Community-Acquired Pneumonia

Introduction

Community acquired pneumonia (CAP) refers to an acute infection of the lung parenchyma in a patient who has acquired the infection outside of a healthcare setting, and developed symptoms and signs in the community or within 48 hours after admission to hospitals, in the absence of recent hospitalisation.

Aetiology

CAP can be caused by a variety of pathogens. In the outpatient setting, the most frequently detected pathogens are *Streptococcus pneumoniae*, *Mycoplasma pneumoniae* and respiratory viruses (e.g. influenza, parainfluenza, respiratory syncytial virus). Less frequent causes include *Haemophilus influenzae* and *Moraxella catarrhalis*. Group A Streptococcus and *Staphylococcus aureus* may cause secondary bacterial pneumonia following influenza.

A recent study on the distribution of the microbial aetiology in relation to the clinical setting and severity, among a total of 3523 adult patients with CAP, 514 (14.6 %) were outpatients. The microbial aetiology was known in 161 outpatients (31 %). Selected frequencies of pathogen are *Streptococcus pneumoniae* (35 %), *Mycoplasma pneumoniae* (17 %), *H. influenzae* (5%), methicillin-sensitive *S. aureus* (1%), respiratory viruses (9 %) and mixed aetiologies (9 %). *M. catarrhalis* was not detected among outpatients in this study. (1)

Clinical features

Common clinical features of CAP include cough, fever, pleuritic chest pain, dyspnoea and sputum production. Mucopurulent sputum production is most frequently found in association with bacterial pneumonia (e.g. *Streptococcus pneumoniae*), while scant or watery sputum production is more suggestive of an atypical pathogen (e.g. *Mycoplasma pneumoniae*). On physical examination, many are febrile, although this finding is frequently absent in older outpatients. Tachypnoea and tachycardia are also common. Chest examination reveals audible crackles in most outpatients. Signs of consolidation, such as decreased or bronchial breath sounds, dullness to percussion, may be present. The presence of an infiltrate on plain chest radiograph is considered as the gold standard for diagnosing pneumonia when clinical and microbiological features are supportive. The chest radiograph appearance of CAP may include lobar consolidation, interstitial infiltrates and/or cavitation.

Severity of illness is the most critical factor in determining the site of care. The clinical judgment of clinicians is crucial in assessing the severity of illness, which can be aided by the CRB-65 score (1 point for each feature present: confusion, respiratory rate $\geq$ 30/min, low blood pressure (systolic blood pressure $<$ 90 mmHg or diastolic blood pressure $\leq$ 60 mmHg), age $\geq$ 65 years). Patients who have a CRB-65 score of 0 are at low risk of death and do not normally require hospitalisation for clinical reasons. Patients who have a CRB-65 score of 1 or 2 are at increased risk of death, particularly those patients with score of 2, and hospital referral and assessment should be considered. Patients who have a CRB-65 score of 3 or 4 are at high risk of death and require urgent hospital admission. Apart from severity of illness, other factors should also be taken into account in determining the site of care. These include the ability to maintain oral intake, likelihood of medication adherence, history of active substance abuse, mental illness, cognitive or functional impairment, and living or social circumstances.

Microbiological testing

Testing for a microbiological diagnosis is important in some clinical or epidemiological settings, suggesting possible infection with antibiotic resistant *Streptococcus pneumoniae* and *Mycoplasma pneumoniae*, or possible infection with an organism that requires treatment different from standard

empirical regimens. For example, exposure to birds suggests possible infection with *Chlamydia psittaci*, while exposure to goats, sheep and cattle suggests possible infection with *Coxiella burnetii*. Furthermore, infection with *Legionella* species, *Mycobacterium tuberculosis*, community-acquired methicillin-resistant *Staphylococcus aureus* or influenza require treatment different from standard empirical regimens.

