Diagnosis and management of lower respiratory tract infections

Chamira Rodrigo BSc, BM, MRCP and Wei Shen Lim DM, FRCP

Lower respiratory tract infections in the community lead to considerable morbidity and days off work. Our Drug review considers the assessment of disease severity, when to prescribe antibiotics and recommended management of LRTIs, followed by sources of further information.

Respiratory complaints are the leading cause of presentations to GPs, and around a quarter of the UK population visit their GP each year because of an acute respiratory tract infection (RTI). Incidence rates are highest at the extremes of age, in the presence of co-morbid illnesses and with greater levels of social deprivation.

Although an overall decline in the incidence of lower respiratory tract infections (LRTIs) has been reported in the UK, more recent studies reveal an increase in the incidence among adults aged >65 years, most likely due to an ageing population.

The associated mortality of RTIs in the community is low (<1 per cent); however, it leads to considerable morbidity and days of work lost (1.5–5.9 days per episode of influenza; 27.5 million days from colds, coughs and flu in 2011).

Of all antibiotic prescriptions in general practice, 60 per cent are attributed to RTIs, and the annual prescription cost for acute cough alone amounts to £15 million.

The spectrum of disease

The main LRTIs affecting adults that are of significance to GPs are acute bronchitis, pneumonia and infective exacerbations of chronic lung disease.

Only 5–12 per cent of patients presenting to GPs with LRTI will have pneumonia, and the absence of clinical features to reliably distinguish between the different types of LRTI makes the accurate diagnosis of pneumonia challenging. That said, labelling an illness as ‘pneumonia’ is often less important than deciding when to prescribe antibiotics. This decision is based on a combination of illness severity and the likely diagnosis (see Table 1).

The further management of infective exacerbations of specific lung diseases, such as COPD or bronchiectasis, is outside the scope of this article.

Assessing disease severity in LRTI

An accurate appreciation of the severity of illness is critical to decisions regarding antibiotic prescription and the need for
hospital admission. Generally, the greater the severity of illness, the higher the likelihood of pneumonia. For patients with suspected pneumonia, the CRB65 (new-onset confusion, respiratory rate ≥30 breaths per minute, BP <90mmHg systolic, ≤60mmHg diastolic, age ≥65 years) score is helpful in guiding the need for hospital admission (see Figure 1).

The range of pathogens identified in LRTIs is similar to that in community-acquired pneumonia (CAP). *Streptococcus pneumoniae* is the commonest pathogen followed by viral pathogens as a group (see Table 2). Although *Chlamydia pneumoniae* is commonly identified in research studies, its clinical significance is uncertain: it may be an innocent ‘bystander’, a co-pathogen or a primary pathogen in different circumstances.

Viruses associated with LRTI include rhinovirus, coronavirus, adenovirus, influenza A and B viruses, respiratory syncytial virus (RSV) and parainfluenza virus. Seasonal variation is recognised: RSV activity starts to increase in the autumn, coinciding with peaks in acute bronchitis, and activity continues throughout the winter months resulting in 5000–7500 estimated deaths from adult LRTI each winter in the UK.

Influenza typically strikes later during the winter months and is associated with higher rates of hospitalisations and excess mortality among adults >65 years and individuals with co-morbid illnesses (estimated 7000–25 000 deaths in all age groups each winter).

Although the presence of certain clinical features is commoner with some pathogens, it is not possible to reliably predict the microbial aetiology of LRTI by clinical features alone. In practice, the main bacterial pathogen to cover is *S. pneumoniae*, and the only viral infection to which there is readily accessible therapy is influenza.

An ‘influenza-like illness’ (ILI) refers to the sudden onset of fever (>38°C) with cough or sore throat, in the absence of other diagnoses. The microbial aetiology of ILI is broad: of adults with an ILI presenting to hospital, a virus other than influenza is identified in a third and a bacterial pathogen in a further third.

