Current treatments for lower respiratory tract infections

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Lower respiratory tract infections are caused by a wide range of organisms and the appropriate choice of antibiotics is important. Our Drug review discusses the current recommended management of LRTIs in the community, followed by sources of further information in Resources.

The term ‘lower respiratory tract infection’ (LRTI) covers a broad spectrum of pathological processes and aetiologies, including acute and chronic bronchitis, bronchiolitis and acute and chronic pneumonia, as well as pleural effusions, empyemas and lung abscesses.

The latter three conditions will usually be managed in hospital initially, and treatment will depend on the likely microbiological cause. In complicated pneumonias, e.g. in immunosuppressed or HIV-infected individuals, and in chronic lung conditions such as cystic fibrosis, decisions on antibiotic therapy should be made by the specialist physician looking after the patient in conjunction with a microbiologist, virologist or infectious disease physician.

This review concentrates on the LRTIs that are seen and managed by GPs. Appropriate patient selection for treatment and the correct use of agents are important, not only in optimising therapy for the individual patient but also in order to keep emergence of
resistance and side-effects to a minimum. The decision to prescribe and the choice of antibiotic used has never been more important than now with the rise in prevalence of aggressive strains of *Clostridium difficile* and the increasing prevalence of multiresistant organisms. The indication for antibiotic use in LRTIs and the type of antibiotic used will depend upon the diagnosis and severity of the disease, which may give clues to the likely aetiology.

The British Thoracic Society (BTS) has published guidelines on the assessment and management of cough in both children and adults, which doctors may find useful in assisting them to differentiate between infective and noninfective causes.

Other factors to be considered in choosing an antibiotic are the spectrum of activity of the drug, the local resistance pattern, the side-effect profile, contraindications, interactions with other drugs that the patient may be taking (see Table 1; refer to the *BNF* for a comprehensive list), tolerability (including the frequency of dosing) and the cost.

**Community-acquired pneumonia**

Community-acquired pneumonia (CAP) is an LRTI with lung parenchymal involvement. CAP affects 5–11 per 1000 of the population per year, with a greater proportion affected at the extremes of age.

Diagnosis of CAP in the community relies on clinical features. Patients may present with some of the following features: cough, fever, sputum production (may be purulent or blood stained), dyspnoea, pleuritic chest pain and localised chest signs. Older patients may present with nonrespiratory symptoms such as confusion, falls or worsening of a chronic illness, and may not have a fever. Very young patients may also present with nonspecific symptoms such as abdominal pain.

**Initial assessment**

A variety of severity assessment tools have been developed that are useful in predicting the prognosis of patients with LRTIs and guiding their management, including the need for hospitalisation. One of the simplest is the CURB-65 severity score summarised in the 2009 update of the BTS guidelines. This has been adapted to the CRB-65 score (see Figure 1) for use in the community where a blood urea is not generally available at the time of initial assessment. When making decisions around admission versus home therapy, clinical judgement should always be applied, taking into account factors such as social circumstances, the wishes of the patient and their relatives, and the patient’s co-morbidities.
Investigations
A diverse selection of pathogens are responsible for CAP. Defining the microbiological cause can be helpful in selecting the most appropriate antibiotic and may have public health and infection control implications. However, in practice, microbiology investigations are not routinely recommended in most CAP patients managed in the community, ie mild CAP, even when available, the delay in obtaining results and the limitations of the available tests in identifying the aetiological agent make empirical therapy necessary (see Table 2).

Microbiological testing may be indicated in patients treated in the community in the circumstances described below. Sputum examination should be considered in patients who have not responded to empirical therapy, and examination for Mycobacterium tuberculosis (TB) should be considered in those with a persistent cough, especially if they also have malaise, weight loss, night sweats or specific risk factors for TB. Legionella and pneumococcal urinary antigen testing, microbiological testing, eg of sputum or throat swabs, for respiratory pathogens and serological testing may be considered during outbreaks, eg Legionella, or epidemic years of Mycoplasma or where there is a specific epidemiological or clinical reason to do the test. However, their routine use in patients with mild pneumonia is not felt to be cost effective.

