GUIDELINE

Management of Community-Acquired Pneumonia in Adults

Working Group of the South African Thoracic Society

Objective. To revise the existing South African community-acquired pneumonia guideline in the light of the following factors:

- Increasing antibiotic resistance
- Introduction of new antibiotics
- International trends based on evidence published since the previous guideline.

The main aim of the guideline is to recommend an initial choice of antibiotics in patients with community-acquired pneumonia encompassing the following subgroups:

- Adults without co-morbid illness
- The elderly and/or those with associated co-morbid illness, including patients with concomitant human immunodeficiency virus (HIV) infection, and
- Patients with severe pneumonia.

Options. Studies comparing patient outcome obtained with the various treatment regimens have been reviewed. The choice of antibiotic is based on the most commonly isolated pathogens, with cost as a consideration.

Outcomes. The empiric antibiotic therapy covers all commonly encountered organisms in patients with community-acquired pneumonia and is likely to achieve the best prognosis.

Evidence. Working group of clinicians and clinical microbiologists, following detailed literature review, particularly of studies performed in South Africa.

Benefits, harms and costs. The guideline pays particular attention to cost-effectiveness in South Africa and promotes rational antibiotic prescribing with the aim of limiting emergence of antibiotic resistance.

Recommendations. These include details of likely pathogens, an appropriate diagnostic approach, indicators of severity of illness, need for hospitalisation and antibiotic treatment options.

Validation. The guideline was updated by a working group of the South African Thoracic Society, which included members of the Critical Care Society of Southern Africa, and the Federation of Infectious Diseases Societies of Southern Africa. Reference was made to the recently updated international guidelines from the UK, Europe, Canada and the USA.

Endorsement. The guideline is endorsed by the South African Thoracic Society, the Federation of Infectious Diseases Societies of Southern Africa, and the Critical Care Society of Southern Africa.

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1. Introduction

Pneumonia is an acute infection of the lung parenchyma distal to the terminal bronchiole, most commonly bacterial in nature, and associated with clinical and/or radiological evidence of consolidation of part or parts of one or both lungs. It remains a cause of considerable morbidity and mortality throughout the world. Mortality is improved by early initiation of antibiotics to which the causative organism(s) are susceptible, and adversely affected by delayed or inappropriate initial therapy.

2. Aim of the guideline

The main purpose of the guideline is to provide rational and cost-effective recommendations regarding choice of initial empiric antibiotic therapy that is likely to improve patient survival.

3. Categories of community-acquired pneumonia (CAP)

This revision of the guideline is presented in recognition of the following:

- Increasing antibiotic resistance among some of the common organisms
- The availability of new antimicrobial agents
- International trends based on evidence published since the previous guideline.

Advice is given for differences associated with age, the severity of the infection and the presence or absence of underlying/coexistent disorders. The following categories are considered separately:

- Adults without co-morbid illness
- The elderly and/or adults with co-morbid illness, including concomitant HIV infection, and
- Severely ill adults.

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4. Causative organisms in CAP

4.1 Although many organisms may cause pneumonia, relatively few pathogens account for most cases. The list of organisms commonly associated with pneumonia includes:

- *Streptococcus pneumoniae*
- Atypical pathogens
  - *Mycoplasma pneumoniae*
  - *Chlamydia pneumoniae*
  - *Legionella* species
- Respiratory viruses
- *Haemophilus influenzae*
- Aerobic Gram-negative bacilli (e.g. *Klebsiella pneumoniae*)
- *Staphylococcus aureus.*

4.2 There is uncertainty about the true incidence of so-called 'atypical infections' in patients with pneumonia in South Africa. Infections with organisms such as *C. pneumoniae* and *M. pneumoniae* are cyclical. There is geographical variation in the incidence of infection with *Legionella* spp. Evidence from academic units in South Africa where the prevalence of *Legionella* infection has been studied suggests this to be low.

4.3 Some differences are noted in the various patient categories. Patients with chronic obstructive pulmonary disease (COPD) may have more infections with *H. influenzae.* In elderly patients more infections with Gram-negative organisms occur. Severely ill patients are infected more frequently with *K. pneumoniae* and *S. aureus.*

4.4 Polymicrobial infections are fairly common, especially in the elderly and in severely ill patients.

4.5 Infections with anaerobic organisms occur more commonly in the elderly and in patients with increased risk of aspiration (for example alcoholism, epilepsy, cerebrovascular accident).

4.6 In HIV-seropositive patients there is an inverse relationship between the CD4 cell count and the frequency of pneumonia, but CAP may occur in HIV-seropositive patients at any stage of the infection. Pneumonia is most common when the CD4+ count falls below 200 cells/µl. The organisms responsible for CAP in HIV-seropositive patients are the same as in HIV-seronegative cases. The most common bacterial causes of pneumonia are *S. pneumoniae* and *H. influenzae.* Infections with *S. aureus* and aerobic Gram-negative bacilli are also relatively common. Unusual causes of CAP are *Pseudomonas aeruginosa* and *Rhodococcus equi.* The possibility of infection with an opportunistic pathogen, notably *Pneumocystis jirovecii,* always needs to be considered. Any of these infections may occur alone or in combination with more usual bacterial pathogens. The risk of opportunistic infections increases as the CD4 cell count falls.

4.7 Risk factors for pseudomonal infections in patients with CAP include the following:

- Patients with structural lung disease, in particular cystic fibrosis and/or bronchiectasis
- Patients who have received broad-spectrum antibiotic therapy for >7 days in the previous month
- Patients who have recently been hospitalised (because of nosocomial colonisation).