### Antibiotic prescription in LRTI

Good antibiotic stewardship was a key topic in the UK Chief Medical Officer’s annual report published in March 2013. Rates of antibiotic prescription in LRTI are affected by clinical need, patient factors (expectation of antibiotics) and clinician factors (perceived levels of patient expectations, time constraints).

Antibiotic prescriptions for LRTIs have been declining in the UK (by 45 per cent between 1994 and 2000) due to a combination of an overall reduction in LRTI consultations and reduced prescribing by GPs. The demedicalisation of self-limiting respiratory illness in the community has helped: some data show that only 34 per cent of adults consulting for RTIs actually want antibiotics. The use of patient information leaflets and delayed prescriptions is also associated with reductions in antibiotic prescription for LRTIs.

More recently, a randomised controlled trial (RCT) of adults aged >18 years with acute LRTI achieved a 31 per cent reduction in antibiotic prescription rates using an internet-based training tool for GPs focusing on ‘gathering of information on patients’ concerns and expectations, exchange of information on symptoms, normal disease course and treatments, agreement of a management plan, summing up, and providing guidance about when to reconsult’. NICE recommends a three-pronged approach of no, delayed or immediate antibiotic prescription for RTIs. An RCT of individuals aged over two years presenting with acute cough in whom pneumonia was not suspected (on the basis of absent focal chest signs and systemic symptoms) found little difference in symptom duration and severity between groups given immediate, delayed or no antibiotics.

A large observational study of adults aged >18 years presenting to primary care with acute cough or symptoms suggestive of an LRTI found no benefit in antibiotic prescription with regard to symptom resolution and time to recovery. Adults who produced discoloured sputum were more likely to be prescribed antibiotics, but treatment on this basis was not associated with better recovery.

More recently, an RCT of adults aged >18 years with acute LRTI in whom pneumonia was not suspected found no benefit from amoxicillin compared to placebo in relation to mean symptom scores or duration of symptoms. A higher rate of drug-related adverse events was reported in the group prescribed amoxicillin. These findings also extended to adults aged >60 years.

It is important to carry out ‘safety netting’ in adults who are not prescribed antibiotics immediately; this should involve advice on the natural history of the condition, clinical features that suggest complications and when to seek further help.

### Antiviral therapy for influenza

A systematic review of RCTs investigating healthy adults exposed to seasonal influenza found that treatment with the neuraminidase inhibitors (NAIs) oseltamivir (Tamiflu) and zanamivir (Relenza) was associated with a shortened duration of influenza-like illness (about one day) compared to placebo.

Microbiological confirmation is not a prerequisite for NAI treatment (see Table 3). Postexposure prophylaxis with NAIs can be offered to at-risk individuals if they are inadequately protected with influenza vaccination and present within 36 hours (zanamivir) or 48 hours (oseltamivir) of close contact with an influenza-affected individual.

---

### Table 1. Recommended use of antibiotics in LRTIs

<table>
<thead>
<tr>
<th>Condition</th>
<th>Antibiotics usually indicated or delayed prescription</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unwell and/or suspected pneumonia</td>
<td>antibiotics usually indicated main pathogen <em>S. pneumoniae</em></td>
</tr>
<tr>
<td>Exacerbation of COPD</td>
<td>antibiotics usually indicated if increased sputum purulence main pathogen <em>Haemophilus influenzae</em></td>
</tr>
<tr>
<td>Exacerbation of asthma</td>
<td>antibiotics not usually indicated</td>
</tr>
</tbody>
</table>

---

**Not severely ill and/or acute bronchitis**

Antibiotics not usually indicated consider delayed prescription

---

**Unwell and/or suspected pneumonia**

Antibiotics usually indicated main pathogen *S. pneumoniae*

---

**Exacerbation of COPD**

Antibiotics usually indicated if increased sputum purulence main pathogen *Haemophilus influenzae*

---

**Exacerbation of asthma**

Antibiotics not usually indicated
A Cochrane systematic review of RCTs investigating NAIs for postexposure prophylaxis found drug effectiveness to be 60–80 per cent.7

NAIs are generally well tolerated with commonly reported side-effects being nausea and rashes.