Clinical, epidemiological and radiographic information is often similarly unhelpful in predicting

| Drug                              | Important interactions                                                                 |
|-----------------------------------|----------------------------------------------------------------------------------------|
| **Beta-lactams, eg amoxicillin**  | • allopurinol – risk of rash with ampicillin and amoxicillin                           |
|                                   | • oral contraceptive pill – possible decreased efficacy of combined oral contraceptive (COC) |
|                                   | • warfarin – increased anticoagulant effect                                              |
| **Erythromycin and other macrolides** | • antiarrhythmics – increased risk of arrhythmias                                        |
|                                   | • antiepileptics – inhibition of metabolism of carbamazepine, phenytoin and possibly sodium valproate |
|                                   | • anxiolytics – inhibition of metabolism resulting in an increased sedative effect, eg midazolam |
|                                   | • cimetidine – increased toxicity of macrolide, eg deafness                            |
|                                   | • statins – increased risk of myopathy                                                 |
|                                   | • warfarin – increased anticoagulant effect                                              |
| **Tetracyclines**                 | • antiepileptics – increased metabolism of doxycycline with carbamazepine, phenytoin and some other antiepileptics |
|                                   | • calcium salts and dairy products – reduced absorption of tetracyclines (less marked with doxycycline and minocycline) |
|                                   | • iron and zinc – reduced absorption of both the metal and the tetracycline            |
|                                   | • COC – possible decreased efficacy of COC                                              |
|                                   | • warfarin – possible increased anticoagulant effect                                    |
| **Quinolones**                    | • antacids – decreased absorption of quinolones                                         |
|                                   | • metal salts, eg iron, zinc and calcium – reduced absorption of quinolones             |
|                                   | • NSAIDs – possible increased risk of convulsions                                       |
|                                   | • theophylline – possible increased risk of convulsions                                 |
|                                   | • warfarin – increased anticoagulant effect                                             |
|                                   | • some of the newer fluoroquinolones, eg moxifloxacin, have an increased risk of arrhythmias with a number of drugs (see BNF) |

Table 1. Some of the more commonly encountered drug interactions to be considered in patients taking antibiotics for the treatment of LRTIs
aetiology, and the differentiation of pneumonia caused by ‘typical’ and ‘atypical’ pathogens on clinical grounds alone has been shown to be unreliable. A chest X-ray is not considered necessary for most patients managed in the community, but should be considered if it would help in the differential diagnosis and management of the acute illness, if progress is not satisfactory at review, and/or if underlying pathology such as lung cancer is considered.\(^4\)

Point-of-care tests are available for influenza (A and B). Specificity is generally excellent but sensitivity may be as low as 50–74 per cent. These rapid tests allow a diagnosis of influenza to be made within 10–30 minutes, such that timely prescription of antivirals can be made and/or the clinician may feel more confident about not prescribing antibiotics.\(^5\)

**Causative agents**

*Streptococcus pneumoniae* is the major cause of CAP, accounting for over a third of cases in the community. *Mycoplasma pneumoniae* exhibits periodicity, with epidemics every four to five years, has a low morbidity and mainly affects younger individuals. Influenza virus, along with a number of other viruses, contributes a sizeable proportion of cases (currently around 13 per cent, but potentially much higher in an influenza pandemic). Other causes of CAP

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**Figure 1.** When to refer patients with CAP. Adapted from the BTS Guidelines for the Management of Community Acquired Pneumonia\(^4\)

| Core feature | Cut-off |
|--------------|---------|
| Confusion    | MMSE ≤8/10 or new disorientation in time, place or person |
| Respiratory rate | ≥30 per min |
| Blood pressure | systolic <90mmHg or diastolic ≤60mmHg |
| Age          | ≥65 years |

- **Assess CRB-65 criteria**
- **Core feature**
  - **1–2 core features**
    - consider additional adverse prognostic features, eg oxygen saturation <94%
    - consider hospital referral
  - **3–4 core features**
    - urgent hospital referral
    - give empirical antibiotics if life threatening
- **Assess pre-existing adverse prognostic features, eg co-existing disease**
  - **no core features**
  - **1–2 core features**
    - consider hospital referral
    - give empirical antibiotics if life threatening
  - **3–4 core features**
    - urgent hospital referral
    - give empirical antibiotics if life threatening
- **Management at home likely to be appropriate provided this is consistent with patient’s wishes and with social circumstances**

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\(^1\) Prescriber 5 March 2011

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include *Haemophilus influenzae* (5 per cent), * Legionella pneumophila*, *Coxiella burnetii*, *Chlamydia species* and *Staphylococcus aureus*, especially when influenza co-exists in the community.

