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COMMUNITY-ACQUIRED PNEUMONIA IN CHILDHOOD GUIDELINES

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SAMJ

CLINICAL GUIDELINE

Diagnosis and Management of Community-Acquired Pneumonia in Childhood – South African Thoracic Society Guidelines

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Background. Community-acquired pneumonia (CAP) is a major cause of morbidity and mortality in South African children. The incidence, severity and spectrum of childhood pneumonia have changed owing to the HIV epidemic. Increasing emergence of antimicrobial resistance necessitates a rational approach to the use of antibiotics in pneumonia management.

Objective. To develop guidelines for the diagnosis, management and prevention of CAP in South African children.

Methods. The Paediatric Assembly of the South African Thoracic Society established five expert subgroups to address: (*i*) epidemiology and aetiology; (*ii*) diagnosis; (*iii*) antibiotic treatment; (*iv*) supportive therapy; and (*v*) prevention of CAP. Each subgroup developed a position paper based on the available published evidence; in the absence of evidence, expert opinion was accepted. After peer review and revision, the position papers were synthesised into an overall guideline which was further reviewed and revised.

Recommendations. Recommendations based on epidemiological factors include a diagnostic approach, investigations, supportive therapy, appropriate antibiotic treatment and preventive strategies. Specific recommendations for HIV-infected children are provided.

Validation. These guidelines are based on the available evidence supplemented by the consensus opinion of South African experts in paediatrics, paediatric pulmonology, radiology, infectious diseases and microbiology. Published international guidelines have also been consulted.

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1. Introduction

Pneumonia is a major cause of morbidity and mortality in South African children,[1] and this burden has been exacerbated by the HIV epidemic. Early and appropriate treatment of pneumonia can reduce morbidity and mortality,[2] which has been the rationale for the development of guidelines for the management of community-acquired pneumonia (CAP). In developing these guidelines, consideration has been given to the high prevalence of HIV infection in South Africa and its impact on childhood pneumonia.[3] These guidelines have also taken into consideration the current policy regarding treatment of pneumonia, including recommendations contained in the Integrated Management of Childhood Illness (IMCI) strategy which is currently being implemented in South Africa.

Published guidelines for the management of CAP in children have been developed by the British Thoracic Society[4] and the Canadian Medical Association;[5] however, there are no published guidelines for children in developing countries or in high HIV prevalence regions.

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2. Evolution of the guideline

2.1 Aim of the guideline

This document aims to provide guidelines for diagnosis and effective management of children with CAP so as to improve pneumonia-associated morbidity and mortality in South Africa. The guidelines aim to provide recommendations for effective therapy and to minimise the development of bacterial resistance through judicious use of antibiotics. The guidelines have been developed for management of children with simple pneumonia without underlying disease, except for HIV infection. The guidelines are aimed at children from birth to 12 years of age, receiving care at primary, secondary or tertiary care facilities. These guidelines do not address the treatment of children admitted to a paediatric intensive care unit (PICU), nor do they cover therapy of nosocomial pneumonia.

2.2 Process of guideline development

Five subgroups covering different aspects of childhood CAP were established under the direction of the Paediatric Assembly of the South African Thoracic Society (SATS). Position papers were developed by a group of experts for each subgroup in the following areas: (*i*) epidemiology and aetiology of CAP; (*ii*) diagnosis of CAP; (*iii*) antibiotic treatment of CAP; (*iv*) supportive treatment of CAP; and (*v*) prevention of CAP.

The papers were based on the best available published evidence; in the absence of evidence, expert opinion was accepted. Each position paper underwent a process of peer review and revision. The position papers were synthesised into this overall guideline, which was peer-reviewed and revised accordingly.

This guideline comprises a summary document for the diagnosis and treatment of children with CAP that can be widely implemented. A second, more detailed, comprehensive document comprising the separate position papers on which the recommendations are based will be published independently. Regular review of the literature and updating of the guideline is foreseen.

3. Definition of CAP

CAP can be defined as acute infection (of less than 14 days' duration), acquired in the community, of the lower respiratory tract leading to cough or difficult breathing, tachypnoea or chest-wall indrawing.

4. Epidemiology of CAP

CAP is a major cause of health care utilisation, hospitalisation and death in children in developing countries including South Africa.[1,3,6,7] This has been exacerbated by the HIV epidemic, which has increased the incidence, severity and case fatality from childhood pneumonia.[3,7] CAP accounts for between 30% and 40% of hospital admissions, with associated case fatality rates of between 15% and 28%.[7,8] Risk factors for CAP are shown in Table I.

Table I. Risk factors for CAP

Medical
Age < 1 year
Prematurity
Malnutrition
Immunosuppression
Social/environmental
Overcrowding
Inadequate housing
Passive tobacco smoke exposure
Indoor fuel exposure
Winter season

5. Aetiology of CAP in children

Rational treatment for pneumonia depends on knowing the most likely pathogens in each community, as the relative frequency of different agents may vary from one geographical region to another. However, identifying the causal pathogen, particularly bacteria, in children with lower respiratory tract infections is particularly difficult. Furthermore, identification of an organism does not establish causality. Mixed bacterial and viral infections may occur in 30 - 40% of cases of childhood CAP. The possible causes of pneumonia in children are presented in Table II. Additional pathogens occurring in HIV-infected children, including opportunistic infections, are listed in Table III.

