Acute Bronchitis?

# Acute Bronchitis

- Self-limited acute respiratory tract infection (ARTI) lasting up to 3 weeks
- Characterized by inflammation of bronchial epithelium
- Clinical diagnosis based on predominance of cough.
- Only diagnosed when other respiratory conditions are ruled out.



In what percentage of cases of suspected acute bronchitis must you rule out  
Pneumonia?





# ALL OF THEM!

Per CDC: Bronchitis is only diagnosed when you rule out more serious illnesses, particularly pneumonia



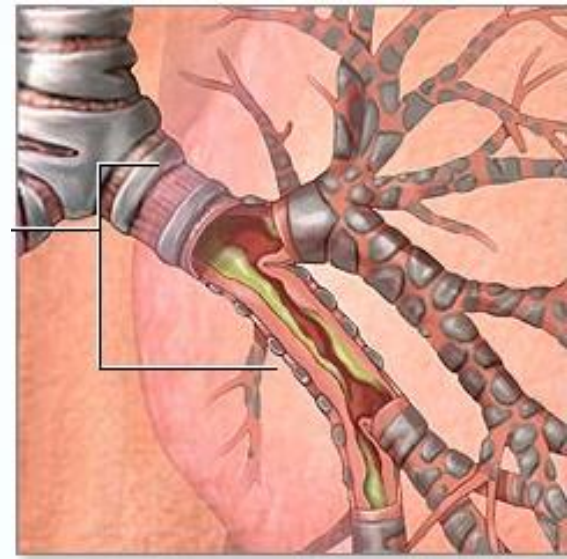
# Etiology

- Etiology is viral in **over 90%** of the cases
  - Influenza A/B, parainfluenza 3, respiratory syncytial virus, corona virus, adenovirus, rhinovirus
- Bacteria only cause 5-10% of cases
  - *Mycoplasma pneumoniae*
  - *Chlamydia pneumoniae*
  - *Bordetella pertussis*
- *CDC only recommends treating pertussis which comprises 1% of the cases*

# Pathophysiology

## Acute phase 1-5 days

- Virus inoculates tracheo-bronchial epithelium
- Leads to inflammatory cell activation
- Characterized by mild constitutional symptoms



# Pathophysiology

## Protracted phase 1-3 weeks

- Hypersensitivity of tracheobronchial epithelium and airway receptors: bronchial hyper-responsiveness
- Thickening of bronchial and tracheal mucosa from inflammation
- Characterized primarily by cough
- Often accompanied by phlegm and wheezing
- Transient ↓ in FEV1 on PFT (40% of pts)

**Think Inflammation!**

# Clinical Presentation

- Cough with or without sputum production < 3 weeks
- Localized symptoms: nasal congestion, runny nose, sore throat
- Systemic symptoms typically absent: fever, myalgia, nausea, malaise, and dyspnea.
- Bronchospasm and wheezing may be present
- No signs of lung consolidation
- Cough typically persists 10-20 days, with mean duration of cough 14- 18 days





# True or False



Purulent or discolored sputum is NOT a good predictor of bacterial etiology in patients with acute bronchitis



# TRUE!

50% of patients with acute bronchitis have purulent or discolored sputum and this finding should not sway you to prescribe an antibiotic.



# True or False

Smokers are more likely to have a bacterial etiology of acute bronchitis and should usually be treated with an antibiotic







**FALSE!**

Yet smokers receive RX 1.5 times more often

# Clinical Practice Guidelines

- American College of Physicians (ACP)
- American College of Chest Physicians (ACCP)
- Centers for Disease Control (CDC)
- Agency for HealthCare Research and Quality (AHRQ)

# Clinical Practice Guidelines apply to:

- Healthy adults age 18-64 y/o
- No significant comorbid conditions which might make an antibiotic appropriate:
  - Immunocompromised
  - Malignancy
  - Chronic lung disease
  - End-organ failure



