

10 ANTIBIOTIC MANAGEMENT

10.1 Introduction

Antimicrobial chemotherapy will be indicated primarily for respiratory complications due to secondary bacterial infections, principally influenza-related pneumonia. The majority of patients with exacerbations of chronic obstructive pulmonary disease (COPD) and other chronic lung conditions such as bronchiectasis, due to secondary bacterial will also require antimicrobial chemotherapy, as will some patients with severe sinusitis.

Few pneumonias and lower respiratory tract infections are defined microbiologically at initial assessment and hence most prescribing is empirical. In broad terms the antimicrobial management of these patients should follow the guidance offered in relevant national guidelines for the management of community acquired pneumonia and COPD, but modified in the light of the different range of pathogenic bacteria that may be implicated, specifically *Staph aureus* infection.

In the minority of cases, the aetiology may be determined after hospital admission, thereby permitting modification of the initial empirical regimen.

Although the pathogens responsible for community acquired pneumonia are diverse, in the case of bacterial pneumonia complicating influenza the principal pathogens which should be covered by any initial empirical antimicrobial therapy include: *S pneumoniae*, *H influenzae* and *Staph aureus*. The latter is said to be more common with combined viral-bacterial pneumonia, as some strains of staphylococci have synergistic effect with the virus. Gram negative enteric bacillary infection is also sometimes seen. Exacerbations of COPD will be largely associated with *S pneumoniae*, *H influenzae*, and *Moraxella catarrhalis*. Severity assessment and the association of pre-existing co-morbid disease is essential in predicting prognosis and in turn determines management, choice of antibiotic therapy and its method of administration (see Section 5).

10.2 Antibiotic resistance of respiratory pathogens

During an influenza pandemic this will be principally related to concerns about the local pattern of antimicrobial resistance of *Staph aureus*, and assessing the possibility of methicillin-resistant *S aureus* (MRSA) being present locally. Clinicians should be kept closely informed of any local shift in antimicrobial resistance patterns, both at the start and during a pandemic. *Staphylococcus aureus* is widely resistant to penicillin (76) and an increasing number are now methicillin-resistant (MRSA); when occurring in the community this generally reflects hospitalisation within the recent past or residence within a nursing home. Hence, β -lactamase unstable penicillins (penicillin G, aminopenicillins) and, in the case of MRSA, isoxazolyl penicillins (flucloxacillin, cloxacillin) and cephalosporins, are inappropriate for such infections. The true incidence of resistance among pathogens in the community is difficult to estimate since most laboratory samples come from selected populations. With this limitation in mind, the presence of β -lactamase production among *H influenzae* varies geographically but ranges from 2–17 % (77;78) in various parts of the UK. *M catarrhalis* has a high rate of β -lactamase production.

Antibiotic resistance among *S pneumoniae* is of concern world wide, owing to the dominance of this organism as a cause of community acquired pneumonia and because penicillin and macrolide resistance are frequently linked.(78;79) However to date it is not a common enough problem in the UK to influence initial antimicrobial management decisions.

Recent data provided by the HPA of antimicrobial sensitivities of respiratory pathogens isolated from blood and respiratory samples during the last 3-4 years (Robert George,

personal communication) found macrolide resistance amongst about 10-14% Methicillin sensitive *Staphylococcus aureus* (MSSA) isolates and 12-19% of *S pneumoniae*. Macrolides apart from clarythromycin have poor in vivo activity against *H influenzae*. By contrast, tetracycline resistance was around 5-8% for *S pneumoniae*, 3% for *H influenzae* and 2-8% for of MSSA.

Fluoroquinolones have activity against methicillin sensitive *Staphylococcus aureus* (MSSA): with MIC 90 figures of 1.0 mg/L for ciprofloxacin, 0.5 mg/L for levofloxacin and 0.12 for moxifloxacin.(80) Modern fluoroquinolones (oral moxifloxacin and oral and IV levofloxacin currently licensed in the UK) are therefore a possible choice for secondary bacterial infections following influenza where MSSA is a likely pathogen. A recent pharmacokinetic and pharmacodynamic in vitro study indicated that moxifloxacin 400mg od had advantages over ciprofloxacin 500mg bd or levofloxacin 500mg od in antimicrobial effects against *Staph aureus*.(81) The quinolones levofloxacin or moxifloxacin also provide cover against *S pneumoniae* and *H influenzae*. MRSA is an unlikely pathogen in the UK in the context of community acquired respiratory bacterial infection following influenza and fluoroquinolones are not sufficiently active against MRSA.