Table II. Common causes of CAP in children*

Bacteria
Streptococcus pneumoniae
Haemophilus influenzae
Staphylococcus aureus
Mycobacterium tuberculosis
Moraxella catarrhalis
Atypical bacteria
Mycoplasma pneumoniae
Chlamydia trachomatis
Chlamydia pneumoniae
Viruses
Respiratory syncytial virus
Human metapneumovirus
Parainfluenza virus types 1 and 3
Adenovirus
Influenza A or B
Rhinovirus
Measles virus

*The predominant pathogens vary for children of different age groups as follows:
For children < 2 months: Gram-negative bacteria, Group B streptococcus, *S. aureus*, *C. trachomatis*, viruses.
For children 2 months - 5 years: *S. pneumoniae*, *H. influenzae*, *S. aureus*, viruses.
For children > 5 years: similar pathogens as 2 mo. - 5 years age group; in addition *M. pneumoniae*, *C. pneumoniae*.

Table III. Additional pathogens causing CAP in HIV-infected children

Bacteria
Non-typhoid salmonella
Klebsiella pneumoniae
Streptococcus milleri
Escherichia coli
Methicillin-resistant *Staphylococcus aureus*
Fungi
Pneumocystis jiroveci (previously *Pneumocystis carinii*)
Candida species
Viral
Cytomegalovirus
Varicella zoster virus

Bacteria are the major cause of pneumonia mortality in both HIV-uninfected and HIV-infected children.[2,3,6] *Streptococcus pneumoniae* is the commonest cause of bacterial pneumonia. Other bacteria isolated are *Staphyloccocus aureus* and less often *Haemophilus influenzae* type b (Hib). The routine immunisation of children against Hib has decreased the incidence of pneumonia due to this bacterium, although non-typable strains are still responsible for a small proportion of pneumonia in South Africa. Based on clinical studies evaluating the efficacy of Hib conjugate vaccine, it is estimated that Hib may be responsible for approximately 20% of childhood pneumonia

associated with alveolar consolidation on chest radiographs (CXRs).[9,10] Similarly, based on recent experience with the pneumococcal conjugate vaccine, it is estimated that at least 20 - 37% of pneumonia associated with alveolar consolidation on CXRs is due to pneumococci.[11-14]

Respiratory syncytial virus (RSV) is the commonest cause of viral CAP, especially in the first 3 years of life. RSV causes significant mortality and morbidity in both HIV-infected and uninfected children, especially in children born prematurely and who are less than 6 months of age at the onset of the RSV season. HIV-infected children with RSV are more likely to develop pneumonia rather than bronchiolitis compared with HIV-uninfected children. Concurrent bacterial infection has been reported in 30 - 40% of children hospitalised with viral pneumonia.[15] A newly described paramyxovirus, human metapneumovirus (hMPV), is emerging as an important respiratory pathogen in children and produces a similar spectrum of disease to RSV.[16,17]

Pneumocystis jiroveci (previously *P. carinii*) pneumonia (PCP) is a common, serious infection among HIV-infected children and is associated with high mortality. Infants aged 6 weeks - 6 months are at highest risk for infection; PCP is the predominant cause of pneumonia mortality in HIV-infected children less than 6 months of age.[18] PCP has also been described in malnourished children and in young HIV-exposed uninfected infants.

Culture-confirmed *Mycobacterium tuberculosis* has been identified in 8% of HIV-infected and HIV-uninfected children hospitalised for acute pneumonia.[19-21]

6. Diagnosis of CAP

The diagnosis of CAP should be considered in any child who has an acute onset of respiratory symptoms, particularly cough, fast breathing or difficulty breathing. Diagnosis includes clinical evaluation, radiographic evaluation and aetiological investigations to: (*i*) establish whether pneumonia is present; (*ii*) assess the severity of pneumonia; and (*iii*) determine the causative organism. In general, diagnostic investigations to determine the cause of pneumonia are indicated only in children requiring hospitalisation.

6.1. Clinical evaluation

6.1.1 Determining whether pneumonia is present and assessing severity

A history and clinical examination are the basis for diagnosing pneumonia and evaluating the severity of illness. In primary care the physical examination should include assessment of the child's general appearance, measurement of the respiratory rate, evaluation of the work of breathing and assessment of oxygenation. Auscultation of the chest should be done where possible.

The principal symptoms of pneumonia are cough, dyspnoea or tachypnoea. For diagnosis of pneumonia and assessment of the severity of respiratory illness simple **clinical signs** (respiratory rate and lower chest-wall indrawing) are sensitive and moderately specific. World Heath Organization (WHO) guidelines[22] recommend the following:

- That pneumonia be diagnosed when a child older than 2 months has a cough or difficult breathing with tachypnoea defined as: (*i*) > 50 breaths per minute (bpm) for infants 2 - 12 months of age; and (*ii*) > 40 bpm for children 1 - 5 years of age.
- That severe/very severe pneumonia be diagnosed when a child has lower chest wall retractions *or* stridor *or* a general danger sign.

The presence of wheezing without bronchial breathing on auscultation is suggestive of a non-bacterial cause for the lower respiratory tract illness.[22]

The presentation of CAP can range from mild to severe life-threatening illness. It is essential to distinguish and refer children needing hospitalisation (Table IV) from those who can be managed as outpatients. Assessment of the **general appearance** of the child is helpful in determining the severity of illness. The WHO IMCI guidelines[23] define specific 'danger signs' that indicate severe disease requiring referral to hospital including inability to drink, convulsions, abnormal sleepiness, or persistent vomiting. All children with pneumonia under the age of 2 months require admission to hospital (Table IV).