4.8 Influenza pneumonia caused by influenza viruses type A or B can present as mild/moderate or as a severe 'flu' or 'flu-like' illness. Prognosis is worse if complicated by bacterial pneumonia. Avian influenza (influenza virus, type A (H5N1)) following close contact with infected poultry, and occasional human-to-human transmission, has been reported. Clinically the infection presents as a fulminant respiratory illness, followed by the development of adult respiratory distress syndrome (ARDS) and death in a large number of patients.

4.9 The possibility of infection with *Mycobacterium tuberculosis* should always be considered. This infection is especially common in immunocompromised patients, such as those with concomitant HIV infection, and may present as an acute infection. Tuberculosis should also be considered as a possible cause of pneumonia in immunocompetent individuals, particularly in those who are not responding to conventional antibiotic therapy. A number of antibiotics commonly used for CAP have antituberculosis activity, particularly the fluoroquinolones, and if used empirically for patients with suspected CAP who actually have tuberculosis, may complicate the diagnosis of tuberculosis as well as be associated with development of resistance of mycobacteria to that agent.

5. Establishing the diagnosis of pneumonia

A chest radiograph is advisable in all patients with pneumonia because it helps to:

- confirm the diagnosis
- delineate the extent of the consolidation
- indicate the presence of underlying disorders
- denote the presence of complications.

The chest radiographic features of CAP are not consistent or characteristic enough to suggest the most likely microbial cause. However, infections with organisms such as *P. jirovecii,* in HIV-seropositive patients, tend to be associated with a diffuse pulmonary infiltrate, rather than with the more characteristic focal consolidation (lobar, segmental or sub-segmental) of the common bacterial pathogens. This may be helpful in suggesting the possibility of this opportunistic infection in immunocompromised cases. However, in HIV-seropositive patients bacterial infections may also present with a more diffuse infiltrate. Pulmonary tuberculosis may

also sometimes present in this way, particularly in cases of disseminated disease, and especially in the setting of immunodeficiency. An approach to the initial assessment and management of pneumonia in HIV-seropositive individuals, based on the chest radiographic appearance, is described more fully in Fig. 1.

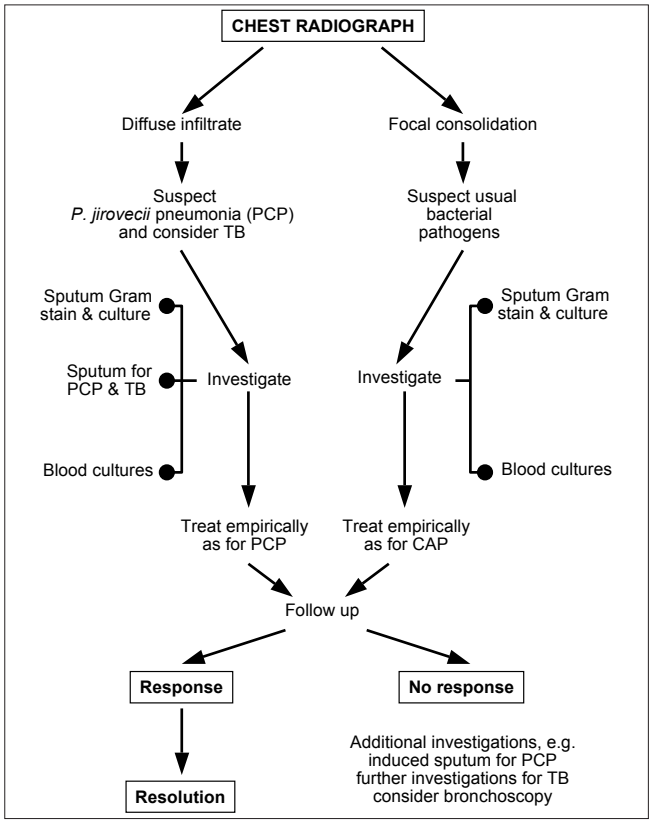

Fig. 1. An algorithmic approach to the evaluation of hospitalised HIV-seropositive patients with community-acquired pneumonia, based on the chest radiographic features. This needs to be considered in conjunction with the clinical features. (Figure from Feldman C. Bacterial pneumonia in the HIV-seropositive patient. CME *2001; 19: 390-394, reproduced with permission.)*

6. Establishing the aetiological diagnosis

6.1 In general, the clinical features and/or other laboratory data are not sufficiently characteristic or consistent to suggest the likely microbial pathogen in patients with pneumonia and therefore cannot be used alone to guide initial therapy.

6.2 However, many HIV-seropositive patients who present with pneumonia have obvious clinical features of HIV infection (such as candidiasis and/or lymphadenopathy) together with a clinical presentation very suggestive of *P. jirovecii* infection: an infection with relatively acute or subacute onset, associated with tachypnoea, tachycardia, and signs of respiratory distress, such as cyanosis, alar flaring and use of accessory muscles, in association with diffuse pulmonary signs and infiltrates. These features are most commonly seen in HIV-seropositive patients not receiving highly active antiretroviral therapy.

6.3 Even with extensive diagnostic testing, the causative organisms are identified in less than half of the cases. An extensive initial diagnostic workup is not recommended.

6.4 In addition to the chest radiograph, the following investigations are recommended in the high-risk patient, in those with underlying co-morbid illness and in more severe infection:

- Gram staining and culture of sputum or other respiratory tract secretions, as well as determination of the susceptibility of any cultured micro-organisms to the antibiotics commonly used and recommended in this guideline for patients with pneumonia.
- Particularly in HIV-seropositive patients, additional specimens need to be submitted for investigation for *M. tuberculosis* (smear and/or culture) and for *P. jirovecii* (immunofluorescence).
- Two sets of blood cultures should be performed in hospitalised cases.
- Haematological and biochemical testing including full blood count and platelet count, serum electrolytes, urea, creatinine, protein, albumin, bilirubin and alanine transaminase should be performed in hospitalised cases.