Antibiotic therapy

Antibiotic therapy should be started as soon as possible once the diagnosis of CAP is suspected or established. (2-8) (Tables 1&2)

Streptococcus pneumoniae is one of the most common pathogens identified in CAP. Hence, the choice of agents for empirical therapy should target on *S. pneumoniae*, which is complicated by the emergence of antibiotic resistance. In Hong Kong, reduced susceptibility to penicillin and resistance to macrolides (60 – 90 %, according to data in antibiogram for common bacterial isolates from outpatient setting of private hospitals and Public Health Laboratory Services Branch of the Centre for Health Protection (9)) are high in the community. (refer to Antibiogram for Common Bacterial Isolates under the Antibiotic Stewardship Programme in Primary Care in the Centre for Health Protection website at https://www.chp.gov.hk/en/features/49811.html)

In 2008, Clinical and Laboratory Standards Institute published revised susceptibility breakpoints for penicillin and *Streptococcus pneumoniae*, and the revised susceptibility breakpoint is ≤ 2 μg/ml for nonmeningeal infections. (10, 11) For pneumococcal pneumonia, pharmacokinetic/dynamic data indicated that isolates with penicillin MIC of up to 2 μg/ml should be considered 'sensitive' to appropriate doses of penicillin G, ampicillin and amoxicillin. Data of susceptibility of 775 invasive pneumococcal isolates between 2012 – 2016 in Hong Kong showed 94.7 – 98.6 % of the *S. pneumoniae* isolates had a penicillin MIC ≤ 2 μg/ml (sensitive), 1.4 – 5.3 % had a penicillin MIC = 4 μg/ml (intermediate susceptibility to penicillin), and 0 – 0.7 % had a penicillin MIC ≥ 8 μg/ml (resistant), among different patient age groups from < 5 to ≥ 65 years. (12)

Patients with pneumococcal pneumonia caused by isolates with penicillin MIC ≤ 2 μg/ml can be treated appropriately with optimal dosage of intravenous penicillin G and several other oral or intravenous beta-lactams. In the outpatient setting, oral amoxicillin is generally viewed as the beta-lactam drug of choice for treating pneumonia caused by *S. pneumoniae* with reduced susceptibility to penicillin. In outpatients without risk factors for reduced susceptibility to penicillin by *S. pneumoniae*, or with isolates having penicillin MIC ≤ 1 μg/ml, initial amoxicillin dosing of 45 mg/kg/day may be used. In outpatients with risk factors for reduced susceptibility to penicillin by *S. pneumoniae*, or with isolates having penicillin MIC = 2 μg/ml, an even higher daily dose of amoxicillin of 90 mg/kg/day is required. Risk factors for reduced susceptibility to penicillin by *S. pneumoniae* include age > 65 years, beta-lactam therapy within past 3 months, alcoholism, multiple medical comorbidities, and exposure to a child in a day care centre. beta-lactam/beta-lactamase inhibitor combinations (e.g. amoxicillin-clavulanate) are active against beta-lactamase-producing organisms (e.g. *H. influenzae*, *M. catarrhalis* and methicillin-sensitive *S. aureus*). Except in outpatients with mixed infections, beta-lactam/beta-lactamase inhibitor combinations offer no additional advantage over amoxicillin for the treatment of pneumococcal pneumonia because beta-lactamase is not produced by *S. pneumoniae*.

At the current level of reduced susceptibility to penicillin by *S. pneumoniae*, oral cephalosporins (e.g. cephalexin, cefaclor, cefuroxime, ceftibuten, cefixime) would not provide reliable coverage for many pneumococci.

Erythromycin-resistant *S. pneumoniae* isolates are regarded as resistant to the newer macrolides such as

clarithromycin and azithromycin. At the current level of macrolide resistance by *S. pneumoniae*, macrolides should not be used as the sole agent for empirical treatment of presumed pneumococcal pneumonia.

Fluoroquinolones may be considered in the treatment of CAP when the first line agent have failed, or when the outpatients are allergic to the first line agent, or have documented infection by *S. pneumoniae* with penicillin MIC ≥ 4 μg/ml (intermediate susceptibility to penicillin). Respiratory fluoroquinolones (e.g. levofloxacin), but not ciprofloxacin or ofloxacin, should be used to treat pneumococcal pneumonia. Use of levofloxacin in suboptimal dose and in divided doses should be avoided as these have been showed to be associated with the emergence of fluoroquinolone-resistant *S. pneumoniae*. Tuberculosis (TB) is prevalent in Hong Kong, and was reported to account for ~ 10 % of CAP in the elderly. Excessive use of respiratory fluoroquinolones in CAP may lead to delay in diagnosis of TB, and increased fluoroquinolone resistance among *Mycobacterium tuberculosis*.