Table IV. Indications for admission to hospital

All children younger than 2 months
Children older than 2 months with:
Impaired level of consciousness
Inability to drink or eat
Cyanosis
Stridor in calm child
Grunting
Severe chest-wall indrawing
Room air $SaO_2 \leq 92\%$ at sea level or < 90% at higher altitudes
Severe malnutrition
Family unable to provide appropriate care
Failure to respond to ambulatory care or clinical deterioration on treatment

Assessment of **oxygenation** is important in the evaluation of a child with pneumonia and pulse oximetry should be performed on all children seen at a hospital. To ensure an accurate reading, a paediatric wrap around probe should be used. Children with a saturation of less than 92% at sea level or less than 90% at higher altitudes (e.g. Johannesburg) should be considered for hospital admission and supplemental oxygen.[24]

6.1.2 Impact of HIV infection on clinical diagnosis of CAP

Clinical signs of CAP are similar in HIV-infected and HIV-uninfected children.[19] However, pneumonia resulting from opportunistic pathogens should also be considered in HIV-infected children. Of these, PCP is the most common and serious infection among infants, occurring commonly at 6 weeks - 6 months of age. PCP is frequently (20 - 40%) the initial presenting feature of AIDS in HIV-infected children not taking co-trimoxazole prophylaxis.[25,26] Although PCP may present with a tetrad of features comprising tachypnoea, dyspnoea, fever and cough, these are not specific for pneumonia caused by *P. jiroveci*. Hypoxia may be prominent and rapidly progressive. Other stigmata of AIDS such as hepatosplenomegaly and generalised lymphadeno-pathy are not always present and adventitious sounds in the chest may be absent despite clinical signs of severe respiratory distress.

6.2 Radiological diagnosis

A CXR may be useful for confirming the presence of pneumonia and detecting complications such as a lung abscess or empyema. CXRs are however less useful for discriminating between causative pathogens and cannot accurately discriminate between viral and bacterial pneumonia.[27] In addition, there is wide inter- and intra-observer variation in the interpretation of CXRs.[28] Overall, a CXR does not result in improved outcome or change of treatment in an ambulatory setting.[29] The cost, radiation exposure, need for infrastructure, staffing and wide observer variation in interpretation all mitigate against routine use of CXRs. There is also no evidence that a routine lateral CXR improves the diagnostic yield in children with acute pneumonia except if tuberculosis (TB) is suspected.[30]

Indications for CXR include: (*i*) clinical pneumonia unresponsive to standard ambulatory management; (*ii*) suspected pulmonary TB; (*iii*) suspected foreign body aspiration; and (*iv*) hospitalised children to detect complications.

CXRs may also be considered in children presenting with high fever, leukocytosis and no obvious focus of infections, since approximately 26% of such children may have radiographic evidence of pneumonia.[31]

6.2.1 Follow-up CXRs

Follow-up films after acute uncomplicated pneumonia are of no value where the patient is asymptomatic.[32] A follow-up CXR should be done: (*i*) in children with lobar collapse; (*ii*) to document resolution of a round pneumonia (as this may mimic the appearance of a Ghon focus); and (*iii*) in those with ongoing respiratory symptoms.

6.2.2 Impact of HIV on radiological diagnosis

The interpretation of CXR changes is even more difficult in HIV-infected children as chronic radiological lung changes are common, especially with increasing age.[33] Increased bronchovascular markings, reticular densities or bronchiectasis are the commonest chronic radiological changes. Diffuse nodular densities and hilar or mediastinal adenopathy occurring in lymphocytic interstitial pneumonia (LIP) may resemble TB, making it difficult to distinguish between the two. Diffuse or scattered ground-glass opacification is a common manifestation of severe PCP, but no radiographic pattern is specific for PCP.[34]

6.3 Aetiological diagnosis

The clinical and radiographic features of CAP cannot reliably determine the aetiology of pneumonia. A causative agent should be sought in hospitalised children (Table V) as identification of a pathogen may allow for more focused effective therapy, provide important epidemiological data and allow for the implementation of infection control measures to reduce the risk of nosocomial transmission of specific pathogens. However, identifying a specific aetiological agent is difficult and may not be possible in most children. Diagnostic testing should not lead to delay in initiation of therapy as this may adversely affect outcome. Empirical treatment should be commenced based on the most likely pathogen and modified according to microbiological results.

The following points should be considered when investigating the aetiology:

- **General tests of infection** including acute phase reactants (erythrocyte sedimentation rate (ESR), C-reactive protein (CRP)), white cell count (WBC), neutrophil count and procalcitonin may not differentiate between bacterial and viral pneumonia.[35-37]
- **Blood culture** may be useful to identify bacterial pathogens and their antimicrobial sensitivity, but only about 5% of blood cultures are positive in HIV-uninfected children with bacterial CAP. The sensitivity of blood cultures is greater in HIV-infected children, in whom approximately 18% of cultures are positive.[14]
- **Pleural fluid**, if present, should be aspirated and investigated for infectious agents.
- Specimens for culture from the lower respiratory tract can be obtained using sputum induction,[38] endotracheal aspiration in intubated children and bronchoalveolar lavage (BAL). The isolation of bacteria from these samples may, however, represent contamination with bacteria that normally colonise the nasopharynx.
- Tuberculin skin testing (Mantoux method) and induced sputum or gastric lavage are indicated when TB is suspected.[39]
- There is a high prevalence (at least 30 - 40%) of bacterial co-infection in children who are hospitalised with viral pneumonia.[40]

