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## Management of community acquired pneumonia (CAP) in children: Clinical practice guidelines by the Paediatric Association of Nigeria (PAN)

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**Abstract:** The Paediatric Association of Nigeria first published management guideline for community-acquired pneumonia in 2015 and covered available evidence at that time.

This update represents a review of available recent evidence statements regarding the management of pneumonia in children, while at the same time incorporating relevant materials from the first edition of the guideline.

The guideline is developed to assist clinicians in the care of children with CAP. The recommendations provided in this guideline may not be the only approach to management, since there are considerable variations among children in the clinical course of CAP. The goal of this guideline is to reduce morbidity and mortality rate of CAP in children by providing recommendations that may be relevant in assisting clinicians to make timely diagnosis and institute appropriate antibiotic therapy of children with CAP.

Summarized below are recommendations made in the new 2021 CAP guideline. As part of the recommendations, the quality of the evidence is provided and the grade of the recommendation indicated. The details of the background, methods and evidence summaries that support each of these recommendations can be found in the full text of the guideline.

## Synopsis of Recommendations

### Clinical Features

- History should explore information on acute respiratory tract infection (ARTI) in the previous 2-3 weeks prior to presentation.
- Appropriate intervention on potential determinants such as health education on exclusive breastfeeding, place of preparation and cooking of food, increasing vaccination coverage, and early control of respiratory tract infection are recommended to prevent those risk factors.
- Pulse oximetry, an essential tool for decision-making should be included in the clinical evaluation of CAP [**Evidence level IVa; Grade C**]
- Serum procalcitonin, where available is a useful tool for decision-making and should be included in the clinical evaluation of CAP. [**Evidence level II; Grade B+**]
- The presence of one or more of: inability to drink/feed, intractable vomiting, convulsions, lower chest in-drawing, central cyanosis, lethargy, nasal flaring, grunting, head nodding, and oxygen saturation <90% should be considered highly suggestive of severe pneumonia requiring hospitalization. [**Evidence level III; Grade B-**]
- Respiratory rates are best determined over a full 60-second period and inconsistencies require repeated observations. This is required in view of the effects of the peculiar behavioural and physiologic factors in children. [**Evidence level III; Grade B-**]
- No single clinical finding is sufficient in determining the presence or absence of pneumonia; combinations of clinical findings are more useful. [**Evidence level II; Grade B+**]
- The best individual clinical findings in children less than 5 years of age are: nasal flaring (age < 12 months); oxygen saturation 90% or less in room air; tachypnoea; and retractions. In the older child with normal respiratory rate or absence of other signs of pneumonia, alternative diagnosis should be sought. However, among children less than 5 years, especially in neonates and those with severe malnutrition pneumonia may be present without signs of respiratory illness. [**Evidence level IVa; Grade C**]
- Bacterial pneumonia should be considered when there is persistent or repetitive fever >38.5°C together with lower chest wall in-drawing and tachypnoea. [**Evidence level IVb; Grade D**]
- Staphylococcal pneumonia should be suspected in children recovering from measles, malnutrition and those with skin or soft tissue infection. [**Evidence level IVb; Grade D**]

### Severity Assessment

- For a child in the community, re-presentation to the general practitioner with persistent fever or parental concern about fever, after an initial consideration of malaria should prompt consideration of CAP, espe-

cially in the presence of respiratory symptoms. [**Evidence level IVb; Grade D**]