10.3 Formulation of these recommendations

There are no robust research studies available to provide evidence based guidance on the best empirical choice of antimicrobial therapy for bacterial complications of influenza. For these reasons the recommendations for treatment have been made on the basis of assessing a matrix of laboratory, clinical, pharmacokinetic and safety data, interpreted in an informed manner and taking account of other published guidelines.(82)

EMPIRICAL THERAPY – IN THE COMMUNITY

10.4 What are the principles and practice of empirical antibiotic choice for adults with bronchial complications of influenza without pneumonia managed in the COMMUNITY?

Features of an acute bronchitis, with cough, retrosternal discomfort, wheeze and sputum production are an integral part of the influenzal illness. In previously well individuals who do not have pneumonia or new focal chest signs antibiotics are not indicated.

If the illness is worsening, for instance with recrudescent fever or increasing breathlessness, a worsening bacterial bronchitis or developing pneumonia is possible and the use of antibiotics should be considered.

Those at high risk (see Appendix 2) of influenza-related complications and super-infection should be strongly considered for early 'prophylactic' antibiotics. The antibiotic prescription should come with clear instructions that the antibiotics should be used if the illness is not starting to settle after 24 hours or if there is worsening of symptoms. The potential advantages of this approach of 'prophylactic' antibiotics is to minimise rates of influenza-related complications and reconsultation.(83)

If, having started antibiotics, patients do not begin to improve over the next 48 hours of antibiotic treatment (or if they get worse) they should be advised to re-contact their GP for assessment of pneumonia and its severity (see sections 3 and 5).

Antibiotics should cover the likely bacterial pathogens including: *S pneumoniae*, *H influenzae*, *M catarrhalis* and *Staph aureus*.

The preferred first choice of antibiotic for non-pneumonic bronchial infections, including those patients with COPD, should include an effective oral β -lactamase stable agent such as co-amoxiclav, or a tetracycline, such as doxycycline. A macrolide (eg. erythromycin or clarithromycin) is an alternative for those intolerant of the preferred first choices, whilst remembering the possibility of antimicrobial resistance. Clarithromycin has better activity against *H influenzae* than azithromycin.

Recommendations

- **Previously well adults with uncomplicated influenza, or acute bronchitis complicating influenza, in the absence of pneumonia, do not routinely require antibiotics.**
- **Antibiotics should be considered in those previously well adults who develop significant worsening of symptoms (particularly recrudescent fever or increasing breathlessness).**
- **A prescription for prophylactic antibiotics should be strongly considered for patients at high risk of complications (see Appendix 2) - to be used if the illness is not starting to improve after 24 hours or there is worsening of symptoms (as above).**
- **Most patients can be adequately treated with a week's course of oral antibiotics**
- **The preferred choice of antibiotic needs also to cover infection with *Staph aureus* - for example either co-amoxiclav, or doxycycline. (see Table 10.0)**
- **A macrolide such as erythromycin (or clarithromycin) is an alternative choice in certain circumstances.**

10.5 What are the principles and practice of empirical antibiotic choice for adults with influenza-related pneumonia managed in the COMMUNITY?

The principles of antibiotic selection for patients with influenza-related pneumonia who can be managed in the community is similar to those for the management of sporadic community acquired pneumonia in general (BTS 2001, 2004), except that adequate cover for *Staph aureus*, in addition to cover for *S pneumoniae*, should be included in any empirical regimen.

For this reason oral co-amoxiclav or a tetracycline, such as doxycycline is the preferred regimen (Table 10.1).

A macrolide (eg. erythromycin or clarithromycin) is an alternative for those intolerant of the preferred first choices.