  These do not help determine aetiology but assist in the assessment of co-morbidity and influence decisions regarding hospitalisation, severity of illness and choice and dosages of antibiotics.
- Thoracocentesis in patients with pleural effusions.

  Pleural fluid examination should include a white cell and differential count and measurement of the pH, protein, glucose and lactate dehydrogenase. Gram staining and culture and Ziehl-Neelsen stain and culture for tuberculosis should be performed. Measurement of adenosine deaminase (ADA) may be helpful in excluding tuberculosis, if a low level is found. ADA levels are elevated in both parapneumonic effusions and tuberculosis and elevated ADA should only be considered strongly suggestive (but not confirmatory) of tuberculosis if there is an associated predominance of lymphocytes representing greater than 50% of inflammatory cells in the pleural fluid differential count.
- Assessment of arterial oxygenation (pulse oximetry or blood gas analysis) in severely ill patients.

6.5 Pneumococcal and *Legionella* urinary antigen detection have good sensitivity and specificity but are expensive and are not recommended for routine use.

6.6 Other investigations *not* routinely recommended include:

- serological testing for 'atypical pathogens'
- additional tests for microbial antigens or antibodies
- invasive diagnostic testing including bronchoscopy
- investigative tools such as polymerase chain reaction techniques.

7. Decision to hospitalise patients

7.1 Not all patients with pneumonia require hospital admission, and it is not always easy to decide which patients can safely be managed at home.

7.2 An important consideration is the patient's socio-economic status and home circumstances.

7.3 Additional factors are:

- Age ≥65 years
- Co-morbid illnesses:
  - HIV infection
  - chronic cardiorespiratory illness
  - renal disease
  - liver disease
  - diabetes mellitus
- Clinical features indicative of severe pneumonia:
  - cyanosis
  - confusion or decreased level of consciousness
  - low blood pressure (<90 mmHg systolic, ≤60 mmHg diastolic)
  - tachypnoea (≥30 breaths/min)
- Multilobar consolidation, bronchopneumonia, pleural effusion, cavitation, and rapidly expanding infiltrates
- Complications of infection, for example empyema and lung abscess
- Laboratory parameters if undertaken:
  - hypoxaemia (<60 mmHg; <8 kPa) or <90% saturation
  - white cell count of <4 or >30×10^9/l
  - abnormal renal function (including urea ≥7 mmol/l)
  - abnormal liver function (including albumin <30 g/l).

8. Severity of illness scores

A number of severity of illness assessment tools have been developed to assist clinicians in assessing the severity of community-acquired pneumonia. Assessment of the severity of infection is important since it will determine appropriate site of care, microbiological work-up and empiric antibiotic treatment. One such scoring system is the CURB-65 score, which was derived from the British Thoracic Society rules. The scoring system uses five components, namely:

- confusion
- urea ≥7 mmol/l
- respiratory rate ≥30 breaths/min
- low blood pressure (systolic <90 mmHg and diastolic ≤60 mmHg, and
- age ≥65 years.

Each parameter is assigned 1 point, if present. Patients with CAP and scores of 0 and 1 are thought to be mild and potentially suitable for management at home. Patients with scores of 2 are considered moderately ill and need to be observed in hospital initially. Patients with scores of >3 are thought to be severely ill, and especially those with a score of 4 or 5 need consideration for admission to a high-care or even intensive care unit. This scoring system has been recommended for use because of its simplicity, but also because its accuracy is similar to that of the more complicated scoring systems, such as the Pneumonia Severity Index. A variation of the CURB-65 is the CRB-65, which does not require the measurement of the urea level, making it more suitable for outpatient use, although it is less accurate. None of the scoring systems replace clinical assessment and important additional factors, such as socioeconomic deprivation and co-morbidity, must influence the decision on hospitalisation and treatment.

9. Suggested empiric antibiotic therapy

Initial antibiotic therapy is empiric and recommendations offered are the result of careful consideration of all relevant local studies and several from abroad (see section 11 and Fig. 2). Different options are offered and individual choice of therapy is best guided by thorough knowledge of commonly encountered pathogens in the region or practice environment and a full appreciation of their usual susceptibility patterns. Significant differences have been noted, not only within the different geographical areas of South Africa, but also between the public and private sector. Few of the recommended treatment regimens have been validated in prospective studies. A further recommendation is that since recent exposure to an antibiotic (in the past 3 months) is a risk factor for antibiotic resistance, particularly to that class of antibiotics, patients presenting with pneumonia should be asked about recent antibiotic exposure. If they have recently been exposed to a particular class of antibiotics, continued or repeated use of that class of antibiotics is not recommended or in the case of a beta-lactam, an agent in that same class with a broader spectrum should be used.

9.1 Patients treated at home

9.1.1 Young patients <65 years of age, without comorbid illness

In young patients, below the age of 65 years and without comorbid illness, the treatment of choice is high-dose oral amoxicillin.