More unusual forms of pneumonia to consider are *Pneumocystis jirovecii* (previously known as *Pneumocystis carinii*) pneumonia in patients with HIV and other forms of immunosuppression (seen much less frequently these days because of the use of prophylactic co-trimoxazole), TB in those with a more chronic pneumonia, and rare fungal and bacterial forms of pneumonia in those who have travelled.

We need to remain alert to emerging causes of pneumonia such as avian influenza (bird flu) and severe acute respiratory syndrome (SARS). These should be considered in all patients presenting with a fever, cough or shortness of breath who have a relevant travel or contact history. Infection control issues will need to be addressed in these patients and an expert should be consulted in cases fitting the diagnostic criteria.

*Pneumonia in children* has a slightly different epidemiological pattern. Neonates may develop pneumonia from organisms acquired from the mother’s genital tract such as Group B *Streptococcus*, Gram-negative organisms and *Chlamydia trachomatis*. These children will usually be admitted to hospital for treatment.

In one-month to four-year-old children most cases of CAP are viral in origin, eg respiratory syncytial virus (RSV), influenza, parainfluenza, rhinovirus, adenovirus and the newly recognised metapneumovirus. These are generally self-limiting and do not require antibiotics. Bacterial pneumonias in this age group are predominantly due to *Strep. pneumoniae*, whereas in the over-fours *Strep. pneumoniae* and *M. pneumoniae* are the most frequently isolated organisms.

*Resistance* Concerns exist over the growing number of resistant bacteria, in particular *Strep. pneumoniae*, *H. influenzae* and methicillin-resistant *Staph. aureus* (MRSA). Penicillin-resistant *Strep. pneumoniae* is of concern, especially as resistance is frequently linked to macrolide resistance. Penicillin resistance in *Strep. pneumoniae* varies widely between countries, communities and groups of patients within those communities. Currently approximately 6–8 per cent of clinical isolates of *Strep. pneumoniae* are resistant to penicillin, and 12–15 per cent resistant to macrolides. Resistance of *Strep. pneumoniae* to tetracyclines and fluoroquinolones is low. Resistance of *H. influenzae* to ampicillin – mainly due to beta-lactamase production – varies geographically, but is around 15 per cent in the UK.

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Treatment

Empirical treatment in the community is based on the fact that *Strep. pneumoniae* remains the leading cause of CAP. Prudent use of antibiotics is important in order to treat infections appropriately, to curb the growing problem of antimicrobial resistance, and to minimise side-effects and maximise compliance. Once a decision is made to treat, local resistance patterns must be taken into account.

BTS recommendations are based on current practice and experience and take into account the cost, tolerability, safety and side-effect profile of the drugs currently available. As yet, the incidence of highly penicillin-resistant strains of *Strep. pneumoniae* in most areas of the UK is sufficiently low to allow amoxicillin (in adequate doses) to remain the first-line therapy for adults and for children over five years of age – provided that the patient has not just returned from an area where the incidence is much greater. Note, however, that the latest BTS guidelines recommend adequate dosing with amoxicillin (500mg–1g three times daily) to cover intermediate-resistant strains. 4,10

Macrolides such as erythromycin are the second-line agents of choice if there are contraindications to amoxicillin or the patient fails to tolerate it. They are also the first-line agents in children over five years in whom *M. pneumoniae* is common. 11 Many people favour clarithromycin over erythromycin because of its better GI tolerance. Azithromycin is another alternative to erythromycin.

Tetracyclines are also alternative agents where there are contraindications to, or failure to tolerate, amoxicillin. Both macrolides and tetracyclines are active against ‘atypical’ pathogens. 4

Tetracyclines have the advantage that resistance rates in pneumococci remain relatively low in the UK, while there is rising *in-vitro* resistance to the macrolides. Care needs to be taken to avoid prescribing tetracyclines in those in whom it is contraindicated, eg pregnant women and children under 12.