Recommendations (see Table 10.1)

- **Co-amoxiclav or a tetracycline is preferred.**
- **A macrolide (erythromycin or clarithromycin) is offered as an alternative choice for those intolerant of penicillins.**
- **Those with features of severe infection (ie. bilateral chest signs or CRB-65 score of 3 or more) should be urgently referred to hospital. (see Section 5)**
- **For those referred to hospital, GPs may consider administering antibiotics immediately where the illness is considered life-threatening or where delays (>2 hours) in admission are likely.**

Table 10.1 Preferred and alternative initial empirical antibiotic treatment regimens for adults with pneumonic and non-pneumonic lower respiratory tract infections (including exacerbations of COPD and acute bronchitis) complicating influenza managed in the community

PREFERRED	ALTERNATIVE ^a
co-amoxiclav 625mg tds PO (for 1 week), OR doxycycline 200mg stat and 100mg od PO	Macrolide (erythromycin 500 mg qds PO or clarithromycin 500 mg bd ^b PO)

a) An alternative regimen is provided for those intolerant of or hypersensitive to preferred regimen

b) Clarithromycin may be substituted for those with gastrointestinal intolerance to oral erythromycin and also has the benefit of twice daily dosage and better cover against *H influenzae*.

Abbreviations: od = once daily; bd = twice; tds = 3 times; qds = 4 times

EMPIRICAL THERAPY – IN HOSPITAL

10.6 What are the principles and practice of empirical antibiotic choice for adults with bronchial complications of influenza without pneumonia managed in HOSPITAL?

The principles are similar to those outlined for such patients managed in the community. (Section 10.4)

In those with chronic lung disease, particularly COPD, bacterial exacerbation will be the commonest cause of admission. It is likely that all such patients sufficiently ill to require hospital admission with an exacerbation will require antibiotics. Management of their underlying condition, such as COPD, should follow standard guidelines, including the use of corticosteroids if indicated.

Antibiotics should cover the likely bacterial pathogens including: *S pneumoniae*, *H influenzae*, *M catarrhalis* and *Staph aureus*. Oral therapy should be sufficient for those without adverse severity features and who are able to take oral medication.

The preferred first choice of antibiotic for non-pneumonic bronchial infections should include an effective oral β -lactamase stable agent such as co-amoxiclav, or a tetracycline, such as doxycycline. A macrolide is an alternative for those intolerant of the preferred first choices, whilst remembering the possibility of antimicrobial resistance. Clarithromycin has better activity against *H influenzae* than azithromycin. A newer generation fluoroquinolone (eg. levofloxacin or moxifloxacin) with enhanced activity against *S pneumoniae* is an alternative choice if there is increased likelihood of resistance or local issues that dictate such a choice (such as local concern regarding the prevalence of antibiotic associated enteropathy linked to β -lactam use).

Recommendations (see Table 10.2)

- **Previously well adults with acute bronchitis complicating influenza, in the absence of pneumonia, do not routinely require antibiotics.**
- **Antibiotics should be considered in those previously well adults who develop worsening symptoms (recrudescent fever or increasing dyspnoea).**
- **Patients at risk of complications or superinfection should be considered for antibiotics in the presence of lower respiratory features. These include patients**

who are within the group currently recommended for influenza vaccination (see Appendix 1).

- Most patients can be adequately treated with oral antibiotics .
- The preferred choice includes co-amoxiclav or a tetracycline.
- A macrolide such as clarithromycin (or erythromycin) or a fluoroquinolone active against *S pneumoniae* and *Staph aureus* is an alternative choice in certain circumstances.

10.7 What are the principles and practice of empirical antibiotic choice for adults with non-severe influenza-related pneumonia managed in HOSPITAL?

Patients will be suffering from primary viral pneumonia, or combined viral-bacterial pneumonia, or secondary bacterial pneumonia. The features of each of these are covered in section 3.

All patients with pneumonic involvement should receive antibiotics. The principles of antibiotic selection for non-severe influenza-related pneumonia is similar to those for the management of sporadic community acquired pneumonia in general (BTS 2001, 2004), except that adequate cover for *Staph aureus* should be included in any empirical regimen. It is also not felt necessary to routinely provide cover for atypical pathogens (*Mycoplasma pneumoniae*, *Chlamydia sp.*, *Coxiella burnetti*, *Legionella sp.*) during a pandemic as the large majority of patients will be hospitalised as a direct result of influenza and its complications caused by bacterial infection.