9.1.2 Elderly patients ≥65 years and/or adults with comorbidity including patients with HIV infection

Alternative agents available for oral outpatient use, which are recommended for use in the elderly (≥65 years), for patients with co-morbid illness, and for sicker patients, are amoxycillin-clavulanate or selected oral cephalosporins (cefuroxime axetil

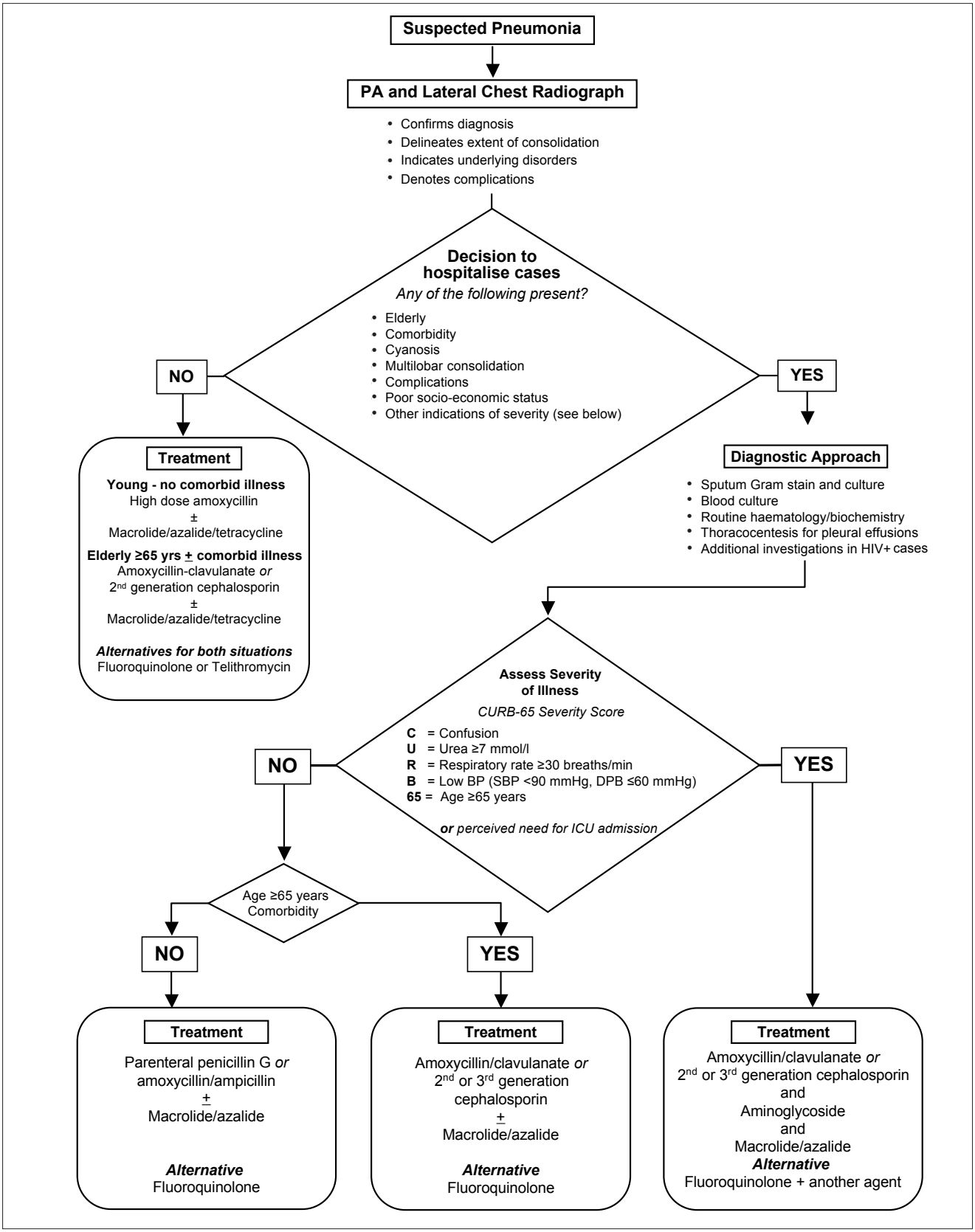

Fig. 2. Algorithm for the management of community-acquired pneumonia in adults in South Africa. This should be read in conjunction with the text.

or cefpodoxime). However, many of these patients may be better treated in hospital (see below).

Other alternative therapies:

- Fluoroquinolones. The fluoroquinolones with extended Gram-positive cover, i.e. moxifloxacin and gemifloxacin, are the preferred agents because of their superior microbiological efficacy against *S. pneumoniae.* Levofloxacin, which is now recommended at the higher dose (e.g. 750 mg daily or 500 mg 12-hourly – see section 11.4), is also a suitable option. However, in order to limit the development of resistance, it is recommended that these agents are not used as routine first-line therapy, but rather are reserved for patients with severe allergy to standard beta-lactam agents, for known or suspected cases of infection with highly penicillin-resistant pneumococci or other resistant infections, and for patients in whom initial therapy with other antimicrobial agents has failed. These antibiotics also provide good cover, as monotherapy, for infections with the so-called 'atypical pathogens'.
- Macrolides/azalides. On the basis of current information on the mechanism, prevalence, and significance of macrolide/azalide resistance in *S. pneumoniae* in South Africa, these agents are not routinely recommended as monotherapy for the treatment of CAP. The prevalence of resistance to these agents appears to be high in many areas, particularly in the private sector in South Africa. In areas known to have a low prevalence of macrolide resistance, such as in many of the public sectors, the continued use of macrolides/azalides as monotherapy in young, previously healthy adults, who have not recently been exposed to antibiotics, may still be acceptable. A thorough knowledge of common pathogens and their usual susceptibility pattern in one's own area of practice is therefore essential.
- Telithromycin. This agent has *in vitro* activity against macrolide/azalide-resistant *S. pneumoniae.* Like the fluoroquinolones, it is recommended that this agent is not used as routine first-line therapy, but reserved for patients with severe allergy to standard beta-lactam agents, for known or suspected cases of infection with highly penicillin- or macrolide-resistant pneumococci, and for cases in which initial therapy with other antimicrobial agents has failed.
- Tetracycline/doxycycline. The considerable and increasing resistance of *S. pneumoniae* to tetracycline/doxycycline in South Africa limits its general use as monotherapy for CAP.