Table V. Investigations in children hospitalised for pneumonia

Investigation	Limitations	Usefulness
Pulse oximetry/ arterial blood gas		Accurate measurement of hypoxia and guide use of O_2
Chest radiograph	Unable to distinguish aetiology	Assess extent of pneumonia Detect complications
Blood culture	Positive in less than 20% of cases Cost	Identification of type and susceptibility of bacterial pathogen/s Targeted antibiotic therapy Epidemiological surveillance
Lower respiratory tract secretions (induced sputum, ET aspirate or BAL) for *P. jiroveci* stain	Cost May be difficult to perform	Diagnosis of PCP, targeted antibiotic and steroid therapy
Lower respiratory tract secretions (induced sputum, ET aspirate or BAL) for *M. tuberculosis* stain and culture	Positive in some cases only Induced sputum preferable to ET aspirate or BAL Infection control to prevent nosocomial transmission needed	Microbiological confirmation of TB Determine sensitivity of isolate for targeted therapy Obtain sputum for AFB stain from mother or caregiver if symptomatic
Three gastric lavages for *M. tuberculosis* stain and culture	Positive in a minority of suspected cases Requires overnight fast, hospitalisation Recommended when induced sputum not possible	Microbiological confirmation of TB Determine sensitivity of isolate for targeted therapy
Tuberculin skin test	False-negative reactions in malnutrition, immunosuppression, overwhelming infection Requires careful technique and reading	Evidence of TB infection
NPA for viral detection	Cost Does not exclude bacterial coinfection	Identification of viral pathogen Cohorting of patients to prevent nosocomial transmission Epidemiological surveillance
NPA for *C. trachomatis*	Cost, limited availability	Confirmation of *C. trachomatis* pneumonia in infants when chlamydia suspected Targeted antibiotic therapy of infant and mother
Aspiration of pleural fluid for WBC, glucose, protein, Gram and AFB stains and for culture	May not be possible in loculated effusions	Identification of pathogen Targeted antibiotic therapy May identify need for intercostal drain insertion
Erythrocyte sedimentation rate, C-reactive protein, WBC, neutrophil count, procalcitonin	Do not accurately distinguish between viral and bacterial pneumonia	Combination of tests may provide some evidence of bacterial infection

BAL = bronchoalveolar lavage; ET = endotracheal; AFB = acid-fast bacillus; NPA = nasopharyngeal aspirate; WBC = white cell count; TB = tuberculosis.

7. Antibiotic use in the treatment of CAP

The choice of antibiotics is influenced by the epidemiology of the infecting organisms in the area, prevalence of drug resistance, HIV prevalence and available resources. As it is difficult to distinguish between pneumonia caused by bacteria and that caused by viral infection, and because of the frequency of mixed bacterial-viral infections (at least 30 - 40%),[40] children with pneumonia require an antibiotic. Most bacterial pneumonia is responsive to amoxicillin, making it the antibiotic of choice. The following additional factors need to be taken into account when prescribing antibiotics for pneumonia.

1. The aetiology of pneumonia in children differs with age. Children younger than 2 months have more Gram-negative infections and therefore require an aminoglycoside or a cephalosporin, while children older than 5 years have more infections caused by *Mycoplasma pneumoniae* and *Chlamydia pneumoniae* and may therefore require a macrolide.[41,42]

2. HIV-infected children requiring hospitalisation may have pneumonia caused by Gram-negative bacteria.[18, 20] Children with a high risk of being HIV-infected or who have symptomatic HIV disease or who are severely malnourished should have an aminoglycoside added to their empirical treatment regimen, or be covered with an alternative regimen that provides adequate effective treatment against Gram-negative bacteria.

3. If PCP is suspected, co-trimoxazole should be added. All HIV-exposed children < 6 months of age should be treated empirically for PCP if hospitalised for severe pneumonia, unless HIV infection status is confirmed to be negative and the child is not breastfed. Empirical treatment with co-trimoxazole in addition to amoxicillin and an aminoglycoside should also be considered for older HIV-infected children with features of AIDS who are not on co-trimoxazole prophylaxis. For children with suspected PCP and hypoxia, corticosteroids may be of benefit.

4. When *S. aureus* is suspected, cloxacillin is the drug of choice. This should be considered if there is radiological evidence of pneumatocele, empyema or abscess formation or if the child remains pyrexial 48 hours after starting amoxicillin. In HIV-infected children, approximately 60% of community-acquired *S. aureus* may be resistant to cloxacillin and require treatment with vancomycin.[21]

5. There is an increase in the incidence of *S. pneumoniae in vitro* resistance to the beta-lactam antibiotics, as well as other classes of antibiotics.[43] However, the favourable pharmaco-dynamic properties of the penicillins when used in the treatment of pneumococcal pneumonia still makes them the preferred antibiotic in the empirical treatment of pneumococcal pneumonia despite the increase in antibiotic resistance.[43,44] This differs from the antibiotic policy for children with pneumococcal meningitis or otitis media. In children with pneumonia, the increasing resistance of pneumococcus to penicillin can be overcome by giving a higher dose of amoxicillin. Although standard doses of amoxicillin (15 mg/kg/dose three times a day) are likely to treat most cases of pneumococcal pneumonia in South Africa, the use of high-dose amoxicillin (30 mg/kg/dose 3 times a day) is advocated so as to overcome and limit the emergence of resistant pneumococci, and to successfully treat those additional few children with high-level pneumococcal resistance (minimal inhibitory concentrations (MICs) of ≥ 2.0 µg/ml).[45]

Antibiotic recommendations are summarised in Table VI and dosages in Table VII.