# National Quality Measures

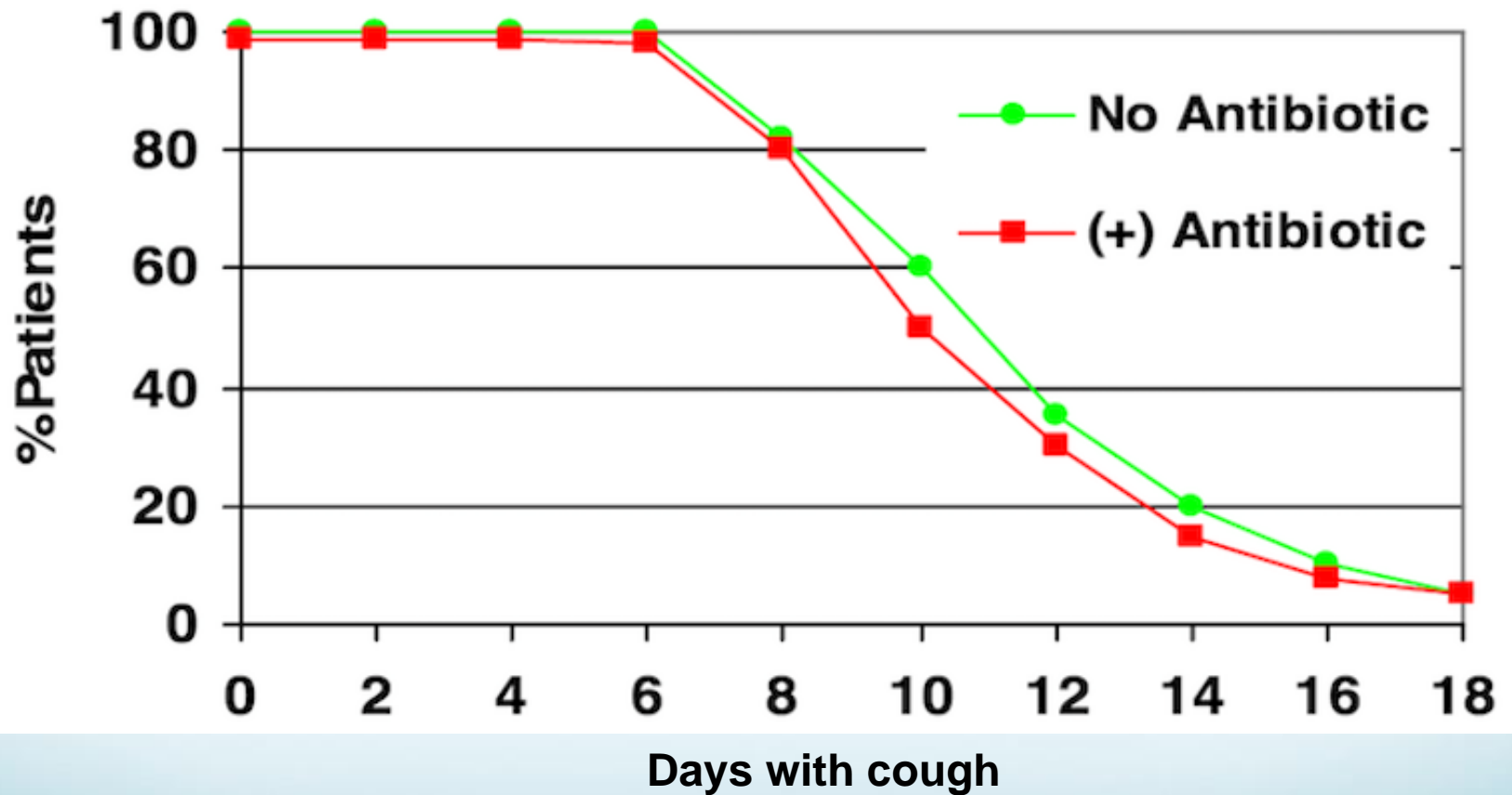
- Healthcare Effectiveness Data and Information Set (HEDIS) since 2007
- According to HEDIS: The rate of antibiotic use for acute uncomplicated bronchitis in adults **should be zero!**

# Do Antibiotics Help?

- No decrease in duration of illness
- No improvement in limitations in activity
- No decrease in time lost from work
- At best, antibiotics decrease the duration of cough by  $\frac{1}{2}$  a day
- Treatment with antibiotics does not have a significant impact on potential complications

# Resolution of Acute Bronchitis

With and without antibiotic



Stott, BMJ, 1976



According to studies,  
how often are antibiotics prescribed  
in outpatient setting  
for acute bronchitis?





Evertsen et al., *Prim Car Resp J*, 2010; 19(3): 237-241  
KroeningRoche et al., *J Emerg Med*, 2011; 43(2): 221-227



So what?



# Consequences of antibiotic over use

- CDC (2013): antibiotic resistance is a global health threat
- Over 2 million illnesses per year
- 23,000 deaths
- Direct health care costs over \$20 billion
- *Clostridium Difficile* infections, adverse drug reactions, increased cost of care.
- Resistant *Streptococcus pneumoniae*



# Case Studies



# Case Study #1



J.B. is 55 y/o WM with cough, fever, malaise, chills, sweats and feeling unwell for 3 days.

