

TREATMENT OF COMMON RESPIRATORY INFECTIONS: THE ANTIBIOTIC DILEMMA

Antibiotics — to use or not to use, a common question.



K T NAIDOO

BSc, MB ChB, FCP(SA),
Certificate in Pulmonology

Specialist

Physician/Lecturer

Nelson Mandela School of
Medicine
University of KwaZulu-
Natal

Pulmonologist

Respiratory Unit
Inkosi Albert Luthuli Central
Hospital

Dr Naidoo obtained his
Pulmonology Certification
in September 2003. His
current interests include
critical care medicine, dif-
fuse pulmonary disease and
pulmonary vascular dis-
ease.



DOUGLAS WILSON

MB ChB, FCP (SA)

Principal Specialist

Pietermaritzburg Hospital
Complex

Honorary Lecturer

University of KwaZulu-Natal

Douglas Wilson trained in
internal medicine, and from
1999 to 2002 in infectious
diseases and as an HIV cli-
nician at Somerset Hospital
and Groote Schuur
Hospital. He started an anti-
retroviral clinic at Somerset
Hospital in 2001, and in
April 2003 moved to Grey's
Hospital in
Pietermaritzburg.

Respiratory tract infections are one of the commonest reasons for a visit to a family physician, and given time constraints and perceived patient expectations many consultations will end with an antibiotic prescription. Antibiotic resistance among the respiratory tract pathogens is clinically significant and increasing rapidly, and clinicians treating outpatients with respiratory tract infections need to grapple with the issue of whether or not an antibiotic should be prescribed (Fig. 1). A recent study from the United States¹ gives insight into the manner in which clinicians respond to these issues. The study reviewed the treatment of more than 24 000 adults presenting with nonspecific respiratory tract infections and revealed that 63% received a prescription for an oral antibiotic. Importantly, the study excluded patients with chronic bronchitis, asthma or chronic obstructive pulmonary disease (COPD), and concluded that interventions are needed to reduce antibiotic prescribing to limit the progression of antibiotic resistance.

How should clinicians responsibly approach the management of viral upper respiratory tract infections (URTIs), sinusitis and bronchitis? Guidelines were developed in the 1980s and 1990s, but were difficult to use in individual cases and did not take into account varying antibiotic resistance in different regions. An alternative approach is to consider each case on merit and, when an antibiotic is necessary, to prescribe effectively.

The following three clinical scenarios will be discussed:

- acute bronchitis
- acute sinusitis
- infective exacerbation of chronic bronchitis, COPD or bronchiectasis.

ACUTE BRONCHITIS

Acute bronchitis is often preceded by a viral URTI. Symptoms progress to include general malaise, retrosternal pain, dry 'tickly' cough and sputum production that is initially mucoid and may later become mucopurulent because of secondary bacterial infection. The microbiological causes of acute bronchitis are shown in Table 1. Management should be based on the following principles:

- assessment of the severity of the symptoms, and colour and quantity of the sputum

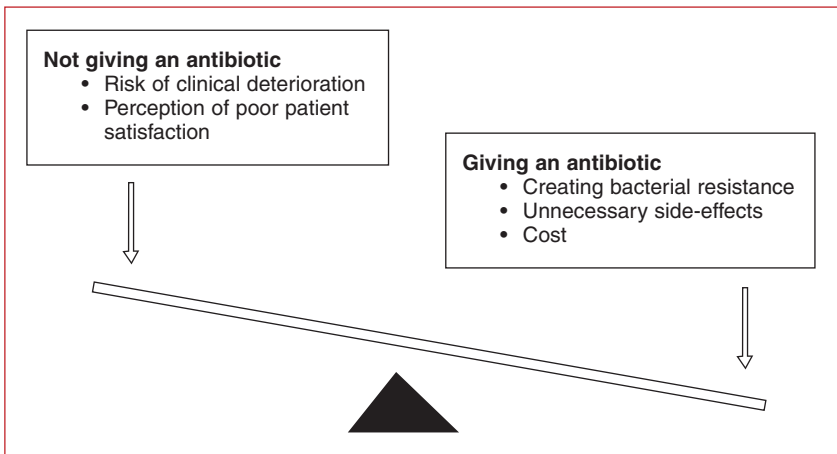


Fig. 1. The clinical dilemma of acute bronchitis.

- evaluation for underlying co-morbidity (Table II)
- exclusion of acute bacterial tonsillitis by looking for purulent tonsillar exudates
- clinical exclusion of pneumonia a chest radiograph (CXR)
- assessment of the clinical severity and access to medical care
- informing the patient that the infection will probably resolve spontaneously and about problems associated with antibiotic over-use and resistance
- antibiotic allergies.