Treatment may be rationalised if a specific pathogen is identified or if sensitivities are at variance with the empirical regimen. This should be guided by local microbiological advice.

Patients should improve on appropriate therapy within 48 hours. It is therefore important to review them at this stage or earlier. If they have failed to improve they should be considered for addition of an agent to cover atypical organisms if not already on one, and for radiography and/or hospital admission. 10

Where a patient has failed to respond to initial empirical therapy, clinical, radiological and microbiological review are recommended to confirm that the correct diagnosis has been made and/or whether

| Condition                      | Causative organism                                      | Empiric therapy                                              | Other considerations                                      |
|--------------------------------|----------------------------------------------------------|--------------------------------------------------------------|-----------------------------------------------------------|
| Pneumonia                      | *Strep. pneumoniae*, influenza virus, *M. pneumoniae*, *H. influenzae*, *L. pneumophila*, *C. burnetii*, *C. pneumoniae*, enterobacteriaceae, *Staph. aureus* | *must be active against* *Strep. pneumoniae*, *eg amoxicillin*, erythromycin | *immunisation against influenza and pneumococcus*<br> *beware of increasing penicillin-resistant *Strep. pneumoniae* |
| Acute exacerbation of COPD     | *most are viral*<br> *some due to* *H. influenzae*, *Strep. pneumoniae* or *M. catarrhalis* | commonly no need for antibiotics<br> see Table 4 for criteria for antibiotics | *immunisation against influenza and pneumococcus*<br> *stop smoking* |
| Acute bronchitis               | *usually viral*<br> *occasionally* *B. pertussis*, *M. pneumoniae* or *C. pneumoniae* | rarely indicated<br> if evidence of pertussis, *Mycoplasma* or *Chlamydia pneumoniae* infection, treat with a macrolide | *consider pertussis as a cause*<br> *immunise as per Green Book against pertussis and influenza* |
| Bronchiolitis                  | *RSV, other viruses*<br> *occasionally Mycoplasma*        | none usually necessary<br> antivirals may be used by hospital doctors | *if in a high-risk group consider prophylaxis on the advice of a paediatrician* |

Table 2. Summary of conditions, causative agents, empirical therapy and other considerations in LRTIs treated in the community.
new complications have occurred. Consideration should be given to whether the patient complied with the original regimen, and/or that absorption took place. If indicated, further specimens should be taken to exclude unusual pathogens, *eg* Legionella, Mycobacteria, and hospitalisation may need to be considered.

In patients with low-severity pneumonia where a change of empirical antibiotics is considered to be required, but continuing care in the community is felt to be appropriate, and where no causative pathogen has been identified, a macrolide is an appropriate agent to add in or use to replace the original empirical therapy.

Over the last few years several new drugs with greatly improved bioavailability and tolerability have become available for use in the treatment of CAP. The fluoroquinolones, *eg* moxifloxacin (Avelox) and levofloxacin (Tavanic), which have antistreptococcal activity, have both an excellent antimicrobial spectrum – they are active against atypical pathogens and *Legionella* species as well as the common ‘typical’ organisms – and advantageous pharmacodynamic characteristics. Moxifloxacin has been licensed for use in nonsevere pneumonia. The BTS does not recommend the use of fluoroquinolones for CAP in the community due to the evidence for rapid onset of fluoroquinolone resistance in pneumococci and other pathogens when they are used.
There are additional concerns in that fluoroquinolones appear to be a significant risk factor in precipitating *C. difficile* infections caused by the hypervirulent 027 strain. Although these data were largely based on ciprofloxacin use, it is likely that the newer fluoroquinolones will have a similar effect. Quinolones are not recommended for use in the under-18s except on the advice of a paediatrician or microbiologist.

Widespread use of the newer macrolides, *eg* azithromycin, is not being encouraged as yet.

There is direct and indirect evidence that delays in antibiotic administration in patients with pneumonia adversely affect mortality. For patients who need to go to hospital, particularly those who are severely ill or in whom delays of more than six hours in the patient being admitted and treated in hospital are likely, antibiotics should be commenced by the GP as soon as possible. If parenteral penicillin G is available, it should be given (1.2 g benzylpenicillin i.m. or i.v.). If not, oral amoxicillin 1 g (or oral clarithromycin 500 mg if penicillin sensitive) should be commenced. Ambulance services should allocate patients with pneumonia a high priority for transfer to hospital.