**Pneumococcal and influenza vaccination**

Childhood pneumococcal conjugate vaccination in most countries has led to reductions in overall rates of pneumococcal disease in children and, through ‘herd protection’, in adults.

A Cochrane systematic review found vaccination of adults with the 23-valent pneumococcal polysaccharide vaccine (Pneumovax II) to be beneficial, especially with regard to lowering the risk of invasive pneumococcal disease.9 The uptake rate of pneumococcal polysaccharide vaccination among adults >65 years in the UK was about 70 per cent over the last three years.

Seasonal influenza vaccination is known to have a good safety record, and numerous studies have demonstrated reductions in mortality and hospitalisations in at-risk individuals.

---

**Clinical diagnosis and severity assessment**

**Clinically well or suspected acute bronchitis**

- Antibiotics not usually indicated
- Consider delayed prescription

**Clinically unwell or suspected pneumonia**

- Antibiotics usually indicated
- *If suspected pneumonia*

- Risk stratify using a combination of clinical judgement and CRB65 score

---

**Low severity (eg CRB65 score 0)**

- Likely suitable for home management
- Consider social circumstances and home support

- Empirical treatment
  - First line: amoxicillin
  - Second line: doxycycline or clarithromycin

**Moderate severity (eg CRB65 score 1–2)**

- Consider hospital admission, especially if CRB65 score is 2

**High severity (eg CRB65 score 3–4)**

- Urgent hospital admission

- If life-threatening illness and not allergic to penicillin, administer penicillin G 1.2g iv or amoxicillin 1g po prior to hospital admission

---

*see section on ‘Management of suspected pneumonia’

**CRB65**: new-onset confusion, respiratory rate ≥30/minute, systolic blood pressure <90mmHg or diastolic blood pressure ≤60mmHg, age ≥65 years

---

*Figure 1. Recommended management of LRTI in the community*
Vaccine uptake rates in adults aged >65 years during the last three years in the UK were about 73 per cent; however, uptake rates were considerably lower in younger ‘at-risk’ groups during this period (about 50 per cent).

Recommendations have been made by the Joint Committee on Vaccination and Immunisation (JCVI) to extend the current influenza vaccination programme to all children. A phased introduction of the childhood influenza vaccination programme commenced in September 2013 when a live attenuated intranasal influenza vaccine (Fluenz) was offered to all children aged two and three years and children aged 2–18 years in clinical risk groups.

Management of suspected pneumonia
Patients with CAP have consistently poorer outcomes in comparison to nonpneumonic LRTI, making identification of this subgroup clinically important. Around 22–42 per cent of all adults with CAP will require admission to hospital. The mortality for CAP managed in the community is about 1 per cent, rising to 10–24 per cent in adults requiring hospital admission.

While there is no group of signs or symptoms that reliably distinguishes CAP from nonpneumonic LRTI, the following clinical features together make the diagnosis of CAP less likely: 1) the absence of abnormal vital signs (fever, tachypnoea, tachycardia); 2) absence of focal signs on examination of the chest; and 3) a short duration of illness (<24 hours).

The gold standard for the diagnosis of CAP remains the chest X-ray, but this is not routinely required. Chest radiography should be reserved for:

- individuals in whom the diagnosis is in doubt
- individuals who fail to respond to treatment
- adults at risk of serious underlying lung pathology such as lung cancer.

A validated tool for assessing CAP severity is the CRB65 score (see Figure 1). Pulse oximetry can also be useful. Low oxygen saturations (<90 per cent) denote worse clinical outcomes; however, the presence of normal oxygen saturations does not rule out severe CAP.

Microbiological tests are generally not required for adults with suspected CAP. S. pneumoniae is the dominant pathogen and antibiotic recommendations reflect this (see Table 4).