9.2 Hospitalised patients

9.2.1 Young patients <65 years of age, with no comorbid illness

The treatment of choice is high doses of parenteral penicillin or ampicillin or amoxycillin.

Alternative therapy may be an intravenous anti-pneumococcal fluoroquinolone, with the same considerations as described above.

9.2.2 Elderly patients ≥65 years and/or adults with comorbidity including patients with HIV infection

The treatment of choice is either amoxycillin-clavulanate or a selected second-generation cephalosporin (cefuroxime) or a selected third-generation cephalosporin (ceftriaxone or cefotaxime) or ertapenem in specific circumstances (see 11.6 below). It is further recommended that these agents be given parenterally initially, at least until the temperature settles. It is best to avoid aminoglycosides in the elderly. An alternative choice is an intravenous anti-pneumococcal fluoroquinolone, particularly in the setting of severe beta-lactam allergy.

9.3 Additional therapy for both non-hospitalised and hospitalised cases

A macrolide, azalide, tetracycline or telithromycin is recommended on its own or as additional therapy for any patient being treated with a beta-lactam antibiotic in the case of suspected or proven infection with the so-called 'atypical pathogens'. While clinical features often do not allow the accurate differentiation of 'atypical infections' from the more common bacterial causes, it may be appropriate to add one of these agents to standard therapy in cases with atypical or unusual features, or in cases not responding to initial antibiotic treatment (see also 9.5 below – combination therapy).

9.4 Severely ill adults

The treatment of choice is a combination of parenteral amoxycillin-clavulanate or a parenteral second-generation cephalosporin (cefuroxime), or a third-generation cephalosporin (ceftriaxone or cefotaxime) or ertapenem in specific circumstances (see 11.6), together with an aminoglycoside (gentamicin or amikacin or tobramycin) and a macrolide (erythromycin, clarithromycin or azithromycin). The aminoglycoside is added initially because of the relatively high prevalence of CAP associated with aerobic Gram-negative bacilli documented previously in various intensive care unit studies in South Africa. The aminoglycoside may be stopped if a micro-organism other than a Gram-negative bacillus is isolated.

Alternative treatment may include an anti-pneumococcal fluoroquinolone, particularly in the setting of severe beta-lactam allergy. However, there are no data on whether these agents are adequately effective as monotherapy in critically ill cases and therefore at present, in this setting, it is recommended that if they are used it should be together with another antibiotic, such as a beta-lactam agent or an aminoglycoside.

9.5 Combination therapy

There is emerging evidence that in patients with more severe pneumonia, combination antibiotic therapy, most commonly the addition of a macrolide agent to standard beta-lactam therapy, may be associated with a better outcome than monotherapy. Although the studies have been retrospective or purely observational in design the benefit in outcome has been shown particularly in sicker, hospitalised patients with pneumonia, including the sub-set of patients with bacteraemic pneumococcal infections. The current guideline recommends combination antibiotic therapy in severely ill patients with pneumonia (see section 8 above), admitted to hospital for intravenous antibiotic therapy, in line with most international pneumonia guidelines.

9.6 Special clinical situations

9.6.1 Aspiration pneumonia

Aspiration may be a factor in the pathogenesis of all categories of CAP, but is a particular problem in the elderly and in the presence of conditions such as alcoholism, epilepsy and various neurological disorders, including cerebrovascular accident. When macro-aspiration is suspected, antibiotic cover for anaerobic organisms must be provided. Amoxycillin-clavulanate alone affords adequate anaerobic cover, but oral or intravenous metronidazole may be added to any of the other regimens mentioned above. An alternative is ertapenem in specific circumstances (see 11.6).

9.6.2 HIV-seropositive patients

Pneumonia, including infections with the common bacterial pathogens, is a common presenting symptom and is the AIDS-defining infection in a significant proportion of HIV-seropositive patients. It is therefore recommended that HIV testing be offered to all patients with pneumonia. It is rarely necessary for this to be done at the time of presentation, and instead it should be offered when the patient has improved from the acute illness and has received appropriate counselling. There is considerable evidence that prophylaxis with co-trimoxazole (recommended dosage is 2 single-strength tablets (trimethroprim 80 mg/sulfamethoxazole 400 mg) daily) in HIV-seropositive patients not only protects against *P. jirovecii* pneumonia, but also significantly reduces the incidence of pneumonia with usual bacterial pathogens. In the absence of antiretroviral therapy, co-trimoxazole prophylaxis reduces hospitalisation and mortality by 40 - 45% in association with the latter infection.

In HIV-infected patients presenting acutely with bilateral pulmonary infiltrates suspected to be due to *P. jirovecii*, empirical therapy with co-trimoxazole should be given, either on its own or in addition to standard antibacterial therapy. The usual dose of co-trimoxazole in adults is 4 tablets (single-strength) orally 6-hourly or 4 ampoules (trimethoprim 320 mg and sulfamethoxazole 1 600 mg) intravenously 6-hourly. Hypoxic patients should also be given adjunctive therapy with corticosteroids.