7.1 Route of antibiotic administration

Parenteral administration of antibiotics is traumatic to children, expensive and does not improve outcome in uncomplicated pneumonia. Parenteral pencillin G has been reported to have similar efficacy to oral amoxicillin in treatment of severe pneumonia.[46] Parenteral administration should only be given to those children who are severely ill and those with gastrointestinal disturbances (vomiting and diarrhoea) in whom absorption may be problematic. There are no randomised trials indicating when to switch from intravenous to oral therapy; in a child receiving intravenous therapy, oral medication should be considered when clinical improvement has occurred and the child is able to tolerate oral intake.

7.2 Duration of treatment

There are no firm data on the duration of treatment, but it is generally recommended that 5 days of therapy is sufficient for uncomplicated pneumonia. A recent study of HIV-uninfected children with uncomplicated pneumonia reported that the clinical efficacy of 3 days of oral amoxicillin (15 mg/kg/dose) was similar to 5 days for outpatient therapy.[47] Children with *S. aureus* pneumonia should be treated for 14 - 21 days depending on clinical response. Children infected with *M. pneumoniae* or *C. pneumoniae* require erythromycin for 10 days; alternatively the newer macrolides such as azithromycin may be used for 3 - 5 days.

8. Supportive treatment in the management of CAP

In addition to antibiotics, careful supportive management is required for children with CAP.

8.1. Oxygen therapy[48-52]

Oxygen therapy should be used to treat hypoxia. Hypoxaemia can only be accurately assessed if a pulse oximeter is used.

1. When pulse oximetry is available start oxygen therapy when transcutaneous saturation is less than 90 - 92% in room air.

2. When pulse oximetry is unavailable, oxygen therapy should be used when there is: (*i*) central cyanosis; (*ii*) lower chest indrawing; (*iii*) grunting; (*iv*) restlessness; (*v*) inability to drink or feed; and (*vi*) respiratory rate > 70 breaths per minute.

8.1.1 Recommendation for oxygen use[48,53,54]

- Oxygen should be available at any health care facility where sick children are seen regularly.
- If oxygen is required infrequently then cylinders are the most practical source of oxygen. Cylinders also allow oxygen therapy to be used while the patient is transferred to a facility with more resources.
- If oxygen is used more frequently, then oxygen concentrators are the preferred source of oxygen.
- In hospitals with oxygen supplies, wall oxygen units should be available.
- Low-flow flow meters must be available to give appropriate oxygen flow to children. In most hospitals these will be variable orifice units, but fixed orifice units may be more practical in some units.
- Pulse oximetry should be performed when the child is resting and not crying or irritable.

8.1.2 Method of oxygen administration

- Nasal prongs are recommended for most children. Nasal prongs give a maximum fractional concentration of inspired

Table VI. Empirical antimicrobial therapy for paediatric pneumonia

	Ambulant	Hospitalised
0 - 2 mo.	Recommend **hospitalise** all children less than 2 months of age	**1. Ampicillin/penicillin iv + aminoglycoside iv** *or* 2. Ceftriaxone/cefotaxime iv
3 mo. - 5 yrs	**1. Amoxicillin po high dose**	**1. Ampicillin iv/amoxicillin po high dose** *or* 2. Cefuroxime iv/amoxicillin-clavulanic acid po or iv 3. Cefotaxime/ceftriaxone iv Add: cloxacillin if suspect *Staphylococcus aureus*
5 yrs onwards	**1. Amoxicillin po high dose** *or* 2. Macrolide po (erythromycin/clarithromycin/azithromycin) – if suspect *Mycoplasma pneumoniae* or *Chlamydia* spp.	**1. Ampicillin iv/amoxicillin po high dose** *or* 2. Cefuroxime iv/amoxicillin-clavulanic acid po or iv 3. Cefotaxime/ceftriaxone iv Add: cloxacillin if suspect *Staphylococcus aureus* Add: macrolide if suspect *Mycoplasma pneumoniae* or *Chlamydia* spp.

po = oral, iv = intravenous.
Notes:
1. **The first antibiotic is the antibiotic of choice.** Other antibiotics represent second- and third-line choices respectively.
2. Add an aminoglycoside to all hospitalised children known to be HIV-infected, to children at high risk of being HIV-infected, or to severely malnourished children. A cephalosporin may be used as an alternative if there is a low prevalence of extended-spectrum β-lactamase-producing organisms.
3. Add a macrolide if *C. trachomatis* is suspected in children younger than 6 months.
4. Add cotrimoxazole if PCP is suspected in an HIV-exposed child less than a year of age and in any HIV-infected child not taking PCP prophylaxis and not on HAART. For children with suspected PCP and hypoxia, corticosteroids (prednisone 1 mg/kg tapered over 10 - 14 days) may be of benefit.
5. *S. aureus* should be suspected in children who fail to respond to therapy within 48 hours or those with suggestive CXR changes e.g. a pneumatocele, empyema or abscess.
6. *M. pneumoniae* and *Chlamydia* spp. should be suspected if no clinical response to a β-lactam within 48 hours of starting treatment, or if there is wheezing in children older than 5 years of age.
7. High-dose oral amoxicillin may be used in hospitalised children who are able to take medicine orally and in whom there is no risk of aspiration.

oxygen (F_IO_2) of 28 - 35% except in small infants when higher concentrations may be obtained. This method does not require humidification of oxygen and ensures that the child receives oxygen during feeding. Oxygen flows of 0.5 - 1 l/min are required in children less than 2 months old and 2 - 3 l/min in children aged 2 months - 5 years.