Vitals: temp 101.3, HR: 120, RR: 24, BP 124/82

His exam reveals a moderately ill appearing WM. Breath sounds reveal RLL crackles with decreased breath sounds and tactile fremitus.

# Suspect Pneumonia

- **T**achycardia: HR > 100
- **T**achypnea: RR > 24
- **T**emp > 100.4
- Signs of focal consolidation
  - Rales/crackles
  - Egophony
  - Fremitus
- Gold standard for pneumonia: chest xray

# Case Study #2

M.L. is a 77 y/o AF with cough and altered mental status. She has a temperature of 99.2, P: 98, RR 26.

Exam reveals a frail, slightly confused AF with decreased breath sounds worse on LLL but no definite crackles, rales, rhonchi.



# Pneumonia in Elderly



- Atypical presentations
- In persons over 75 y/o obtain chest xray if:
  - RR >24
  - Decreased mental status and/or
  - Change in behavior

*regardless of temperature*

# Case Study #3

J.G. is a 59 y/o BM. He c/o a cough for almost 2 weeks. He states his cough was initially intermittent, but now he has severe “coughing fits” followed occasionally by vomiting. His vitals are: T: 99.2, P: 92, RR 18, O2 sat 98%.

On exam, he has normal breath sounds.





# Pertussis

- CDC: 1% of cases of bronchitis
- High index of suspicion with outbreaks or known contacts
- Consider dx if cough illness lasting 2 or more weeks including 1 or more of following:
  - Paroxysms of cough
  - Inspiratory “whoop”
  - Posttussive vomiting

# Case study #4



A.L. is a 19 y/o WF who is home from college on Christmas break. She states her roommate was sick at the beginning of the week, now she “has it” for the past 2 days.

She c/o sudden onset of fevers, headache, chills, s/t, fatigue, and states OMG “my whole body hurts!”

Temp 102, P 99, RR 18, O2 sat 99%

Exam reveals a tired, moderately ill appearing, slightly diaphoretic WF with occasional cough. Lung exam is normal.

# Influenza



- Most common pathogen isolated in patient with uncomplicated acute bronchitis
- Peak fall and winter months
- Sudden onset
- Annual epidemics
- Fever, myalgia, headache, s/t
- During outbreaks, the positive predictive values of clinical judgment is as good as a rapid test. (Snow, 2001)

# Case study #5



R.V. is a 30 y/o HF with c/o cough, wheeze, and slight shortness of breath for 10 days.

She states her symptoms started like a cold, but now her cough persists and she is wheezing for the past week or so. She gets “bronchitis” at least twice a year and wants her zpack. Denies fevers, chills, or malaise.

VS: T: 99.0, P: 78, RR: 16, O2 sat: 97%

Exam: Healthy appearing HF with productive cough. Breath sounds reveal moderate expiratory wheezing and slight rhonchi throughout.

# Consider Asthma



- Many patients with acute bronchitis actually have asthma.
- Consider asthma if
  - Wheezing
  - Female gender
  - One or more episode of wheeze, dyspnea in past year
  - Allergy induced symptoms
  - H/o 2 diagnosed cases of “acute bronchitis” in past 5 years (65% chance of asthma)

# Treatment of Acute Uncomplicated Bronchitis

- Antitussive agents (mixed results but reasonable)
- Bronchodilators if evidence of airflow obstruction (wheezing)
- Mucokinetic agents (no consistent favorable effect)
- NSAIDS (helps with some symptoms but not cough)
- Inhaled corticosteroids (may be some benefit to high dose inhaled corticosteroids)
- No data to support use of oral corticosteroids in acute bronchitis when there is no asthma

How can we communicate  
with our patients  
Who might expect an antibiotic?



# Supportive strategies

## What Patients want:

- To have their symptoms listened to
- To discuss worries and concerns
- To have their self-knowledge respected
- To have the severity, nature, and expected length of their illness explained
- To discuss treatment options
- To have their concern handled in one visit
- To be able to f/u with their provider by phone or email