For these reasons oral co-amoxiclav or a tetracycline, such as doxycycline is the preferred regimen (Table 10.1). When oral therapy is inappropriate, parenteral co-amoxiclav or a second or third generation cephalosporin is offered as an alternative. Based on in-vitro data, the activity of selected cephalosporins against MSSA in the UK in descending rank order is cefuroxime (MIC90 1 – 2 mg/l) > cefotaxime (MIC90 2mg/l) > ceftriaxone (MIC90 16mg/l). (Robert George, personal communication) Only cefuroxime and cefotaxime are recommended as cephalosporins offering adequate MSSA cover within an empirical regimen.

A macrolide or one of the new fluoroquinolones, are identified as an alternative in hospitalised patients, in specific circumstances. These include those intolerant of penicillins, where local microbiological surveillance suggests they are better choices or where there are local concerns over *C difficile* associated diarrhoea. At the time of completing these guidelines, only levofloxacin and moxifloxacin are licensed and available in the UK for pneumonia.

Regardless of the regimen selected it is critical that the antibiotics be administered promptly (within 4 hours of admission), and in the case of the patient with severe pneumonia without delay, by the admitting doctor in the Admissions Ward or by the general practitioner if delays are expected in the hospital admission process. Delays in administration of antibiotics are related adversely to mortality in some studies, particularly when managing elderly patients. (84;85)

Following initial assessment and empirical therapy, progress should be monitored carefully. The route and choice of antibiotic treatment will require adjustment, either by stepping up and broadening the spectrum of microbiological activity in the light of clinical deterioration or as a result of positive microbiological information, or stepping down with improvement as discussed below. The review of antibiotic therapy forms an obvious and essential part of the regular clinical review of patients with community acquired pneumonia.

Recommendations (see Table 10.2)

- Most patients can be adequately treated with oral antibiotics.
- Oral therapy with co-amoxiclav or a tetracycline is preferred.
- When oral therapy is contra-indicated, recommended parenteral choices include intravenous co-amoxiclav, or a second or third generation cephalosporin (cefuroxime or cefotaxime respectively).
- A macrolide (erythromycin or clarithromycin) or a fluoroquinolone active against *S pneumoniae* and *Staphylococcus aureus* is an alternative regimen for those intolerant of penicillins or where there are local concerns over *C difficile* associated diarrhoea. Currently levofloxacin and moxifloxacin are the only recommended fluoroquinolones licenced in the UK.
- Antibiotics should be administered within 4 hours of admission.

10.8 What are the principles and practice of empirical antibiotic choice for adults with severe influenza-related pneumonia managed in HOSPITAL?

Mortality is greatly increased in those with severe pneumonia (Section 5). The illness may progress before microbiological information is available.

Preferred and alternative initial treatment regimens are summarised in Table 10.1. The recommendation of broad-spectrum β -lactam regimens plus a macrolide in those with severe influenza-related pneumonia is based on the following rationale:

- a. While *S pneumoniae* and *Staph aureus* remain the predominant pathogens, Gram negative enteric bacilli, although uncommon, carry a high mortality.(86)
- b. The recommended empirical regimen will offer double cover for the likely pathogens implicated in influenza-related pneumonia and there is some evidence to indicate that combination therapy is associated with better outcomes in severe pneumonia.(87)
- c. Although there is no evidence of an increased incidence of infection by atypical pathogens in influenza-related pneumonia, in severe pneumonia, it is felt necessary to include cover for atypical pathogens, particularly Legionella sp. as it may not be possible at the outset to distinguish between patients with sporadic severe community acquired pneumonia in whom Legionella infection is important, and influenza-related pneumonia.

Parenteral administration of antibiotic is recommended in those with severe community acquired pneumonia regardless of the patient's ability or otherwise to take oral medication. This is to ensure prompt, high blood and lung concentrations of antibiotic.

A fluoroquinolone is offered as an alternative, despite limited data on their use in severe pneumonia.(88) Levofloxacin is the only licensed and available agent in the UK at the time of writing. It is marketed in parenteral and oral formulations. However, until more clinical experience is available we recommend combining it with another agent active against *S pneumoniae* and *Staphylococcus aureus* such as a broad spectrum β -lactam or macrolide when managing severe influenza-related pneumonia.