Crucially, patient satisfaction has been shown to relate to the quality of the doctor-patient interaction rather than the prescription of an antibiotic. The use of an antibiotic for acute bronchitis is widely discouraged.

If the assessment justifies the administration of an antibiotic, either amoxicillin or doxycycline should be prescribed for 5 days. In order to achieve the concentration of amoxicillin in the bronchial secretions above the minimum inhibitory concentration (MIC) (for pneumococcus), the adult dose should be 500 mg 3 times daily. Erythromycin can be prescribed with amoxicillin if there is an outbreak of mycoplasma or chlamydia infection in the community. Doxycycline will cover both the typical respiratory tract pathogens and the mycoplasma/chlamydia. Importantly, treatment for the 'atypical' pathogens should be continued for 14 days.

ACUTE SINUSITIS

Mucoid nasal discharge with post-nasal drip and nasal congestion is a prominent feature of the common cold, and is not an indication for antibiotic treatment. Patients should be informed that these symptoms should resolve spontaneously within 3 - 4 days. Persisting symptoms for more than 1 week and a purulent nasal discharge suggest that acute bacterial sinusitis has developed. Facial pain, which is exacerbated by bending forward, or by direct pressure over the sinuses, is also highly suggestive of this condition.

Table I. Causes of acute bronchitis

Primary infection	Secondary infection
Adenovirus Rhinovirus Influenza Mycoplasma Chlamydia	<i>Streptococcus pneumoniae</i> (pneumococcus) <i>Haemophilus influenzae</i>
In the elderly	
Respiratory syncytial virus Para-influenza virus	

Table II. Conditions associated with increased risk of progression to severe lower respiratory tract infection

Immunocompetent individuals	Immunocompromised individuals
Persons > 65yrs Chronic cardiovascular disease Chronic respiratory disease Other chronic medical conditions Diabetes mellitus Cirrhosis Alcoholism Special environments Nursing homes Mines Hostels Prisons	HIV infection Leukaemia/lymphoma Myeloma Other malignancies Chronic renal failure Nephrotic syndrome Organ transplants Immunosuppressive medication

Certain patients develop sinusitis more readily; the threshold for using an antibiotic should be lower if the patient has a history of:

- sinus surgery
- sinus polyps
- bloodstained nasal discharge during the current URTI
- mucociliary disorders (rare).

If acute sinusitis is diagnosed, antibiotic treatment is indicated using amoxicillin (at least 500 mg 3 times daily), co-amoxiclav (with 500 mg of the amoxicillin component) or cefuroxime.

INFECTIVE EXACERBATIONS OF UNDERLYING LUNG DISEASE

Patients with underlying lung disease experiencing an infective exacerbation are more likely to need an antibiotic. The following points should raise the suspicion of underlying chronic lung disease:

- smoking
- daily sputum production for > 3 months yearly for the last 2 years
- gradually increasing effort intolerance
- previous pulmonary tuberculosis
- history of working underground in the mines.

Clinical features suggesting chronic lung disease include:

- prolonged expiration, hyperinflated chest and wheezing
- fixed coarse inspiratory crackles (also heard at the mouth) and finger clubbing.

Symptoms suggesting an infective exacerbation include increasing breathlessness, increased volume of sputum production and more purulent sputum. Patients with the following clinical features should be treated with an antibiotic:

- severe underlying COPD
- markedly purulent sputum
- evidence of systemic infection (fever, raised white cell count, raised erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP)
- new infiltrate on chest radiograph
- co-morbidity or an increased risk of developing pneumonia.

The use of an antibiotic is associated with the following benefits:

- more rapid improvement in peak expiratory flow rate
- lower risk of clinical failure and progression to pneumonia
- two-day reduction in duration of illness
- lower relapse rate.

An appropriate antibiotic will also eradicate infections that accelerate lung destruction and chronic airway obstruction. Importantly, treatment should also include inhaled/nebulised beta₂-agonists with ipratropium, prednisone 40 mg daily for 14 days, and inhaled oxygen if the patient is severely hypoxaemic. (Note that oxygen supplementation should be used cautiously if hypercarbia is present.)

The appropriate choice of antibiotic is detailed in Table III. Intravenous antibiotics may be required in severe cases, but can be 'switched' to oral therapy when clinical improvement occurs. Moxifloxacin (400 mg daily) and gatifloxacin (400 mg daily) have excellent absorption from the gastrointestinal tract, but are very expensive and resistance develops rapidly; hence their use should be restricted to patients who are allergic to beta-lactam antibiotics. If co-amoxiclav is used a minimum of 500 mg of the amoxicillin component should be given. Duration of therapy for severe disease should be 10 - 14 days.