It is important that antibiotics are administered in a high enough dose and for a sufficient duration that the patient does not relapse after stopping the therapy.
and that antibiotic resistance does not develop. This needs to be balanced with the risk of side-effects, particularly the risks of *C. difficile* infection. There is no robust evidence to support the optimal duration of therapy, and it will vary between patients according to a number of factors. For low to moderately severe uncomplicated pneumonia the current recommendation is to treat for seven days, whereas 7–10 days is proposed for more severe microbiologically undefined forms of pneumonia, though 14-21 days may be required in some patients based on the organism concerned and the clinical response. Two weeks’ treatment is recommended for the treatment of pneumonia due to ‘atypical’ pathogens.

Table 3 lists the benefits and drawbacks of some drugs available to treat LRTIs.

Viruses contribute to about 13 per cent of cases of CAP, of which influenza A and B account for about 8 per cent. In the over-65s and those with concomitant chronic disease or immunosuppression, influenza contributes to a particularly high mortality. Patients

| Drug                  | Pros                                                                 | Cons                                                                 |
|-----------------------|-----------------------------------------------------------------------|-----------------------------------------------------------------------|
| Beta-lactams, eg amoxicillin | cheap, safe, proven efficacy with much experience among prescribers | ineffective against atypical organisms and penicillin-resistant pneumococci |
|                       | effective against intermediate-resistant strains of pneumococci provided given at adequate dose (500mg–1g 3 times daily) | GI side-effects, hypersensitivity, rashes |
| Macrolides, eg erythromycin, clarithromycin | active against atypical pathogens and pneumococci – useful in penicillin-allergic patients | poor efficacy against *H. influenzae* |
|                       | erythromycin is cheap                                                   | erythromycin has marked GI side-effects resulting in poor compliance rates; other side-effects include cholestatic jaundice |
|                       | GI side-effects less frequently seen with newer macrolides, eg clarithromycin | erythromycin requires 4-times-daily dosing |
|                       |                                                                      | interact with a number of drugs                                      |
| Tetracyclines         | effective against atypical pathogens                                   | increasing resistance of pneumococci                                  |
|                       | twice-daily dosing                                                     | contraindicated in children and pregnant women due to discoloration of developing teeth |
|                       | cheap                                                                 | side-effects: nausea, vomiting, diarrhoea, photosensitivity, oesophageal irritation, interactions with a number of foods and medications |
| Fluoroquinolones      | good cover against Gram-negative organisms, eg *H. influenzae*, *M. catarrhalis* | ciprofloxacin and ofloxacin have inadequate Gram-positive cover to treat pneumococci or staphylococci |
|                       | newer agents have improved efficacy against *Strep. pneumoniae*, including penicillin-resistant pneumococci | issues exist concerning cost, side-effects and interactions |
|                       | active against typical and atypical pathogens and *Legionella* species | thought to be drivers of new aggressive strains of *C. difficile*     |
|                       | once- or twice-daily dosing                                            | side-effects include dizziness, photosensitivity, hepatotoxicity and cardiotoxicity (QT prolongation), lowering of seizure threshold, tendon inflammation |
|                       |                                                                      | avoid in G6PD deficiency, myasthenia gravis, pregnancy, breast-feeding and children and adolescents |

Table 3. Advantages and disadvantages of some drugs available to treat LRTIs in the community
at risk of severe influenza who present within 48 hours (36 hours in children) of the onset of a flu-like illness at a time when influenza A and B strains are known to be circulating, may be candidates for oseltamivir (Tamiflu) or zanamivir (Relenza); see www.hpa.org.uk/infections/topics_az/influenza for the latest guidelines.

In addition to specific antibiotic or antiviral therapies, patients may need to be advised about taking adequate rest, maintaining hydration by drinking plenty of fluids and taking simple analgesics. Smoking cessation advice should be offered to all current smokers with CAP.