Recommendations (see Table 10.2)

- Patients with severe pneumonia should be treated immediately after diagnosis with parenteral antibiotics.
- An intravenous combination of a broad spectrum beta-lactamase stable antibiotic such co-amoxiclav or a second (eg cefuroxime) or third (eg cefotaxime) generation

cephalosporin together with a macrolide (clarithromycin or erythromycin) is preferred.

- An alternative regimen includes a fluoroquinolone with enhanced activity against pneumococci together with a broad spectrum β -lactamase stable antibiotic or a macrolide. Currently levofloxacin is the only such fluoroquinolone licenced in the UK.

10.9 When should the IV route be changed to oral?

There can be no rigid recommendation concerning the timing of transfer to oral therapy and further studies of this area are needed.(89) Any decision must be individualised on the basis of assessing all factors, including the absence of any contraindications to oral administration, the availability of any microbiological information regarding aetiology of the infection and clear evidence that the patient is responding to initial therapy. The recommended guideline is that oral therapy be considered in a patient who has shown clear evidence of improvement and whose temperature has resolved for a period of 24 hours.

Recommendations

- Patients treated initially with parenteral antibiotics should be transferred to an oral regimen as soon as clinical improvement occurs and the temperature has been normal for 24 hours, providing there is no contra-indication to the oral route.

10.10 How long should antibiotics be given for?

Until there are more precise methods to reliably identify microbiological and clinical end-points, the duration of therapy will remain subject to clinical judgement and custom. For these reasons the duration of therapy will vary by individual patient, disease severity and speed of resolution.

Recommendations

- For most patients admitted to hospital with non severe and uncomplicated pneumonia, 7 days of appropriate antibiotics is recommended.
- For those with severe, microbiologically undefined pneumonia, 10 days treatment is proposed. This should be extended to 14 to 21 days where *S aureus* or Gram negative enteric bacilli pneumonia is suspected or confirmed.

10.11 Failure of initial empirical therapy

In those patients who fail to respond to initial empirical therapy, several possibilities need to be considered, the first of which is whether the correct diagnosis been made. Radiographic review is recommended for the community and hospital-managed patient. This may also indicate complications of pneumonia such as pleural effusion/empyema, lung abscess or worsening pneumonic shadowing, which will be more common in the presence of staphylococcal infection.

The initial empirical antibiotic regimen may need to be reassessed. However compliance with, and adequate absorption of an oral regimen should first be considered.

Microbiological data should be reviewed and further specimens examined, with a view to excluding *Staph aureus* and Gram negative bacillary infection.

In the hospital managed, non-severely ill patient, changing to a new fluoroquinolone such as levofloxacin provides a second alternative.

In the severely ill patient already receiving a β -lactam/clarithromycin regimen, it is recommended that further staphylococcal cover is added to include cover for MRSA. In addition, urgent referral to a respiratory physician should be made for clinical assessment including the possible need for bronchoscopic sampling. Other rapid MRSA diagnostic techniques are in the evaluation stage.

Recommendations

- **For those with non-severe pneumonia in hospital on combination therapy, changing to a fluoroquinolone with effective pneumococcal and staphylococcal cover is an option.**
- **Adding further antibiotics effective against MRSA is an option for those with severe pneumonia not responding to combination antibiotic therapy.**

SPECIFIC PATHOGEN DIRECTED ANTIBIOTIC THERAPY

10.12 What are the optimum antibiotic choices when specific pathogens have been identified?

When a pathogen has been identified specific therapy as summarised in Table 10.3 is proposed. In transferring patients from empirical to pathogen targeted therapy, the regimen and route of administration will be determined by the continued need for parenteral therapy and known drug intolerance. These recommendations are again based on a synthesis of information, which includes *in vitro* activity of the drugs, appropriate pharmacokinetics and clinical evidence of efficacy gleaned from a variety of studies. The choice of agent may be modified following the availability of sensitivity testing or following consultation with a specialist in microbiology, infectious disease or respiratory medicine. Close liaison with the local microbiology service will be essential during a pandemic.