- Nasal catheters are usually well tolerated and humidification is not required, but they can be blocked by mucus. Oxygen via nasal catheters gives a maximum F_IO_2 of 35 - 40%
- Nasopharyngeal catheters[55-61] have the advantage of requiring the lowest flow rate to achieve a given oxygen concentration in the airways. Infants under 2 months can usually be treated with 0.5 l/min and infants up to 1 year with 1 l/min. However, humidification of oxygen is required and the catheter may easily block. Further, potentially lethal complications including gastric distention, airway obstruction, apnoea, pneumo-orbitus and pneumocephalus may occur. Continuous skilled nursing is therefore necessary to prevent these complications. Consequently, oxygen administration via nasopharyngeal catheter is *not* recommended.
- Headbox oxygen is well tolerated by young infants. Headbox oxygen requires no humidification but requires a high flow and a mixing device to ensure that the correct F_IO_2 is delivered. This is the *least preferred* method as there is wastage of oxygen and the delivered F_IO_2 is unpredictable.
- Facemask oxygen is designed to deliver 28% - 65% oxygen at a flow rate of 6 - 10 l/min.
- In severely hypoxic infants who are not ventilated, oxygen should be administered using a polymask whereby F_IO_2 concentrations of 60 - 80% may be achieved. The flow rate should be regulated to keep the bag of the mask inflated during inspiration and expiration.

Using the prone position for infants may improve hypoxia and the respiratory system compliance[62] and should be attempted if hypoxia is difficult to treat.

Oxygen should be discontinued when the child is improving clinically and the transcutanous saturation is above 90% in room air.

8.2. Antipyretics and analgesics

An elevated temperature may be useful in fighting infection.[63,64] Temperature should be treated when: (*i*) > 39°C; (*ii*) there is a known risk of febrile convulsions; or (*iii*) there is central nervous system pathology that may be aggravated by high temperature.

Pain associated with pneumonia may be due to pleurisy or to pathology involving the upper airways. Pain or discomfort

Table VII. Antibiotic treatment for CAP

Antibiotic class	Antibiotic	Dosage/kg **per dose**	Maximum dosage **per dose**	Number of daily doses	Route¶
Aminoglycosides	Amikacin	Load 20 mg/kg, then 15 mg/kg	240 - 360 mg trough level < 5 mg/l	1	iv
	Gentamicin	7.5 mg/kg, then 5 mg/kg	240 - 360 mg trough level < 1 mg/l	1	im or iv
Beta-lactams	Amoxicillin*	30 mg/kg	500 mg	3	oral
	Ampicillin	50 mg/kg	2 000 mg	4	iv
	Amoxicillin*-clavulanic acid	30 mg/kg of amoxicillin	500 mg of amoxicillin and 125 mg of clavulanic acid	3	oral or iv
	Cefuroxime	15 mg/kg	500 mg	2	oral
		50 mg/kg	2 000 mg	3	iv
	Ceftriaxone†	50 mg/kg	1 000 mg	1 - 2‡	im or iv
	Cefotaxime†	50 mg/kg	2 000 mg	3	iv
	Cloxacillin	25 mg/kg	500 mg	4	oral
		50 mg/kg	2 000 mg	4	iv
	Crystalline penicillin G§	50 mg/kg	2 000 mg	4	iv
Macrolides	Azithromycin	15 mg/kg first day then 7.5 mg/kg	500 mg day 1, then 250 mg	1	oral
	Clarithromycin	15 mg/kg	500 mg	2	oral
	Erythromycin	10 mg/kg	500 mg	4	oral or iv
Others	Cotrimoxazole for PCP treatment	Loading dose 10 mg/kg of trimethoprim (TMP), then 5 mg/kg TMP	160 mg TMP	4	iv or oral**
	Cotrimoxazole for PCP prophylaxis	5 mg/kg of TMP	80 mg TMP	Daily or 3 times/week	oral
	Vancomycin	10 mg/kg	500 mg trough level < 5 mg/l	3	iv

*High-dose amoxicillin should be used to prevent emergence of pneumococcal resistance.
†Ceftriaxone or cefotaxime is indicated for high-level pneumococcal resistance (MIC ≥ 2 µg/ml).
‡Although ceftriaxone may be given daily, its pharmacokinetic properties support a twice-daily dosing in very ill subjects.
§Crystalline penicillin G may be given 6 times daily for severe infections.
¶For intravenous administration of antibiotics, a saline locked intravenous cannula is optimal.
**Higher doses may be required for oral therapy (20 mg/kg TMP load, then 10 mg/kg).
iv = intravenous; im = intramuscular.

should be treated as it may severely compromise respiratory function and adequate clearance of secretions. The most appropriate agent is paracetamol at a dose of 15 mg/kg/dose given 4 - 6-hourly. If this does not provide adequate analgesia a mixture of paracetamol and codeine (0.5 mg/kg/dose 8-hourly) is very effective. Aspirin is contraindicated in most children because of the association with Reye's syndrome.

8.3. Blood transfusions

Children with haemoglobin levels above 7 g/dl should only be transfused if there is tissue hypoxia or cardiovascular compromise.