Respiratory tract infections caused by *Mycoplasma pneumoniae* are primarily a disease of school-age children and adolescents. The infections are often self-limiting even without specific antibiotic therapy. Initial empirical therapy that covers *M. pneumoniae* is considered optional for outpatients with mild CAP. It may be indicated if first line agent has failed, or the outpatients have severe CAP, or are children ≥ 5 years and adolescents. Up to 40 % of CAP in children ≥ 5 years of age has been attributed to *M. pneumoniae*. (13) In Hong Kong, macrolide resistance rate among *M. pneumoniae* is high in the community. Doxycycline is recommended for the treatment of macrolide resistant *M. pneumoniae* (MRMP) associated CAP in children > 8 years old, adolescents and adults. Doxycycline may be given orally at 2 mg/kg (maximum = 100 mg) twice daily. For children aged 5 – 8 years old, adolescents and adults infected with MRMP associated CAP, fluoroquinolone (e.g. levofloxacin) is an alternative. Levofloxacin may be given orally at 8 mg/kg (maximum = 500 mg) once daily. Both doxycycline and fluoroquinolones have the potential to cause toxicities in children. Clinicians should explain the reasons for their use and potential side effects to the parents before prescribing the drugs to children.

Duration of antibiotic therapy

Clinical judgment is required in determining the duration of antibiotic therapy. Factors that need to be considered include patient's clinical response, severity of infection, causative pathogen, in-vitro susceptibility of the pathogen, presence of complications and side effects. Most outpatients with CAP will have an adequate clinical response within 72 hours. For most outpatients, appropriately chosen initial antibiotic therapy should not be changed in the first 72 hours, unless there is marked clinical deterioration. In clinical trials, the total duration of antibiotic therapy is often 7 to 10 days, although shorter courses may be just as effective for milder disease managed on an outpatient basis. Longer treatment courses (> 10 days) may be required for CAP complicated by parapneumonic effusion, empyema or lung abscess, which may require surgical drainage.

All persons aged 6 months or above, except those with known contraindications, are recommended to receive seasonal influenza vaccine for personal protection. Outpatients with risk factors for invasive pneumococcal infection are recommended to receive pneumococcal vaccination.

Table 1. Antibiotics recommendation for treatment of Community-Acquired Pneumonia in adults

Drug (Route)	Dosage and Frequency, Adults (Usual)	Duration (Usual)	Remarks
First line			
Amoxicillin (oral)	500 or 1000 mg three times daily	7–10 days	High-dose amoxicillin is used for coverage of drug-resistant *S. pneumoniae* (DRSP). Risk factors for DRSP include age > 65 years, beta-lactam therapy within past 3 months, alcoholism, multiple medical comorbidities, and exposure to a child in a day care centre. For aspiration pneumonia, Amoxicillin-clavulanate (or other BLBLIs) is recommended for anaerobic coverage. If levofloxacin is used, metronidazole should be added (oral 400mg three times daily).
Amoxicillin-clavulanate or other BLBLIs# (oral)	1g (875 mg /125 mg) twice daily	7–10 days	
Doxycycline (oral)	100 mg twice daily	7–10 days	As a combination treatment with beta-lactams for atypical pneumonia coverage. Initial empirical therapy that covers *M. pneumoniae* is considered optional for outpatients with mild CAP.
Second line			
Ceftriaxone (IV or IM)	1-2g/day in 1 to 2 divided doses (maximum: 4000 mg per day)	7–10 days	For failed initial therapy, ill presentation, non-type 1 penicillin allergy. Daily doses greater than 2g are divided into 2 doses.
Levofloxacin (oral)†	500 mg once daily	7–10 days	For outpatients who have failed the first line agent, or are allergic to the first line agent, or have documented infection by *S. pneumoniae* resistant to penicillin.