Currently *S pneumoniae* highly resistant to penicillin (MIC ≥ 4 mg/L) is uncommon in the UK. However it is important that the situation is monitored and in future higher doses of penicillins or alternative regimens may need to be considered.

Staphylooccus aureus is an uncommon cause of sporadic community acquired pneumonia in the UK, but will assume much greater potential importance during a pandemic. Most community isolates are methicillin-sensitive although the recent increase in MRSA in hospitalised patients may result in subsequent readmission with an MRSA infection, secondary to influenza. Options for methicillin-sensitive and -resistant infections are based on parenteral administration in view of the serious nature of staphylococcal pneumonia.

Recommendations

- **If a specific pathogen has been identified, the antibiotic recommendations are summarised in Table 10.3.**

Table 9.1
Antiviral agents for influenza

Antiviral Agent	Trade Name	Manufacturer	Influenza Spectrum	Route of Administration	Daily Dosage for Adults		Most Common Side Effects
					Prevention	Treatment	
Amantadine	Symmetrel Lysovir	Endo Pharmaceuticals (USA) Alliance (UK)	Type A	Oral	200mg	200mg	Gastrointestinal and central nervous system
Rimantadine†	Flumadine	Forest Laboratories (USA)	Type A	Oral	200mg	200mg	Gastrointestinal
Zanamivir	Relenza	GlaxoSmithKline	Types A and B	Oral inhalation	10mg	20mg	None
Oseltamivir	Tamiflu	Roche	Types A and B	Oral	75mg	150mg	Gastrointestinal

† Not available in the UK

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Table 9.2

Neuraminidase inhibitors in the treatment of adults with community-acquired influenza – summary of trial data

Treatment	Patients (% with proven influenza)	Age range (mean)	Duration of illness	Reduction in days to alleviation of symptoms in patients with influenza (median)	Comments	Investigator
Inhaled zanamivir 10mg bid for 5 days	417 (63%)	≥13 years (32 years)	≤48 h	1 (5 vs 4) 3 (7 vs 4 in febrile)	3 days reduction in patients treated ≤30 h	Hayden <i>et al</i> (1997)(22)
Inhaled zanamivir 10mg bid for 5 days	455 (71%)	≥12 years (37 years)	<30 h and >30 h	1.5 (6.5 vs 5.0) 2.0 (6.5 vs 4.5 in febrile)	Reduced complications and antibiotics (15% vs 38%) in patients with underlying conditions. No effect in patients with symptoms > 30 h	MIST Study Group (1998)(69)
Oseltamivir 75mg or 150mg bid for 5 days	629 (60%)	18-65 years	≤ 36 h	1.4 (4.3 vs 2.9 vs 2.9)	Reduced complications	Treanor <i>et al</i> (2000)(23)
Oseltamivir 75mg or 150mg bid for 5 days	719 (66%)	18-65 years	≤ 36 h	1.2-1.5 days (4.9 vs 3.6 vs 3.4)	No difference between doses	Nicholson <i>et al</i> (2000)(68)

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Table 10.2: Preferred and alternative initial empirical antibiotic treatment regimens and parenteral to oral switch regimens for pneumonic and non-pneumonic lower respiratory tract infections complicating influenza managed in HOSPITAL