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Streptococcus pneumoniae</td>
<td>47.3</td>
</tr>
<tr>
<td>Viral</td>
<td>35.3</td>
</tr>
<tr>
<td>Chlamydia pneumoniae</td>
<td>31.8</td>
</tr>
<tr>
<td>Mixed infections</td>
<td>24.3</td>
</tr>
<tr>
<td>Haemophilus influenzae</td>
<td>17.3</td>
</tr>
<tr>
<td>Mycoplasma pneumoniae</td>
<td>13.3</td>
</tr>
<tr>
<td>Moraxella catarrhalis</td>
<td>4.0</td>
</tr>
</tbody>
</table>

Table 2. Pathogens detected in LRTIs in the community (after reference 3)

Evidence of influenza circulation (see Public Health England surveillance data at phe.gov.uk)

**Individual at risk** (any of the following):
- ≥65 years
- chronic respiratory disease
- chronic heart disease
- chronic kidney disease
- chronic liver disease
- chronic neurological condition
- diabetes
- immunosuppression

**Presentation with influenza-like illness within 48 hours of symptom onset**

Patients should be advised regarding smoking cessation (if relevant), rest and adequate oral hydration. Analgesics may be required to alleviate pleuritic chest pain. A review 48–72 hours following commencement of treatment (see Table 4) may help identify patients in whom clinical response is inadequate and who may require a longer course of antibiotics, further investigations to identify complications (e.g. chest X-ray) or hospital referral.

**Conclusion**

The morbidity and healthcare burden associated with LRTIs in the community is considerable. Preventive strategies such as influenza and pneumococcal vaccination should be utilised and encouraged in at-risk individuals.

The key step in the management of adults presenting with LRTIs is assessment of disease severity, which in turn informs decisions regarding antibiotic prescription and the need for hospital admission. Empirical antibiotic therapy should be targeted towards S. pneumoniae and, if antibiotics are not prescribed immediately, ‘safety netting’ should be incorporated. LRTIs due to a viral aetiology lead to a significant number of excess deaths during the autumn and winter months. Antiviral therapy should be considered during the influenza season in accordance with NICE guidance on the use of antivirals.

**References**

5. Little P, et al. Lancet 2013. Published online 2013/08/07. doi:
Table 4. Antibiotic recommendations for suspected community-acquired pneumonia

<table>
<thead>
<tr>
<th>Life-threatening illness or high-severity CAP and possible delays of &gt;6 hours to first antibiotic dose in hospital, in adults who are not allergic to penicillin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug</td>
</tr>
<tr>
<td>penicillin G</td>
</tr>
<tr>
<td>amoxicillin</td>
</tr>
</tbody>
</table>

**Declaration of interests**

Dr Rodrigo has received salaries part funded by an unrestricted grant from Pfizer and a National Institute for Health Research grant; Dr Lim’s department has received research funding from the National Institute for Health Research and unrestricted investigator-initiated research funding from Pfizer.

*Dr Rodrigo is clinical research fellow and specialist registrar in respiratory medicine, and Dr Lim is consultant respiratory physician, Nottingham University Hospitals Trust*
For each section, one of the statements is false – which is it?

1. The incidence of RTIs is highest at the extremes of age, in the presence of co-morbid illnesses and with greater levels of social deprivation.
   a. True
   b. False

2. Twenty per cent of antibiotic prescribing in general practice is attributed to the treatment of RTI.
   a. True
   b. False

3. The proportion of patients presenting to GPs with an LRTI who have pneumonia is 5–12 per cent.
   a. True
   b. False

4. The CRB65 score is helpful in assessing the need for hospital admission.
   a. True
   b. False

5. In the prevention and treatment of influenza:
   a. A neuraminidase inhibitor does not shorten the duration of flu-like illness compared with placebo.
   b. To be eligible for postexposure prophylaxis with oseltamivir, the patient should present within 48 hours of contact with an individual who has flu.
   c. NICE criteria for treatment with oseltamivir include evidence of circulating influenza.
   d. True