8.4. Fluids

Children with uncomplicated pneumonia should receive normal maintenance fluids. Appropriate rehydration is required in children who are dehydrated.

8.4.1 Enteral feeds

Children with pneumonia should be encouraged to feed orally unless they are: (*i*) too distressed to drink or swallow safely; (*ii*) having frequent severe coughing episodes that may be associated with vomiting and possible aspiration of gastric contents; or (*iii*) hypovolaemic with associated poor perfusion.

Breastfeeding should be continued where appropriate. If children are too distressed to take fluid and feeds orally, continuous enteral feeds via a nasogastric tube may be provided. Ensuring adequate caloric intake is essential as there is an excessive demand on the energy reserves in children with pneumonia, in whom the work of breathing is increased. Children should not be starved for more than 24 hours.

8.4.2 Intravenous fluids[65-68]

Intravenous fluids must be used with great care and only if there is adequate monitoring available.

Indications for intravenous fluid in a child with pneumonia include: (*i*) shock; and (*ii*) inability to tolerate enteral feeds.

In children with severe or complicated pneumonia, serum urea and electrolytes should be measured before instituting intravenous fluids as the syndrome of inappropriate antidiuretic hormone secretion (SIADH) is common. In these children, intake should be restricted to 40 - 60% of normal

requirements, i.e. 50 ml/kg/day of intravenous fluids. If hyponatraemia is a problem, fluids containing half normal or isotonic saline should be used.

8.5 Nutrition

Nutrition is of particular concern especially when there are underlying factors such as HIV disease or malnutrition.

8.5.1 Caloric requirements

A minimum of 50 - 60 kcal/kg/day is required by children with pneumonia. In the presence of malnutrition, and following several days of poor nutrition, this needs to be increased considerably. In the early phase of pneumonia, ketosis should be avoided by ensuring adequate carbohydrate intake. With time, a greater proportion of intake can be lipids. The intake of calories should be adequate to meet metabolic requirements and growth.

8.5.2 Vitamin supplementation

Vitamin A should not be given to children with acute pneumonia unless this is measles associated.[69,70] For measles, 200 000 IU vitamin A given on 2 days substantially reduced overall and pneumonia-specific mortality.[70] There is no evidence that vitamin A improves outcome in non-measles pneumonia.[69]

8.5.3 Micronutrient supplementation

In children with acute pneumonia, adjuvant treatment with 20 mg zinc per day until discharge was found to accelerate recovery from severe pneumonia, reducing the duration of hypoxia.[71-73] Zinc should therefore be considered for use in children hospitalised with pneumonia, particularly if there is coexisting malnutrition.[72]

8.6 Indications for transfer and admission to a PICU

A very small proportion of children will require ventilatory support for severe CAP. A child should be transferred to an institution where ventilatory support is possible in the following circumstances: (*i*) failure to maintain a saturation of > 90% on an F_IO_2 of > 70% (i.e. on a polymask); or if the partial pressure of arterial oxygen $(P_aO_2):F_IO_2$ ratio is < 100 (normal is 350); (*ii*) apnoea; (*iii*) hypercarbia with resulting acidaemia (pH < 7.25); and (*iv*) exhaustion, which may be difficult to judge, but should be considered if a child maintains a high respiratory rate or severe chest-wall indrawing.

8.7 Measures of *no value* in the treatment of CAP

- There is no evidence that chest physiotherapy is of benefit in uncomplicated CAP.
- Mucolytic agents are not advised.
- There is no evidence for the use of a head-down position for postural drainage.
- Nebulised bronchodilators or saline do not improve the outcome of CAP.
- There is no evidence to support the use of oral or inhaled corticosteroids.

9. Prevention of childhood CAP

9.1 General preventive strategies[74]

General preventive strategies that may reduce the incidence and severity of pneumonia include the following.

9.1.1 Nutrition

Attention to adequate nutrition and growth monitoring should be encouraged as malnutrition frequently predisposes children to pneumonia. Breastfeeding has been shown to decrease the incidence of pneumonia in young children by up to 32%.[75] Breastfeeding should be encouraged for the first 6 months of life in HIV-unexposed children.

9.1.2 Micronutrient supplementation

HIV-infected or malnourished children should receive micronutrient supplementation as part of routine care. Specific micronutrients that may play a role in prevention of pneumonia include the following.

Vitamin A. Current evidence supports use of vitamin A supplementation for reducing the severity of respiratory complications of measles.[76] However, the association between vitamin A and non-measles pneumonia is unclear. A meta-analysis[77] of the impact of vitamin A supplementation on pneumonia morbidity and mortality reported no consistent overall protective or detrimental effect on pneumonia-specific mortality and no effect on the incidence or prevalence of pneumonia. Routine supplementation with vitamin A for prevention of non-measles pneumonia is therefore currently not recommended.

Zinc. Daily prophylactic elemental zinc, 10 mg to infants and 20 mg to older children, may substantially reduce the incidence of pneumonia, particularly in malnourished children.[78] A pooled analysis[79] of randomised controlled trials of zinc supplementation in children in developing countries found that zinc-supplemented children had a significant reduction in pneumonia incidence compared with those receiving placebo (odds ratio (OR) 0.59 (95% confidence interval (CI): 0.41 - 0.83)).

9.1.3 Reduction in passive smoking and indoor fuel exposure[80]

Caregivers and household members should be encouraged to refrain from smoking and advised on smoking cessation programmes. Exposure to fumes from indoor cooking fuels should be avoided.