PREFERRED	ALTERNATIVE ^a
[1] Hospital-treated, non-pneumonic bronchial complications (including exacerbations of COPD and acute bronchitis) requiring antibiotic therapy	
<ul style="list-style-type: none"> co-amoxiclav 625mg tds PO, OR doxycycline 200mg stat and 100mg od PO 	<ul style="list-style-type: none"> Macrolide (erythromycin 500 mg qds PO or clarithromycin 500 mg bd ^b PO) OR Fluoroquinolone with enhanced pneumococcal activity e.g. levofloxacin 500 mg od PO or moxifloxacin 400mg od PO^c
[2] Hospital-treated, not severe pneumonia	
<ul style="list-style-type: none"> co-amoxiclav 625mg tds PO OR doxycycline 200mg stat and 100mg od PO <p>OR if IV needed</p> <ul style="list-style-type: none"> co-amoxiclav 1.2 g tds IV OR cefuroxime 1.5 g tds IV or cefotaxime 1g tds IV 	<ul style="list-style-type: none"> Macrolide (erythromycin 500 mg qds PO or clarithromycin 500 mg bd ^b PO) OR Fluoroquinolone with enhanced pneumococcal activity e.g. levofloxacin 500 mg od PO or moxifloxacin 400mg od PO^c Macrolide (erythromycin 500 mg qds PO or clarithromycin 500 mg bd ^b PO) OR levofloxacin 500 mg od IV ^c
[3] Hospital-treated, severe pneumonia	
<ul style="list-style-type: none"> co-amoxiclav 1.2 g tds IV or cefuroxime 1.5 g tds IV or cefotaxime 1g tds IV PLUS Macrolide (erythromycin 500 mg qds PO or clarithromycin 500 mg bd ^b PO) 	<ul style="list-style-type: none"> Fluoroquinolone with some enhanced pneumococcal activity e.g. levofloxacin 500 mg bd IV, PO ^c PLUS, EITHER Macrolide (erythromycin 500 mg qds PO or clarithromycin 500 mg bd ^b PO) OR Beta-lactamase stable antibiotic (co-amoxiclav 1.2 g tds IV or cefuroxime 1.5 g tds IV or cefotaxime 1g tds IV)

a) An alternative regimen is provided for those intolerant or hypersensitive to preferred regimen, or where there are local concerns over *C difficile* associated diarrhoea related to beta-lactam use

b) Clarithromycin may be substituted for those with gastrointestinal intolerance to oral erythromycin and also has the benefit of twice daily dosage and better cover against *H influenzae*.

c) Levofloxacin and moxifloxacin are the only currently UK licensed fluoroquinolones with enhanced activity against *S pneumoniae*, in addition to cover for *Staphylococcus aureus*. Levofloxacin comes in an oral and parenteral formulation and is licensed for severe pneumonia. Moxifloxacin comes in an oral formulation only in the UK and is not licensed for severe pneumonia. In the future other fluoroquinolones such as gemifloxacin and gatifloxacin are likely to extend this choice, when licensed in the UK.

Abbreviations: od = once daily; bd = twice; tds = 3 times; qds = 4 times; IV = intravenous; PO = oral

Switch from parenteral drug to the equivalent oral preparation should be made as soon as clinically appropriate, in the absence of microbiologically confirmed infection. In the case of the parenteral cephalosporins, the oral switch to co-amoxiclav 625 mg tds is recommended rather than to oral cephalosporins.

Table 10.3: Recommended therapy of most likely microbiologically defined causes of pneumonia complicating influenza.* Local specialist advice should always be sought

PATHOGEN	PREFERRED	ALTERNATIVE
<i>S pneumoniae</i>	amoxicillin 500 mg – 1.0 g ^a tds PO or benzylpenicillin 1.2 g qds IV	cefuroxime 0.75-1.5 g tds IV or cefotaxime 1-2 g tds IV or ceftriaxone 2g od IV or erythromycin 500 mg qds PO or clarithromycin 500 mg bd PO
<i>S aureus</i>	Non-MRSA: flucloxacillin 1-2 g qds IV ± rifampicin 600 mg od or bd, PO/IV MRSA: vancomycin 1 g bd IV (dose monitoring) ± rifampicin 600 mg od or bd PO/IV	Consult local microbiologist for further advice.
<i>H influenzae</i>	Non-β-lactamase-producing: amoxicillin 500 mg td or ampicillin 500 mg qds IV β-lactamase-producing: co-amoxiclav 625 mg tds PO or 1.2g tds IV	cefuroxime 750 mg -1.5g tds IV or cefotaxime 1-2 g tds IV or ceftriaxone 2 g od IV or fluoroquinolone ^b PO or IV
Gram negative enteric bacilli	cefuroxime 1.5 g tds or cefotaxime 1-2 g tds IV or ceftriaxone 1-2 g bd IV	fluoroquinolone ^b IV or imipenem 500 mg qds IV or meropenem 0.5-1.0 g tds IV
<i>P aeruginosa</i>	ceftazidime 2 g tds IV ± gentamicin or tobramycin (dose monitoring)	EITHER ciprofloxacin 400 mg bd IV OR piperacillin 4 g tds IV ± gentamicin or tobramycin (dose monitoring)

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