6. In the management of suspected pneumonia:
   a. The mortality of CAP in individuals admitted to hospital is 10–24 per cent.
   b. Clinical features that make a diagnosis of CAP less likely include duration of illness <24 hours.
   c. The presence of normal oxygen saturation rules out a diagnosis of severe CAP.
   d. True

7. When prescribing an antibiotic to treat a patient with LRTI in primary care:
   a. The GP’s decision to prescribe is influenced by his/her perception of the patient’s expectation of treatment.
   b. Prescribing an antibiotic on the basis of presentation with discoloured sputum has been shown to improve recovery in patients with LRTI in primary care.
   c. Some data show that 34 per cent of adults presenting with an LRTI expect a prescription.
   d. One trial found that, compared with placebo, amoxicillin did not reduce the severity or duration of symptoms in adults with acute LRTI in whom pneumonia was not suspected.
   a. True
   b. False

For each section, one of the statements is false – which is it?

2. Considering the pathogens that may cause LRTI:
   a. Streptococcus pneumoniae is the commonest identified pathogen.
   b. The clinical significance of isolating Chlamydia pneumoniae in a patient with LRTI is uncertain.
   c. Clinical features are a good guide to the identity of the likely pathogen.
   d. The incidence of respiratory infections due to respiratory syncytial virus starts to increase in the autumn.
   a. True
   b. False

3. In the prevention and treatment of influenza:
   a. A neuraminidase inhibitor does not shorten the duration of flu-like illness compared with placebo.
   b. To be eligible for postexposure prophylaxis with oseltamivir, the patient should present within 48 hours of contact with an individual who has flu.
   c. NICE criteria for treatment with oseltamivir include evidence of circulating influenza.
   d. True

4. In the management of suspected pneumonia:
   a. The mortality of CAP in individuals admitted to hospital is 10–24 per cent.
   b. Clinical features that make a diagnosis of CAP less likely include duration of illness <24 hours.
   c. The recommended duration of a course of doxycycline to treat CAP is five to seven days.
   d. The presence of normal oxygen saturation rules out a diagnosis of severe CAP.
   a. True
   b. False

For each section, one of the statements is false – which is it?

5. When prescribing an antibiotic to treat a patient with LRTI in primary care:
   a. The GP’s decision to prescribe is influenced by his/her perception of the patient’s expectation of treatment.
   b. Prescribing an antibiotic on the basis of presentation with discoloured sputum has been shown to improve recovery in patients with LRTI in primary care.
   c. Some data show that 34 per cent of adults presenting with an LRTI expect a prescription.
   d. One trial found that, compared with placebo, amoxicillin did not reduce the severity or duration of symptoms in adults with acute LRTI in whom pneumonia was not suspected.
   a. True
   b. False

For each section, one of the statements is false – which is it?

6. Considering the pathogens that may cause LRTI:
   a. Streptococcus pneumoniae is the commonest identified pathogen.
   b. The clinical significance of isolating Chlamydia pneumoniae in a patient with LRTI is uncertain.
   c. Clinical features are a good guide to the identity of the likely pathogen.
   d. The incidence of respiratory infections due to respiratory syncytial virus starts to increase in the autumn.
   a. True
   b. False

For each section, one of the statements is false – which is it?

7. In the prevention and treatment of influenza:
   a. A neuraminidase inhibitor does not shorten the duration of flu-like illness compared with placebo.
   b. To be eligible for postexposure prophylaxis with oseltamivir, the patient should present within 48 hours of contact with an individual who has flu.
   c. NICE criteria for treatment with oseltamivir include evidence of circulating influenza.
   d. True

For each section, one of the statements is false – which is it?

8. In the management of suspected pneumonia:
   a. The mortality of CAP in individuals admitted to hospital is 10–24 per cent.
   b. Clinical features that make a diagnosis of CAP less likely include duration of illness <24 hours.
   c. The recommended duration of a course of doxycycline to treat CAP is five to seven days.
   d. The presence of normal oxygen saturation rules out a diagnosis of severe CAP.
   a. True
   b. False