10. Initiation and duration of antibiotic therapy and switch to oral agents

It is recommended that empiric therapy for patients with CAP is initiated as soon as possible. Some studies have suggested that in patients with pneumonia started on antibiotics within 4 - 8 hours of presentation to hospital there is a better outcome. The optimal duration of parenteral antibiotic therapy and overall duration of antibiotic treatment is uncertain. The usual recommendation is that antibiotics be given for 5 - 7 days for 'usual' bacterial infections and for 14 days for severe *Legionella* infections. In patients initially on IV therapy 'switch' to oral agents may be made earlier in milder cases, particularly in those demonstrating a satisfactory clinical response in the first 48 - 72 hours. Switching from a parenteral to an oral antibiotic is made easier by the availability of agents such as amoxycillin-clavulanate, cefuroxime, and moxifloxacin or levofloxacin which have both parenteral and oral forms, particularly because of their high systemic bioavailability.

11. Additional consideration in antibiotic therapy and dosages

The current guideline is designed to ensure the recommendation of effective antibiotic cover for the most common micro-organisms involved in CAP. However, cognisance also needs to be taken of the problem of increasing antibiotic resistance, both locally and internationally. Inappropriate selection of antibiotics, dosing schedules and length of treatment are the major reasons for emergence of resistance. It is hoped that the appropriate use of antibiotics will reduce this phenomenon. The following notes regarding antibiotics are intended for guidance in their correct selection.

11.1 Penicillin and aminopenicillins

There is increasing resistance of *S. pneumoniae* to penicillin on the basis of alterations in the penicillin-binding proteins. Most of the current resistance is in the intermediate range. For respiratory tract infections the recommended higher doses of parenteral penicillin and aminopenicillins will still provide more than adequate cover for these resistant pneumococcal infections. Risk factors for infection with beta-lactam-resistant pneumococci in CAP for which such higher doses of intravenous and oral beta-lactams are mandatory include:

- age >65 years
- β-lactam therapy within past 3 months
- alcoholism
- immune suppression (including the use of corticosteroids)
- multiple medical comorbidities
- exposure to children in day care.

Emerging resistance among *H. influenzae* isolates to the aminopenicillins, on the basis of beta-lactamase production, has been documented. In situations where there is concern about beta-lactamase production by the infecting organisms, e.g. in patients with COPD colonised by such organisms, amoxycillin-clavulanate is the preferred antibiotic.

Parenteral

Penicillin G	2 - 4 million units 6-hourly
Ampicillin or amoxycillin	1 - 2 g 6-hourly
Amoxycillin-clavulanate	1.2 g 8-hourly.

Oral

Amoxycillin	1 g 8-hourly
Amoxycillin-clavulanate	1 g 12-hourly or 2 g sustained release (SR) 12-hourly (other dosing regimens, which may be less costly in some settings, such as the public hospitals, include 625 mg tablets given 8-hourly or 375 mg tablets together with 500 mg amoxycillin given 8-hourly). Amoxycillin-clavulanate slow-release increases the time above the minimum inhibitory concentration (MIC) of amoxicillin, thus enhancing bacteriological efficacy in resistant pneumococcal strains.

11.2 Macrolide or azalide

There is more than one mechanism of resistance, including both low-level (efflux-mediated) and high-level (ribosomal-mediated) resistance. More recently isolates with both mechanisms of resistance have been described. The commonest mechanisms in South Africa are associated with high-level resistance, which cannot be overcome by increasing the dose of the antibiotic. These antibiotics may therefore be unsuitable as monotherapy for CAP in some parts of South Africa, particularly in the private sector. Their use as alternative monotherapy may still be considered in areas where the prevalence of resistance is known to be low, such as in many parts of the state sector, especially in young, otherwise previously healthy patients who have not recently been exposed to antibiotics. They are nevertheless the drugs of choice for 'atypical infections' and are recommended as an important part of combination therapy, as discussed above.

Parenteral

Erythromycin	4 - 5 mg/kg 6-hourly (usually administered as 1 g 6-hourly)
Clarithromycin	500 mg 12-hourly
Azithromycin	500 mg daily.

Oral

Erythromycin	500 mg 6-hourly
Clarithromycin	500 mg 12-hourly
Clarithromycin	1 g extended release (XL) daily
Azithromycin	500 mg daily.

11.3 Ketolides

Telithromycin is an antibacterial agent that belongs to a new chemical family – the ketolides. It has a broad spectrum of antibacterial activity, which encompasses penicillin-resistant and erythromycin-resistant *S. pneumoniae,* as well as 'atypical' micro-organisms.

Oral

Telithromycin	800 mg daily.

11.4 Fluoroquinolones

The earlier drugs in this class such as ciprofloxacin offered activity against Gram-negative organisms, but relatively poor Gram-positive cover. The newer agents have enhanced antipneumococcal activity. The most active appear to be gemifloxacin and moxifloxacin followed by levofloxacin. These agents provide a spectrum of activity against both typical and atypical organisms found in CAP. In order to limit the development of resistance to these agents, it is suggested that their use be restricted to the indications discussed above.

Because of fluoroquinolone failures in this setting, it has been recommended that recent exposure of a patient to this class of antibiotic should be considered a contraindication to the use of another fluoroquinolone for the empiric treatment of CAP in the same individual.

Parenteral

Levofloxacin (high doses)	500 mg 12-hourly or 750 mg daily
Moxifloxacin	400 mg daily.

Oral

Gemifloxacin	320 mg daily
Levofloxacin (high doses)	500 mg 12-hourly or 750 mg daily
Moxifloxacin	400 mg daily.