Table 2. Antibiotics recommendation for treatment of Community-Acquired Pneumonia in children

Drug (Route)	Dosage and Frequency, Children^ (Usual)	Duration (Usual)	Remarks
First line			
Amoxicillin (oral)	45 mg/kg/day or 90 mg/kg/day (maximum: 3000 mg/day) in divided doses every 8 or 12 hours	7–10 days	In outpatients without risk factors for DRSP, amoxicillin dosing of 45 mg/kg/day may be used. In outpatients with risk factors for DRSP, amoxicillin dosing of 90 mg/kg/day is required. Risk factor for DRSP: antibiotic consumption in recent 3 months. Choose the preparation that could provide the required amoxicillin dose with the least amount of clavulanate to reduce side effects e.g. diarrhea
Amoxicillin-clavulanate or other BLBLIs# (oral)	45 mg/kg/day or 90 mg/kg/day of the amoxicillin component (maximum: 3000 mg/day) in divided doses every 12 hours	7–10 days	

Azithromycin or other macrolides e.g. clarithromycin (oral)	For children <15 kg (<3 years): 10 mg/kg once daily For children ≥ 15 kg: 15-25 kg (3-7 years): 200 mg once daily; 26-35 kg (8-11 years): 300 mg once daily; 36-45 kg(12-14 years): 400 mg once daily; Over 45 kg: Dose as per adults	3–5 days	As a combination treatment with beta-lactams for atypical pneumonia coverage. Initial empirical therapy that covers *M. pneumoniae*[§] is considered optional for outpatients with mild CAP. It may be indicated if the patients have severe CAP or are children ≥ 5 years and adolescents.
Second line			
Ceftriaxone (IV or IM)	50 to 100 mg/kg/ day IV or IM in divided doses every 12 or 24 hours (maximum: 4000 mg per day)	7–10 days	For failed initial therapy, ill presentation, non-type 1 penicillin allergy. Daily doses greater than 2g are divided into 2 doses.
Cefpodoxime (oral)	Infants >3 months of age and Children <12 years of age: Oral: 5 mg/kg/dose (maximum: 200 mg/dose) every 12 hours Children ≥12 years of age and Adolescents: refer to adult dosing	7–10 days	For non-type 1 penicillin allergy. Certain *S. pneumoniae* isolates may not be reliably covered by oral cephalosporins in the local setting.
Cefuroxime (oral)	Infants >3 months of age and Children <40 kg: 15 mg/kg/dose (maximum : 250 mg/dose) every 12 hours; Children ≥40 kg: maximum: 500 mg/dose every 12 hours	7–10 days	
Clindamycin@ (oral)	30 to 40 mg/kg/day in divided doses every 6 to 8 hours	7–10 days	For empirical treatment of suspected pneumococcal pneumonia with severe (type 1) allergy to penicillin (rare). Certain *S. pneumoniae* isolates may not be reliably covered by oral clindamycin in the local setting.

^Dosages listed are not appropriate for neonates.
[§]Doxycycline is recommended for the treatment of macrolide-resistant *M. pneumoniae* (MRMP) associated CAP in children > 8 years old, adolescents and adults. Doxycycline may be given orally at 2 mg/kg (maximum: 100 mg) twice daily.
[†]Beware of possible serious side effects (e.g. joint or tendon pain, muscle weakness, tingling or pricking sensation, numbness in the arms or legs, confusion, and hallucinations).
#Beta-lactam-beta-lactamase inhibitor combinations e.g. ampicillin-sulbactam.
@Only capsule (not syrup) preparation is available locally. The capsule is dosed as 150mg each.

Clinicians should tailor make drug treatment based on clinical judgment. Definitive therapy should be based on microbiological and antibiotic sensitivity results if available.
Management of outpatients with infections should be individualised. Doctors should check, document and get outpatients well informed about antibiotic treatment (e.g. indication, side effect, allergy, contraindication, potential drug-drug interaction, etc.). Outpatients should be reminded to take

antibiotics exactly as prescribed by their family doctors.

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Disclaimer:

This guidance notes is intended for medical professionals for reference only and is not intended to be prescriptive or a substitute for clinical judgment on management of individual patient. It is not a complete authoritative diagnostic or treatment guide. Medical professionals are recommended to obtain relevant information from other sources, and provide patient management based on clinical judgment.

This guidance notes will be kept updating thereafter. Please visit the website of Centre for Health Protection, Department of Health for the latest update and other information.

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