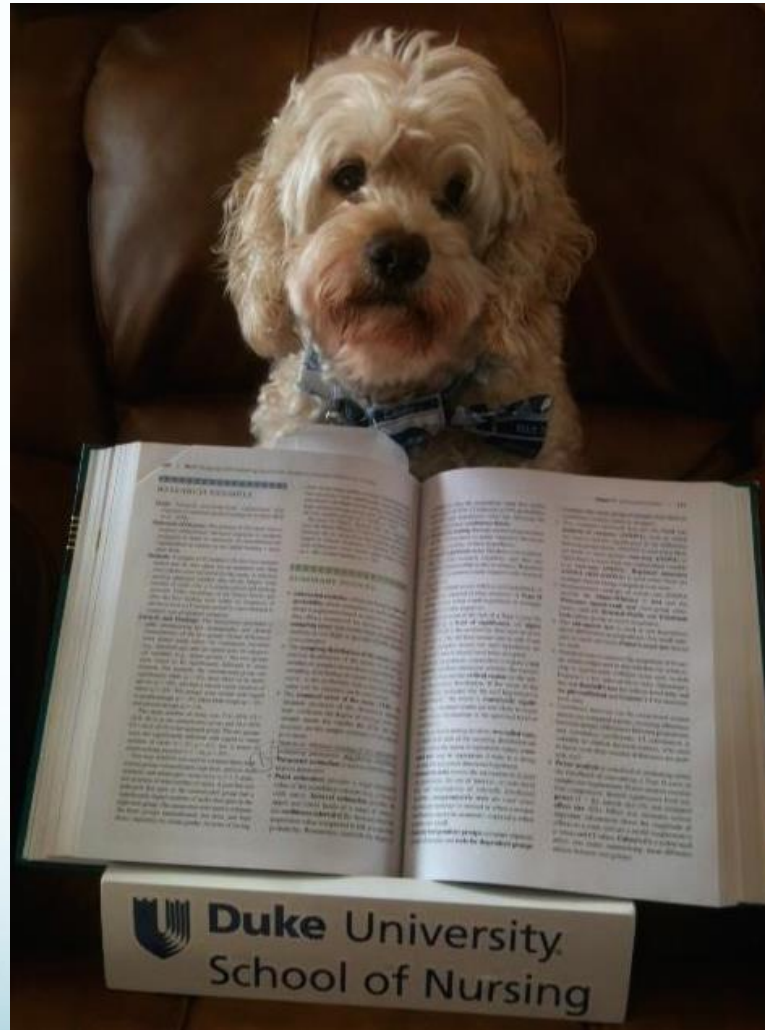
# Communication

- Call it a “chest cold” or “viral respiratory infection”
- Let them know what to expect
  - Duration of cough typically 10-14 days (up to 3 weeks)
  - Cough subsides in 75% by 2 weeks
- Explain that antibiotics do not significantly reduce the duration of symptoms

# More communication

- Explain that antibiotics may cause adverse effects and lead to antibiotic resistance.
- Recent antibiotic use places your family at risk for carrying antibiotic resistant bacteria
- Consider delayed “pocket” prescription