Prevention

Emphasis needs to be placed on primary prevention of LRTIs. Influenza vaccination has been shown to reduce hospital admissions, death rates from pneumonia and flu, prevent pneumonia and decrease outpatient visits for all respiratory conditions in over-65s and patients with chronic disease. Vaccination should be offered on an annual basis to: all those aged 65 or over; all those six months of age or over and in a clinical risk group; individuals in long-stay residential or care facilities where rapid dissemination with a high morbidity and mortality is likely if influenza were introduced; and carers of individuals whose welfare would be at risk if the carer were to fall ill. Please refer to the section on influenza in the Green Book for more details (www.dh.gov.uk/dr_consum_dh/groups/dh_digitalassets/@dh/@en/documents/digitalasset/dh_118770.pdf).

Please note that the seasonal vaccine is now also recommended for pregnant women not falling into a high-risk group who have not received the monovalent H1N1v vaccine (2009 ‘swine flu’ vaccine), and to those working in close contact with poultry. Most influenza vaccines are made using hens’ eggs and vaccination is contraindicated in those with a confirmed anaphylactic reaction to egg products. Celvapan, which confers protection against influenza A (H1N1)v, does not contain egg and is therefore not contraindicated in this group.

In at-risk persons of 13 years or older who have not been vaccinated, and in institutionalised individuals, when influenza A or B is known to be circulating in the community, oseltamivir may be used for postexposure prophylaxis within 48 hours of exposure.

Pneumococcal vaccine should also be offered to selected individuals. The pneumococcal polysaccharide vaccine (PPV) is recommended for all those of 65 years and over, and those between 2 and 65 years with risk factors of invasive pneumococcal disease. This includes individuals with asplenia or functional asplenia, chronic renal, heart, lung and liver disease, diabetics treated with insulin or hypoglycaemic agents, immunosuppression, cochlear implants and CSF leaks. Any adults admitted with CAP who are unimmunised

| Lung function and other considerations | Aetiology | Antibiotics | Persistent symptoms |
|----------------------------------------|-----------|-------------|---------------------|
| normal lung function and ≤60 years old | usually viral | none | try a macrolide in case C. pneumoniae or Mycoplasma |
| FEV₁ ≥50% predicted and <4 exacerbations per year and ≤60 years old | H. influenzae or Strep. pneumoniae | beta-lactam (but add beta-lactamase inhibitors in regions with high rates of beta-lactamase-producing H. influenzae) | beta-lactam + beta-lactamase inhibitor, second- or third-generation cephalosporin |
| FEV₁ ≤50% predicted or 50–65% but with significant concomitant medical disease or ≥4 exacerbations per year* or >60 years old | H. influenzae, Strep. pneumoniae or M. catarrhalis | beta-lactam + beta-lactamase inhibitor, quinolone, second- or third-generation cephalosporin, second-generation macrolide | |

*people fitting into this category who have continuous sputum production all year round may also be colonised with coliform bacilli or pseudomonads, and this will need to be taken into account when choosing an antibiotic

Table 4. Stratification of patients with acute exacerbation of COPD (adapted from Wilson19 and Grossman20)

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despite fitting the criteria for immunisation should receive a dose during convalescence.

Since September 2006 immunisation with the pneumococcal conjugate vaccine (PCV) has been recommended in the under twos, the schedule being a dose at 2, 4 and 13 months, with a catch-up regimen for anyone who has missed earlier doses. Immunisation should not be given to those who have had a confirmed anaphylactic reaction to a previous dose or to any of the components of the vaccine.14

Chronic pneumonia
In cases of chronic pneumonia where a pulmonary parenchymal process has been present for weeks to months, other causes need to be considered including TB and a host of both infectious and noninfectious causes.15 Exacerbations of infection in patients with cystic fibrosis should be treated in conjunction with the specialist involved in their care.

Empyemas and lung abscesses
The majority of empyemas are secondary to pneumonia, but can result from other causes such as trauma, oesophageal perforation or subdiaphragmatic infections, and the bacterial agent(s) isolated will depend upon the aetiology of the disease. This is a complex condition with a poor prognosis if missed or mismanaged. Patients with these conditions should be managed in hospital in the first instance.