9.2 Specific preventive strategies

9.2.1. Immunisation

9.2.1.1 Routine immunisations

All children should be given routine immunisations including BCG, measles, diphtheria-pertussis-tetanus toxoid (DPT), and Hib conjugate vaccines. The nature and degree of immunosuppression determine the safety and efficacy of vaccination in HIV-infected children. The effectiveness and duration of protection may be reduced in HIV-infected subjects who are not on highly active antiretroviral therapy (HAART). Symptomatic HIV-infected children should not receive BCG.

9.2.1.2 Specific vaccines

Pneumococcal vaccine.

Polysaccharide vaccine (Imovax pneumo 23, Pneumovax 23) should be given to all children older than 2 years at risk of developing invasive pneumococcal disease, including children with chronic pulmonary and cardiovascular disease. For children aged 2 - 9 years, polysaccharide vaccine should be preceded by a single dose of the pneumococcal conjugate vaccine given at least a month prior. Vaccination of African HIV-infected adults was found to result in more episodes of pneumonia in the vaccinated than placebo group, so this vaccine is not recommended for HIV-infected children.[81]

Conjugate vaccines. Pneumococcal conjugate vaccines are extremely effective in preventing radiographically confirmed pneumonia (20 - 37% reduction) in HIV-uninfected children.[11-13,82] The sensitivity of CXRs in detecting the burden of pneumococcal pneumonia prevented by vaccination is however only 37%, hence the true burden of pneumococcal pneumonia prevented by vaccination is 2 - 3-fold greater than that detected by CXRs.[14] The vaccine also prevents 13% of all clinically diagnosed severe pneumonia in HIV-infected children.[14] Furthermore, the vaccine is effective in preventing 85% of invasive pneumococcal disease in HIV-uninfected children and 65% in HIV-infected children.[11] Efforts should be made to vaccinate all HIV-infected and uninfected children with pneumococcal conjugate vaccine at 6, 10 and 14 weeks of age. A booster dose of the vaccine may be required during the second year of life in HIV-infected children.

Influenza vaccine. Children with chronic pulmonary, cardiovascular or immunosuppressive disease or those on aspirin should be vaccinated annually at the start of the influenza season. Children between 6 months and 9 years of age who have not been vaccinated previously require 2 immunisations of a single dose given 1 month apart (children under 3 years should receive half the adult dose on each of the 2 occasions); children who are older than 9 years or those who have been immunised previously require only a single immunisation. Vaccination has been found to be effective in HIV-infected adults who are moderately immunosuppressed (CD4 counts between 200 and 500 cells/μl).[83] Current evidence suggests that influenza vaccination is safe in HIV-infected children; therefore HIV-infected children should also receive influenza vaccine annually.

Varicella vaccine. HIV-infected children who are asymptomatic or mildly immunosuppressed may be given varicella vaccine at 12 - 15 months. Varicella should not be administered to symptomatic immunosuppressed HIV-infected children because of the potential for disseminated disease.

9.2.2 Prophylaxis

9.2.2.1 *Pneumocystis jiroveci* pneumonia (PCP) prevention

Co-trimoxazole prophylaxis for PCP is indicated for:

1. All HIV-exposed infants from 6 weeks of age until HIV infection has been excluded in the child and the mother is no longer breastfeeding.

2. All HIV-infected children from 6 weeks of age until a year. HIV-infected children older than a year should receive prophylaxis if their CD4 counts are less than 15% of lymphocytes or if they have symptomatic HIV disease. A recent study suggested that prophylaxis should be continued indefinitely irrespective of age or CD4 counts when HAART is not available.[84]

3. Prophylaxis should be continued in children taking ARVs for at least 6 months of HAART. There is little information on the safety of discontinuing prophylaxis once immune reconstitution has occurred. Discontinuation of prophylaxis may be considered in those with confirmed immune restoration for 6 months or more as indicated by 2 measurements of CD4% > 25% at least 3 - 6 months apart in children older than 2 years.[85]

4. Lifelong prophylaxis should be given to all children who have had an episode of PCP; the safety of discontinuing secondary prophylaxis in the context of immune reconstitution has not been established.

9.2.2.2 Prevention of mycobacterial disease

INH prophylaxis is currently not routinely recommended for prevention of TB, unless a child has been exposed to a household contact with TB. All children under 5 years of age exposed to a household TB contact should be given INH prophylaxis (10 mg/kg) daily for 6 months once active TB disease has been excluded. HIV-infected children exposed to a household contact should be given prophylaxis for 6 months irrespective of their age. Prophylaxis should also be given to HIV-infected tuberculin skin test-positive children even in the absence of a known household contact.

9.2.2.3 Prevention of RSV

Although the humanised monoclonal-specific antibody for the prevention of RSV infections (Palivizumab) is available there are no studies on the cost benefit for children in developing countries. Children most likely to benefit are those at risk for severe RSV infection, i.e. babies born prematurely (< 32 weeks'

gestational age) who are under 6 months of chronological age at the onset of the RSV season and children with chronic lung disease or congenital cardiac disease who are less than 1 year of age at the onset of the RSV season.[86] A dose should be given monthly for the duration of the RSV season, which spans from February to July in most of South Africa.

9.2.3 Highly active antiretroviral therapy (HAART)

The use of HAART to reconstitute immunity is very effective for decreasing the incidence of pneumonia and opportunistic infections in HIV-infected children. HAART should be given to all HIV-infected children at the appropriate stage of their disease who meet medical, immunological and social criteria for HAART according to national guidelines.

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