# Summary

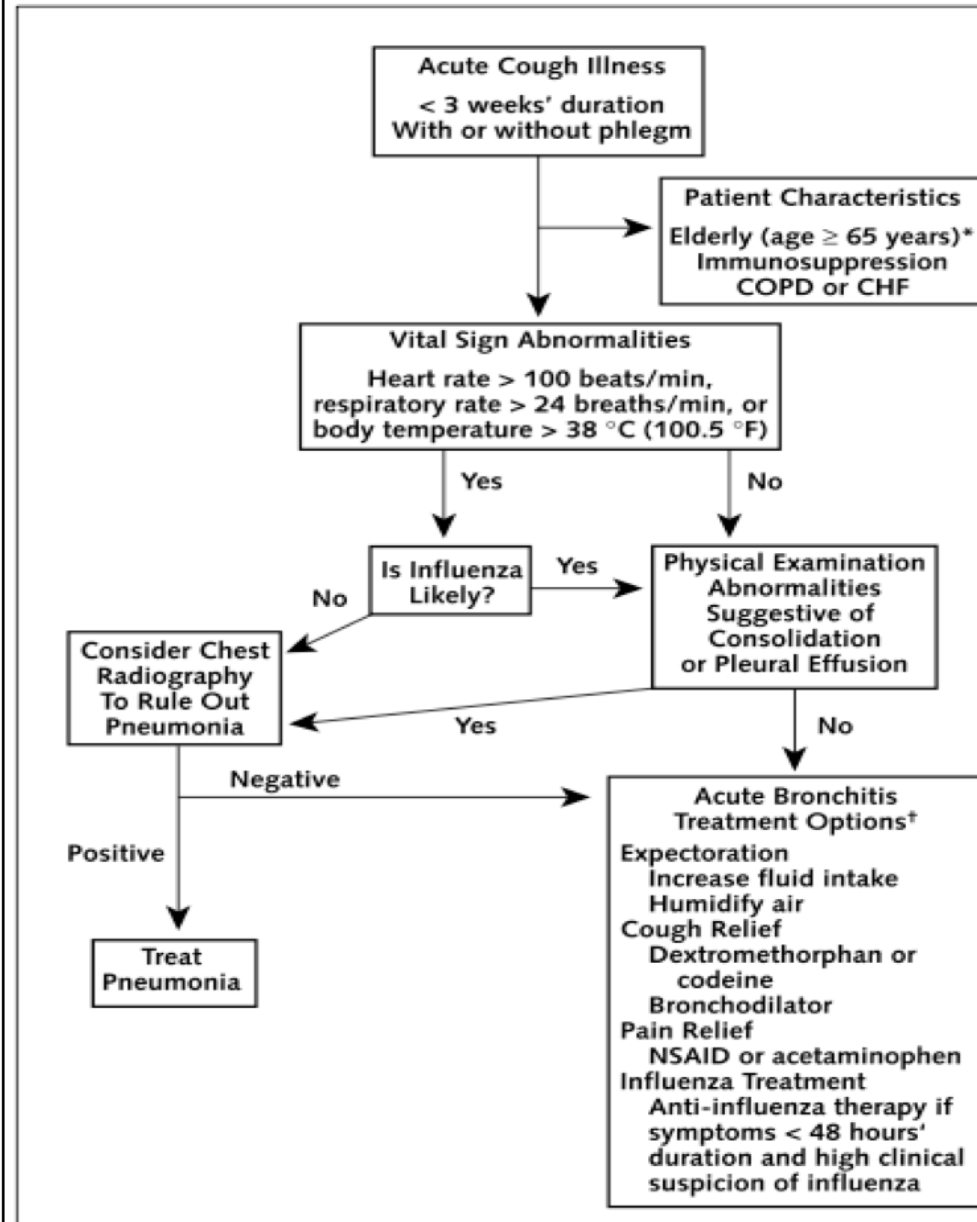


# Acute Uncomplicated Bronchitis in Adults

## Age 18-64

- Acute bronchitis is a self-limited ARTI lasting up to 3 weeks with cough as predominant symptom
- Viruses cause more than 90% of the cases
- Antibiotics are not indicated (except if you suspect pertussis, an unusual circumstance).
- Rule out other respiratory illnesses
- Antitussives, bronchodilators, and inhaled steroids can be used in some patients

**Figure.** Proposed algorithm for evaluation and management of adults with acute cough illness.



# EVIDENCE-BASED MANAGEMENT OF ACUTE RESPIRATORY TRACT INFECTIONS

## Assess clinical probability of pneumonia

*Among elderly patients:  
Also consider pneumonia when altered mental status (clouded thinking), increased falls, loss of appetite or new urinary incontinence is present*

### LOW

(< 5%)

No abnormal vital signs and normal chest exam

- No CXR
- No ABx

### INTERMEDIATE

(5% - 30%)

One or more abnormal vital signs OR abnormal chest exam

- Consider CXR\*
- ABx based on CXR results

### HIGH

(> 30%)

One or more abnormal vital sign(s) AND abnormal chest exam

- Perform CXR
- Consider empiric ABx\*\*

\* CXR should be ordered on all patients with focal lung findings on physical examination.

\*\* Abnormal vital signs are common with uncomplicated influenza infection when influenza is circulating in the community

## In the absence of pneumonia, consider the following diagnoses in adults with acute cough illness

### URI or Rhinosinusitis

#### Dx criteria

- cough plus nasal, throat and/or ear Sx
- no dominant Sx

### Acute bronchitis

#### Dx criteria

- cough dominant
- +/- phlegm
- rhonchi/mild wheezing common

### Influenza

#### Dx criteria

- if cough + fever + myalgias/fatigue present, prevalence  $\geq$  60%

### Acute bacterial sinusitis

#### Dx criteria

- illness > 7 days
- purulent nasal discharge
- facial, head or teeth pain

National Committee for Quality Assurance. (2011). An algorithm to improve appropriate antibiotic use for patients with acute bronchitis. Retrieved from [http://www.ncqa.org/Portals/0/Education/An\\_Algorithm\\_To\\_Improve\\_Appropriate\\_Antibiotic\\_Use\\_for\\_Bronchitis\\_Archived\\_Manual.pdf](http://www.ncqa.org/Portals/0/Education/An_Algorithm_To_Improve_Appropriate_Antibiotic_Use_for_Bronchitis_Archived_Manual.pdf)

# Post-test Question 1

You should consider treating a healthy adult patient with acute bronchitis with an antibiotic when their cough exceeds 10 days.

- A. True
- B. False

# Post-test Question 2

Acute bronchitis in healthy adults is caused by a viral etiology in more than 90% of the cases.