11.5 Cephalosporins

The cephalosporin antibiotics recommended in the various sections of the guideline include second-generation agents, cefuroxime or cefpodoxime and the non-pseudomonal third-generation agents, ceftriaxone and cefotaxime. The advantage of the second-generation cephalosporins is that they retain Gram-positive cover and so still provide adequate cover (although they are not the antibiotic of choice) for *S. aureus* infections. They may also be given orally or parenterally, which allows flexibility in their use and rapid-switch therapy. Owing to emerging resistance to cephalosporins, it is suggested

that these agents be given in high dosages. The advantages of the third-generation cephalosporins include greater Gram-negative cover and ease of use. Cost considerations need to be taken into account in the final choice.

Parenteral (second- or third-generation cephalosporin)

Second generation	
Cefuroxime	1.5 g 8-hourly.
Third generation	
Ceftriaxone	2 g daily (up to a maximum of 4 g daily)
Cefotaxime	3 - 4 g daily in 2 - 4 administrations.

Oral (second-generation cephalosporins)

Cefuroxime axetil	750 mg - 1 000 mg 12-hourly
Cefpodoxime	400 mg 12-hourly.

11.6 Ertapenem

Ertapenem is a broad-spectrum carbapenem, active against most common pathogens including pneumococci and anaerobes but not enterococci, non-fermenters (e.g. *P. aeruginosa*) or methicillin-resistant staphylococci. It remains active against most Enterobacteriaceae with extended-spectrum beta-lactamases (ESBLs). In contrast to the other carbapenems it is administered once a day either intravenously or intramuscularly. In the case of CAP, this agent may be indicated in the following specific circumstances, as alternative to the standard therapies described above:

- The elderly, especially high risk-cases with underlying comorbid illness and/or those living in long-term care facilities (LTCF), or in alcoholics where no risk factors for pseudomonal infections are present (see paragraph 4.7, risk factors for pseudomonal infections)
- Aspiration pneumonia/suspected anaerobic infection/lung abscess, such as may occur in patients with neurological disorders or swallowing dysfunction
- Cases known to be, or suspected of being, infected with pathogens resistant to standard antimicrobial agents but retaining susceptibility to ertapenem, especially in cases where Gram-negative pathogens are involved
- Patients who have failed standard first-line antibiotic therapy for CAP, particularly as part of directed antibiotic therapy based on the results of microbiological testing.

Parenteral (intravenous or intramuscular)

Ertapenem	1 g daily.

11.7 Aminoglycosides

These agents are recommended only as part of combination therapy for seriously ill patients in the intensive care unit, with suspected infections with *K. pneumoniae.* Single daily dosing is recommended for the aminoglycosides, together with routine monitoring of trough serum drug levels. Aminoglycosides may be discontinued if organisms other than Gram-negative bacteria are isolated. The maximum duration of therapy in any situation should not exceed 5 days. Aminoglycosides are best avoided, or used with extreme caution, in the elderly and in patients with renal impairment.

Parenteral

Amikacin	15 mg/kg/day (usually 1.5 g daily)
Gentamicin	5 - 7 mg/kg/day (usually 320 mg daily)
Tobramycin	5 - 7 mg/kg/day (usually 320 mg daily).

11.8 Tetracycline

Doxycycline retains activity against *H. influenzae.* There is considerable and increasing resistance of *S. pneumoniae* to this agent. It may still be used as an add-on therapy for patients with infections with 'atypical' pathogens.

Oral

Doxycycline	200 mg stat followed by 100 mg bd.

12. Additional considerations in therapy

Additional supportive measures that may be needed include bed rest, analgesia, attention to nutrition and hydration, support of cardiovascular and renal function and improvement of oxygenation.

13. Assessment of response to therapy

13.1 With appropriate therapy, some improvement in the clinical features should be evident within 24 - 72 hours. In the elderly or in patients with comorbidity, resolution of the clinical features and the chest radiograph is considerably slower.

13.2 Additional considerations in patients who fail to respond to therapy include:

- Use of inappropriate therapy (e.g. specific antibiotics for organisms such as *S. aureus* may be required)
- Presence of unusual pathogens (e.g. opportunistic pathogens such as *P. jirovecii*)
- Associated tuberculosis
- Non-infective illness (e.g. pulmonary embolism, sarcoidosis and lung carcinoma)
- Complications of pneumonia (e.g. empyema, sepsis syndrome).