Prevention

Preventing influenza and severe bacterial infections is a crucial component of the management of patients with underlying lung disease. The influenza vaccine should be given yearly at the start of the influenza season to all high-risk patients. The 23 serotype pneumococcal vaccine (Pneumovax 23 or Imovax Pneumo 23) should also be given every 5 years to high-risk patients. The role of the new heptavalent pneumococcal vaccine in adults is still unclear. Long-term physiotherapy and postural drainage are important in patients with bronchiectasis.

Clinical example

A 45-year-old woman has bilateral bronchiectasis diagnosed in childhood. Extensive, bilateral lower lobe disease was seen on a recent high-resolution CT scan of the lungs. Her cur-

Table III. Antibiotic therapy recommended for patients with infective exacerbations of COPD

Condition	Patient profile	Pathogens	Appropriate antibiotic therapy
Simple chronic bronchitis	Younger patient, near normal lung function, few exacerbations	<i>Streptococcus pneumoniae</i> <i>Haemophilus influenzae</i> <i>Moraxella catarrhalis</i>	High-dose amoxicillin or amoxicillin/clavulanic acid or macrolide/azalide
Complicated chronic bronchitis	Older patient, impaired lung function, frequent exacerbations > 4/year	As above, but antibiotic resistance more common	Amoxicillin/clavulanic acid, or 2nd or 3rd generation cephalosporin, or new respiratory fluoroquinolone
Bronchiectasis	As above, plus continuous purulent sputum production, possible structural damage/bronchiectasis	As above, plus Gram-negative organisms, including Enterobacteriaceae and <i>Pseudomonas aeruginosa</i>	Ciprofloxacin or new fluoroquinolone, or other agent according to sputum culture

Antibiotic resistance among the respiratory tract pathogens is clinically significant and increasing rapidly, and clinicians treating outpatients with respiratory tract infections need to grapple with the issue of whether or not an antibiotic should be prescribed.

Acute bronchitis is often preceded by a viral URTI. Symptoms progress to include general malaise, retrosternal pain, dry 'tickly' cough and sputum production that is initially mucoid and may later become mucopurulent because of secondary bacterial infection.

Crucially, patient satisfaction has been shown to relate to the quality of the doctor-patient interaction rather than the prescription of an antibiotic. The use of an antibiotic for acute bronchitis is widely discouraged.

rent effort tolerance is good and she describes grade 2 exertional dyspnoea. Over the years she has had many courses of antibiotics as an outpatient and inpatient, and a recent sputum culture grew *Pseudomonas aeruginosa* resistant to amoxicillin, cotrimoxazole, doxycycline, co-amoxiclav, cefuroxime, and sensitive to ofloxacin, ceftriaxone, gentamicin, amikacin and piptazobactam.

Comment

This patient has been colonised by *Pseudomonas* resistant to multiple antibiotics. This organism would have acquired the antibiotic resistance genes (which it does with notorious ease) during previous courses of treatment. During this patient's next infective exacerbation another sputum culture will have to be taken and an urgent Gram stain done. If the stain does not clearly show another organism (e.g. Gram-positive pneumococcus) the clinician will have to presume that the infecting organism is the *Pseudomonas* and treat accordingly.

Outpatient treatment can be given with ofloxacin, but both the clinician and the patient need to understand that in time the organism will become resistant to this drug. Inpatient treatment should be with intravenous ceftriaxone and gentamicin: both are given in an attempt to prevent the organism acquiring resistance to these valuable drugs. The amikacin and piptazobactam can be kept in reserve.

'Surveillance' sputum culture and sensitivity testing should be done twice yearly. Treatment should also include chest physiotherapy and appropriate vaccination. The ultimate goal of treatment is to slow the progression of the bronchiectasis and to preserve as much healthy lung tissue as possible.

Reference available on request.

IN A NUTSHELL

Antibiotic over-prescribing for acute upper respiratory tract infections (URTIs) is common and promotes antibiotic resistance.

In patients without underlying comorbidity the majority of URTIs will resolve spontaneously. Patient satisfaction is related to the quality of the doctor-patient interaction rather than to receiving an antibiotic prescription.

Mucoid sputum or nasal discharge in itself is not an indication for an antibiotic.

Acute bacterial sinusitis can be diagnosed 7 - 10 days after an URTI, when nasal discharge becomes purulent and congestion persists, and is associated with facial pain worsened by bending forward. A history of sinus surgery or nasal polyps suggests that the patient may develop sinusitis more readily, especially if the discharge is bloodstained.

Patients with acute bronchitis and severe underlying lung disease or co-morbidity may benefit from being treated early with an antibiotic to prevent pneumonia or to limit ongoing lung damage.

Sputum culture and sensitivity testing allow rational antibiotic selection for patients with structural lung disease (chronic bronchitis, emphysema and bronchiectasis) and recurrent respiratory tract infections.