- A. True
- B. False



# Post-test Question 3

Discolored or purulent sputum alone in a patient with acute bronchitis is a good predictor of a bacterial etiology.

- A. True
- B. False

# Post-test Question 4

Studies show that patient's are usually dissatisfied with their visit if they expect an antibiotic prescription but don't get one.

- A. True
- B. False

# QUESTIONS?



# References

- Agency for Healthcare Research and Quality. (2006). Technical Review No. 9: Closing the Quality Gap: A Critical Analysis of Quality Improvement Strategies. Volume 4-Antibiotic Prescribing Behavior (AHRQ Publication No. 04[06]-0051-4). Retrieved from <http://www.ncbi.nlm.nih.gov/books/NBK43956/pdf/TOC.pdf>
- Agency for Healthcare Research and Quality. (2013). *Management of uncomplicated acute bronchitis in adults*. Retrieved from <http://www.guideline.gov/content.aspx?id=38688>
- Agency for Healthcare Research and Quality. (2014). *Avoidance of antibiotic treatment in adults with acute bronchitis: percentage of adults 18 to 64 years of age with a diagnosis of acute bronchitis who were not dispensed an antibiotic prescription*. Retrieved from <http://www.qualitymeasures.ahrq.gov/content.aspx?id=48611>.
- Arnold, S.R. & Straus, S.E. (2005). Interventions to improve antibiotic prescribing practices in ambulatory care (Review). *Cochrane Database of Systematic Reviews 2005* (4), 1-78. doi: 10.1002/14651858.CD003539.pub2
- Albert, R.H. (2010). Diagnosis and treatment of acute bronchitis. *American Family Physician*, 82 (11), 1345-1350.
- Aspinall, S.L., Good, C. B., Metlay, J.P., Mor, M.K., & Fine, M.J. (2009) *American Journal of Emergency Medicine*, 27, 544-55. doi: 10.1016/j.ajem.2008.04
- Barnett, M.L. & Linder, J.A. (2014). Antibiotic prescribing for adults with acute bronchitis in the United States, 1996-2010. *JAMA*, 311(19), 2020-2022.
- Braman, S.S. (2006). Chronic cough due to acute bronchitis: ACCP evidence-based clinical practice guidelines [Supplement]. *CHEST*, 129(1), 95S-103S.
- Butler et al. (2011). Antibiotic prescribing for discoloured sputum in acute cough/lower respiratory tract infection. *Eur Respir Journal*, 38, 119-125. doi: 10.1183/09031936.00133910
- Centers for Disease Control and Prevention. (2013). *Antibiotic Resistance Threats in the United States, 2013*. Retrieved from <http://www.cdc.gov/drugresistance/threat-report-2013/pdf/ar-threats-2013-508.pdf>
- Centers for Disease Control. (2011). National Hospital Ambulatory Medical Care Survey: 2011 Outpatient Department Summary Tables. Retrieved from [http://www.cdc.gov/nchs/data/ahcd/nhames\\_outpatient/2011\\_odp\\_web\\_tables.pdf](http://www.cdc.gov/nchs/data/ahcd/nhames_outpatient/2011_odp_web_tables.pdf)
- Colgan, R. & Powers, J.H. (2001). Appropriate Antimicrobial Prescribing: Approaches that Limit Antibiotic Resistance. *American Family Physician*, 64, 99-1004.
- Dosh, S.A, Hickner, J.M, Minous, A.G., & Ebell, M. (2000). Predictors of antibiotic prescribing for nonspecific upper respiratory infections, acute bronchitis, and acute sinusitis. *The Journal of Family Practice*, 49(5), 407-414.
- Evertsen, J., Baumgardner, D.J., Regnery, A., & Banerjee, I. (2010). Diagnosis and management of pneumonia and bronchitis in outpatient primary care practices. *Primary Care Respiratory Journal*, 19(3), 237-241.
- File, T.M. (2015). Acute bronchitis in adults. *UpToDate*.
- Gonzales, R. et al., (2013). A cluster-randomized Trial of decision support strategies for reducing antibiotic use for acute bronchitis. *JAMA Internal Medicine*. 174 (4), 267-274. doi:10.1001/jamainternmed.2013.1589

Gonzales R., Bartlett J.G., Besser R.E., Cooper, R.J., Hickner, J.M., Hoffman, J.R., & Sande, M.A. (2001). Principles of appropriate antibiotic use for treatment of uncomplicated acute bronchitis: Background [Position paper]. *Ann Intern Med* 134(6),521-529.