Acute exacerbation of COPD
Acute exacerbations of chronic obstructive pulmonary disease (AECOPD) are characterised by increased cough, sputum production, purulence of sputum and dyspnoea in someone with a background of excessive cough productive of sputum on most days of more than three months of at least two consecutive years. Infections account for most exacerbations, but allergens, pollutants and irritants can also contribute.

Aetiology
The majority of exacerbations are self-limiting with a viral aetiology and do not require antibiotic therapy, despite the presence of neutrophils and bacteria in the sputum. Three bacterial pathogens are predominant in AECOPD and account for over 70 per cent of the bacteria isolated: *H. influenzae*, *Strep. pneumoniae* and *Moraxella catarrhalis*. Less commonly, *Staph. aureus*, Gram-negative bacilli, other streptococci, *Mycoplasma* and *Chlamydia pneumoniae* play a role.
Antibiotic therapy

NICE has produced guidance on the management of COPD and recommends that antibiotics should be used to treat exacerbations in those in whom the sputum is more purulent, and/or when there is either clinical or radiological evidence of pneumonia. They recommend the use of aminopenicillins, tetracyclines or macrolides, taking into account local microbiology guidance that should reflect local sensitivity patterns. Patients who experience frequent exacerbations are more likely to have resistant organisms and may require broad-spectrum antibiotics.

Recommendations regarding other aspects of patient management, eg indications for steroids or bronchodilators, can be found in the NICE guidance.

Acute bronchitis

Acute bronchitis is an inflammatory condition of the tracheobronchial tree characterised by a severe cough, frequently lasting several weeks. Patients may also have a fever, hoarseness, sputum production, dyspnoea or a wheeze, with a background of a preceding upper respiratory tract infection (URTI).

Aetiology

Acute bronchitis is usually due to respiratory viruses, eg rhinovirus, coronavirus, influenza, parainfluenza, respiratory syncytial virus (RSV), adenovirus and, though rarely seen nowadays, measles. Nonviral causes include Bordetella pertussis, M. pneumoniae and C. pneumoniae. The role of Streptococcus pneumoniae and H. influenzae in acute bronchitis remains unclear – these organisms are commonly isolated from specimens, but this is likely to reflect the fact that they are normal commensals of the upper respiratory tract. Symptoms are worse in those exposed to cigarette smoke and other pollutants.

Noninfectious conditions that may mimic acute bronchitis and should be considered include foreign body aspiration and malignancy. In those at risk, TB should also be excluded.

Management

The majority of patients with acute bronchitis do not require anything other than symptomatic therapy, and antibiotics are not indicated for the majority of cases, even in the presence of purulent sputum.

Studies have suggested that up to one-fifth of adults with acute severe cough have pertussis. Adults whose immunity to pertussis is waning are a major reservoir for B. pertussis. It is therefore important to consider this as a diagnosis in those with a persistent cough and to take a nasopharyngeal swab/aspirate for culture if indicated. Treatment for pertussis is 14 days of erythromycin and is primarily aimed at eliminating carriage. It is also effective in decreasing the duration and severity of disease in the catarrhal phase, but may not alter the course once patients are in the paroxysmal stage.

Patients with acute bronchitis due to M. or C. pneumoniae should also receive antibiotics. Macrolides are the first-line therapy for these conditions. Tetracyclines can be used in the groups in which they are not contraindicated (children under 12 years old...
and pregnant women). In patients with significant co-morbidity, first-line antibiotics are amoxicillin, erythromycin or tetracyclines. If patients do not respond to these, consider co-amoxiclav, tetracyclines, clarithromycin or azithromycin. Anti-influenza agents may be considered in those in whom a swift diagnosis is made.

**Prevention**
Immunisation against influenza and pertussis as guided by current DoH recommendations will reduce some of the burden of this disease, and discouraging smoking is another important preventive strategy.

**Acute bronchiolitis**
Bronchiolitis is an acute LRTI characterised by acute onset of wheeze, cough, rhinorrhea, tachypnoea and respiratory distress, although it may manifest as lethargy, irritability, poor feeding and apnoeic episodes. RSV is the most important cause of bronchiolitis in infants and young children. Other aetiological agents include parainfluenza, adenovirus, rhinovirus and occasionally *Mycoplasma*.