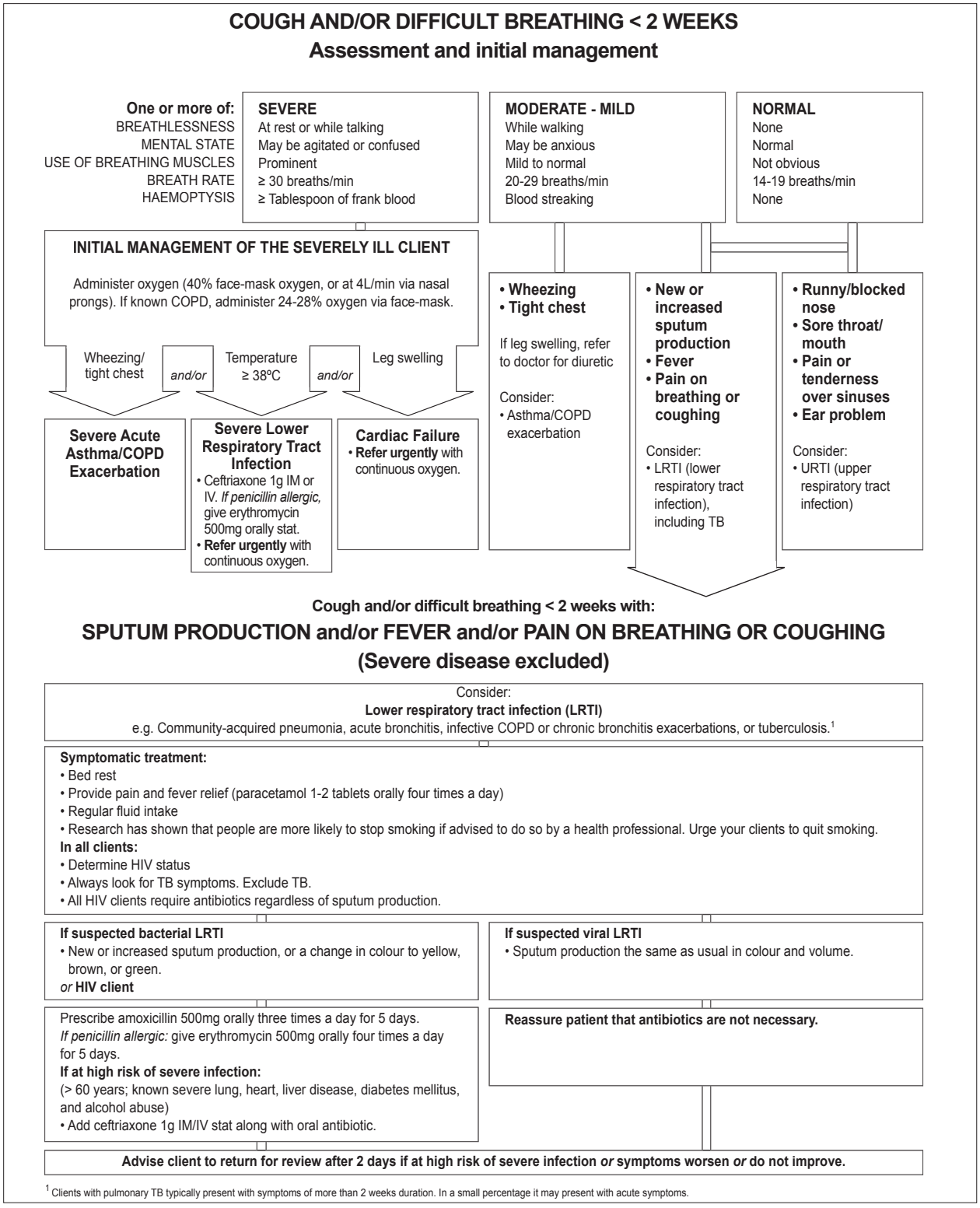

Fig. 3. Algorithm for the diagnosis and initial management of lower respiratory tract infections in primary care – from the PALSA PLUS guideline developed for use in primary care clinics in South Africa. The initial step is recognition and grading of symptoms of lower respiratory tract infection. In patients with features of severe disease, urgent referral is preceded by a single dose of broad-spectrum antibiotic to cover common community-acquired pathogens. For those with milder presentations, amoxicillin (or erythromycin in penicillin-allergic patients) is recommended, but advice on smoking cessation and testing for HIV is offered to all. Sputum examination for tuberculosis is performed on those with suggestive symptoms.

14. Influenza and pneumococcal vaccination guidelines

Implementation of the South African National Guideline for the prevention of influenza and pneumococcal infections may assist in preventing CAP (see www.pulmonology.co.za).

15. Disclaimer

This statement is published for educational purposes only. The recommendations are based on currently available scientific evidence together with the consensus opinion of the authors.

Annexure A: Working Group

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Annexure B: Methodology

A decision to revise the existing national clinical guidelines on the management of community-acquired pneumonia in adults was taken by the Executive Committee of the South African Thoracic Society. C Feldman, A J Brink and G A Richards undertook an initial redraft of the original document. The redrafted guideline was circulated to the members of the working group who still resided in South Africa. Additional members were added. The group was chosen to ensure adequate national representation, particularly from members of the South African Thoracic Society, the Critical Care Society of Southern Africa, and the Federation of Infectious Diseases Societies of Southern Africa. The redraft was then edited to include suggestions and recommendations from the working group. Any contentious issues were dealt with by circulation to the working group. The final document was sent to all members for final approval.

Annexure C: Assessment and initial management of suspected pneumonia in primary care clinics

A large proportion of patients with CAP in South Africa present to primary care clinics. Early recognition and treatment with an effective antimicrobial, particularly in those at risk because of concurrent disease (e.g. HIV infections), is likely to improve clinical outcomes and reduce mortality. Management and treatment is provided in accordance with diagnostic methods and essential drugs (specified in the Essential Drug List for Primary Care of the National Department of Health) at these facilities. Consequently, the approach in primary care clinics, though similar to the standard recommendations provided in this CAP guideline, differs in several respects.

Primary care clinic staff are provided with an integrated management plan for the diagnosis and management of patients with respiratory symptoms (PALSA PLUS – a local adaptation of the Practical Approach to Lung Health (PAL) developed by the World Health Organization). The management algorithm from the PALSA PLUS, which details the recognition of patients with lower respiratory tract infections, particularly those with severe disease who require immediate management including initiation of antibiotics, and referral, are presented in Fig. 3. The need to establish HIV status through testing in all patients with respiratory tract infections, and to look for symptoms of tuberculosis is emphasised. The selection of antibiotics (amoxicillin or erythromycin in penicillin-allergic patients, and a single dose of IM or IV ceftriaxone in those who are in a high risk category) is consistent with the EDL Standard Treatment Guidelines for these facilities.