Gonzales, R., Camargo, C.A., MacKenzie, T., Kersey, A.S., Maselli, J., ... and the IMPAACT trial Investigators. (2006). Antibiotic treatment of acute respiratory infections in acute care settings. *Academic Emergency Medicine*, 13(3), 238-294.

Gonzales, R. & Sande, M.A. (2000). Uncomplicated Bronchitis. *Annals of Internal Medicine*, 133 (12), 981-991.

Grover, M.L., Mookadam, M., Rutkowski, R.H., Cullan, A.M., Hill, D.H., ... Noble, B.N. (2012). Acute respiratory tract infection: a practice examines its antibiotic prescribing habits. *Journal of Family Practice*, 61 (6), 330-335.

Hare, M.E., Gaur, A.H., Somes, G.W., Arnold, S.R., & Shorr, R.J. (2006). Does it really take longer not to prescribe antibiotics for viral respiratory tract infections in children? *Ambulatory Pediatrics* 6 (3), 152-156.

Hart, A.M. (2014). Evidence-based diagnosis and management of acute bronchitis. *The Nurse Practitioner* 39 (9), 33-39.

Holzinger, F., Beck, S., Dini, L., Stoter, C., & Heintze, C. (2014). Clinical practice guideline: The diagnosis and treatment of acute cough in Adults. *Deutsches Arzteblatt International*, 111, 356-363. doi: 10.3238/arztebl.2014.0356

Huang, H., Weintraub, A., Fang, H., & Nord, C.E. (2009). Antimicrobial resistance in *Clostridium difficile*. *International Journal of Antimicrobial Agents*. 34, 516-522. doi:10.1016/j.ijantimicag.2009.09.012

Interagency Task Force on Antimicrobial Resistance (2011). *2011 Progress towards implementation of: A public health action to combat antimicrobial resistance*. Retrieved from <http://www.cdc.gov/drugresistance/pdf/annual-progress-report-2011.pdf>

Kroening-Roche, Soroudi, A., Castillo, E.M., & Vilke, G.M. (2012). Antibiotic and bronchodilator prescribing for acute bronchitis in the emergency department. *The Journal of Emergency Medicine*, 43(2), 221-227. doi:10.1016/j.jemermed.2011.06.143

Ladd, E. (2005). The use of antibiotics for viral upper respiratory tract infections: An analysis of nurse practitioner and physician prescribing practices in ambulatory care, 1997-2001. *Journal of the American Academy of Nurse Practitioners*, 17 (10), 416-424.

Lee, G.C., Reveles, K.R., Attridge, R.T., Lawson, K.A., Mansi, I.A., Lewis II, J.S. & Frie, C.R. (2014). Outpatient antibiotic prescribing in the United States: 2000 to 2010. *BMC Medicine*, 12(96). doi: 10.1186/1741-7015-12-96

Li, J., Anindya D., Ketchum, K., Fagnan, L.J., Haxby, D.G., & Thomas, A. (2009). Antimicrobial prescribing for upper respiratory infections and its effect on return visits. *Family Medicine*, 41 (3), 182-187.

Linder, J.A., Singer, D.E., & Stafford, R.S. (2003). Association between antibiotic prescribing and visit duration in adults with upper respiratory tract infections. *Clinical Therapeutics*, 25 (9), 2419-2430. doi [http://dx.doi.org/10.1016/S0149-2918\(03\)80284-9](http://dx.doi.org/10.1016/S0149-2918(03)80284-9)

Llor, C. et al. (2013). Efficacy of anti-inflammatory or antibiotic treatment in patients with non-complicated acute bronchitis and discoloured sputum: Randomised placebo controlled trial. *British Medical Journal* 347, 1-12. doi: 10.1136/bmj.f5762