**Management**
Many cases can be managed in the community, but children may need admission for greater supportive therapy, such as oxygen and intravenous hydration. Risk factors
for more severe disease include cyanotic or complicated congenital heart disease, underlying pulmonary disease, prematurity and immunodeficiency due to underlying disease or therapy, and children falling into these categories should be admitted in most cases. Some very unwell children may be treated with antivirals, eg ribavirin (Virazole). The monoclonal antibody palivizumab (Synagis) has been used as a prophylactic agent. No vaccines are currently available to prevent RSV.

Preventive measures should be taken to reduce the risk of exposure of these children to infected individuals. Particular attention should be paid to hand-washing to reduce transmission if someone in the household is suffering from a URTI.

Out-patient parenteral antibiotic therapy (OPAT)
OPAT, which is well established in countries such as the USA and Italy, is becoming increasingly widespread within the UK and Ireland and is already widely used by many respiratory departments to manage patients with cystic fibrosis and bronchiectasis. OPAT services are frequently overseen by infectious disease physicians and microbiologists and, in most cases, the care of the patient remains with the hospital rather than the GP.

Appropriately selected patients who require, usually long, courses of intravenous therapy can be discharged to their normal place of residence. Antibiotics are administered by a trained district nurse or family
member (sometimes the patient him/herself) via a line, and are usually given in the patient’s home, but sometimes at a local community hospital or surgery. This gives patients significantly more freedom and reduces their risks of hospital-associated problems such as infections, deep vein thromboses and institutionalisation.

Although GPs are generally not primarily responsible for this aspect of patient care, they may occasionally become involved. They need to be alert to potential complications with the lines, eg infection or blockage, and side-effects from the antibiotics, which can include antibiotic fevers, blood disorders, eg neutropenia, and deranged renal or liver function, as well as the possibility that the underlying infection has relapsed.

In general referral should be directed back to the OPAT team or to the doctors with overall responsibility for the patient. With the increasing emphasis on out-of-hospital care, GPs should expect to see more patients on intravenous therapy in the community in the future.26

**Conclusion**

LRTIs encapsulate a wide range of pathologies caused by a broad spectrum of organisms and need differentiating in order to decide on the most appropriate empirical therapy. CAP is a common infection with significant mortality and, because of the proportion of cases that are due to *Strep. pneumoniae*, therapy should always include adequate cover against this organism.

Most cases of acute bronchitis and exacerbations of COPD are viral in origin and do not require antibiotic therapy. However, certain groups of patients are more vulnerable and antibiotics may be warranted. Lung function, age and premorbid condition should be taken into account when assessing such patients.

Preventive measures, such as immunisation against influenza and *Strep. pneumoniae*, should be considered in at-risk individuals, and smoking discouraged.

With the increasing prevalence of hypervirulent strains of *C. difficile* and increasing rates of antimicrobial resistance, it has never been more important that antibiotics are used appropriately. Local policies should be used to ensure that empirical regimens take into account local resistance patterns. A risk/benefit analysis should be performed whenever antibiotics are prescribed and treatment regimens should be revised on the basis of culture results. Antibiotics should not be continued for longer than necessary.

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Resources

Groups and organisations
British Lung Foundation (BLF), 73–75 Goswell Road, London EC1V 7ER funds research into all lung diseases, provides patient support and information and promotes lung health. Information leaflets for patients are available on COPD and pneumonia. www.lunguk.org.

British Thoracic Society (BTS), 17 Doughty Street, London WC1N 2PL. Official body of respiratory specialists; funds research and promotes good practice. Website provides patient information on chronic bronchitis, emphysema and COPD and also has useful links to other relevant web pages. www.brit-thoracic.org.uk.

Further reading
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Recommendations for the management of cough in adults. Morice AH, et al. Thorax 2006; 61:i1–i24; doi:10.1136/thx.2006.065144.

Prescribing of antibiotics for self-limiting respiratory tract infections in adults and children in primary care. CG69. National Institute for Health and Clinical Excellence. July 2008.

Useful website
Health Protection Agency (HPA). Antibiotic prescribing guidance for primary care. www.hpa.org.uk/infections/topics_az/antimicrobial_resistance/guidance.htm.