- Mehrotra, A.M., Gidengil, C.A., Setodji, C.M., Burns, R.M., & Linder, J.A. (2015). Antibiotic prescribing for respiratory infections at retail clinics, physician practices, and emergency departments. *American Journal of Managed Care*, 21(4), 294-302.
- Meropol, S.B., Localio, R., & Metlay, J.P. (2013). Risks and benefits associated with antibiotic use for acute respiratory infections: A cohort study. *Annals of Family Medicine*, 11 (2), 165-172. Retrieved from <http://www.annfammed.org/content/11/2/165.full>
- Metlay, J.P., Camargo, C.A., MacKenzie, T., McCullough, C., Maselli, J.,... and the IMPAACT Investigators. (2007). Cluster-randomized trial to improve antibiotic use for adults with acute respiratory infections treated in emergency departments. *Annals of Emergency Medicine*, 50(3), 22-230.
- Newhauser, M., & Roselle, G. (2013, April 21). VA's Antimicrobial Stewardship Program [Web blog post]. Retrieved from <http://www.blogs.va.gov/VAntage/13770/vas-antimicrobial-stewardship-program>
- Ong, S., Nakase, J., Moran, G.J., Karras, D.J., Kuehnert, M.J., Talan, D.A., & the EMERGENCY ID Net Study Group. (2007). Antibiotic use for emergency department patients with upper respiratory infections: Prescribing practices, patient expectations, and patient satisfaction. *Annals of Emergency Medicine*. 50 (3), 213-220. doi:10.1016/J.annemergmed.2007.03.026
- Pan, Q., Ornstein, S., Gross, A., Hueston, W.J., Ruth, G., Arch, G., & Silverstein, M.D. (2000). Antibiotics and return visits for respiratory illness: a comparison of pooled versus hierarchical statistical methods. *The American Journal of the Medical Sciences*, 319(6), 360-365.
- Ranji SR, Steinman MA, Shojania KG, & Gonzales R. (2008). Interventions to reduce unnecessary antibiotic prescribing: A systematic review and quantitative analysis. *Med Care*, 46(8), 847-862. doi: 10.1097/MLR.0b013e318178eabd
- Roth, S. et al. (2012) Unintended consequences of a quality measure for acute bronchitis. *The American Journal of Managed Care*, 18 (6), 217-224.
- Safdar, N., Tape, T.G., Fox, B.C., Svenson, J.E., & Wigton, R.S. (2014). Factors affecting antibiotic prescribing for acute respiratory infection by emergency physicians. *Health*, 6, 774-780. Retrieved from <http://dx.doi.org/10.4236/health.2014.6809>
- Shapiro, D.J., Hicks, L.A., Pavia, A.T., & Hersh, A.L. (2013). Antibiotic prescribing for adults in ambulatory care in the USA, 2007-09. *Journal of Antimicrobial Chemotherapy*, 69, 234-240.
- Smith, S.M., Fahey, T., Smucny, J., & Becker, L.A. (2014). Antibiotics for acute bronchitis (Review). *The Cochrane Collaboration*. John Wiley & Sons, Ltd.
- Snow V., Mottur-Pilson C., & Gonzales R., for the American College of Physicians-American Society of Internal Medicine. (2001). Principles of appropriate antibiotic use for treatment of acute bronchitis in adults [Position paper]. *Annals of Internal Medicine*, 134(6), 134:518.
- Tonkin-Crine, S., Yardley, L., & Little, P. (2011). Antibiotic prescribing for acute respiratory tract infections in primary care: A systematic review and meta-ethnography. *Journal of Antimicrobial Chemotherapy*, 66, 2215-2223. doi:10.1093/jac/dkr279
- Thiadians, H.A., Postma, D.S., de Bock, G.H., Huysman, D.A., van Houwelingen, H.C. & Springer, M.P. (2000). Asthma in adult patients presenting with symptoms of acute bronchitis in general practice. *Scandinavian Journal of Primary Health Care*, 18, 188-192.
- Thoolen, B., de Ridder, D., & van Lensvelt-Mulders, G. (2012). Patient-oriented interventions to improve antibiotic prescribing practices in respiratory tract infections: A meta-analysis. *Health Psychology Review*, 6(1), 92-112.
- Van der Velden, A.W., Pijpers, E.J., Kuyvenhoven, M.M., Tonkin-Crine, S.K., Little, P., & Verheij, T.J. (2012). Effectiveness of physician-targeted interventions to improve antibiotic use for respiratory tract infections. *British Journal of General Practice*, 62(605), 801-807. doi: 10.3399/bjgp12X659268
- Vinnard, C., Linkin, D.R., Localio, A.R., Leonard, C.E., Teal, V.L., Fishman, N.O., & Hennessy S. (2013). Effectiveness of interventions in reducing antibiotic use for upper respiratory infections in ambulatory care practices. *Population Health Management* 16 (1) 22-27. doi: 10.1089/pop.2012.0025
- Wang, E.E., Kellner, J.D., & Arnold, S. (1998). Antibiotic-resistant Streptococcus pneumonia: Implications for medical practice. *Canadian Family Physician*, 44, 1881-1888.
- Yardley, L., Douglas, E., Anthierens, S., Tonkin-Crine, S., O'Reilly, G... on behalf of the GRACE consortium. (2013). Evaluation of a web-based intervention to reduce antibiotic prescribing for LRTI in six European countries: quantitative process analysis of the GRACE/INTRO randomized controlled trial. *Implementation Science*, 8, 134. Retrieved from <http://www.implementationscience.com/content/8/1/134>