- Children with CAP in the community or in hospital should be reassessed if symptoms persist and/or they are not responding to treatment. [**Evidence level IVb; Grade D**]
- Children who have oxygen saturations <92% should be referred to hospital for assessment and management. Those already in the emergency room with saturations of <92% should be admitted into the hospital. [**Evidence level II; Grade B+**]
- Auscultation revealing absent breath sounds with a dull percussion note should raise the possibility of a pneumonia complicated by effusion and should trigger a referral to hospital, and for those already in the emergency room should trigger admission for inpatient care. [**Evidence level II; Grade B+**]
- A child in hospital should be reassessed medically if there is persistence of fever 48 hours after initiation of treatment, increased work of breathing or if the child is becoming distressed or agitated. [**Evidence level IVb; Grade D**]
- Any child with a general danger sign requires hospitalization. All children <2 months of age with signs of pneumonia require hospital admission
- Children living with HIV (CLWH), those with other immuno-suppressive conditions and those malnourished require referral for hospital admission.
- If child's clinical state does not improve or worsens within 48 hours
- When the child requires mechanical ventilation at presentation
- Evidence of de-saturation ((saturations <90% at sea level, or <92% at altitude),) or presence of cyanosis
- If blood pressure remains low
- If the child has altered mental status
- Presence of any complications
- For a child in the community, with repeated or persistent fever and malaria has been excluded, prompt consideration for CAP diagnosis and onward referral to a general practitioner must be considered. [**Evidence level IVb; Grade D**]
- Children with CAP in the community or in hospital should be reassessed if symptoms persist and/or they are not responding to the treatment. [**Evidence level IVb; Grade D**]
- Children who have oxygen saturations <90% (at sea level) or <92% (at altitude) should be referred to hospital for assessment and management. [**Evidence level II; Grade B+**]
- Absent breath sounds on auscultation with accompanying dull percussion note should raise the possibility of a pneumonia complicated by effusion and should trigger a referral to hospital. [**Evidence level II; Grade B+**]. A child in hospital should be reassessed medically if there is persistence of fever 48 hours after initiation of treatment, increased work of breathing, if danger signs develop, or if the child becomes distressed or agitated. [**Evidence level IVb; Grade D**]

- Discharge should be considered when clinical features such as fast breathing, respiratory distress, requirement for supplemental oxygen, and fever have resolved for at least 24 hours [**Evidence level IVb; Grade D**]
- When the child is feeding by mouth and tolerates oral medications and the caregiver is comfortable about discharge from hospital and capable of administering oral medication if required. [**Evidence level IVb; Grade D**]

#### *Diagnostic Evaluation/ Investigations*

- While non-specific inflammatory markers may be of clinical benefit, they should not be routinely requested<sup>54</sup> [**Evidence level Ia; Grade A+**]
- Chest radiography should not be requested routinely in children with CAP. [**Evidence level Ia; Grade A+**]
- Children with signs and symptoms of pneumonia who are not admitted to hospital should not have a chest radiograph performed. [**Evidence level Ia; Grade A+**]
- A lateral chest radiograph should not be performed routinely. [**Evidence level II; Grade B+**]
- Follow-up radiography is not required in those who were previously healthy and who are recovering well, but should be considered in those with a round pneumonia, volume loss on initial chest radiograph, or persisting symptoms. [**Evidence level II; Grade B+**]
- In settings where chest radiography is not available, lung ultrasound may fill an important diagnostic gap for children presenting with suspected pneumonia.
- Lung ultrasound may be considered a substitute to chest radiography in children with suspected pneumonia, and preserves the option of chest radiography based on clinical judgement.
- In a setting where both modalities are available as diagnostic options, lung ultrasound holds the potential to decrease the use of chest radiographs, both in the diagnosis and follow-up of children with pneumonia.

#### *Management of a Child with CAP*

- Families of children who are well enough to be cared for at home should be given information on management of fever, prevention of dehydration and identification of any signs of deterioration. [**Evidence level IVb; Grade D**]

#### *Antibiotic Therapy for CAP*

- All children with a clinical diagnosis of pneumonia should receive antibiotics, as bacterial and viral pneumonia cannot be reliably distinguished from each other. [**Evidence level II; Grade B+**]
- High dose oral amoxicillin (90 mg/kg/day in 2 di-

vided doses for at least 3 days) should be used in the treatment of children aged 2 months to 5 years for 5 days in areas with high HIV prevalence, and for 3 days in areas with low HIV prevalence. [**Evidence level Ib; Grade A-**]

- CLWH should still receive oral co-trimoxazole preventive therapy alongside amoxicillin for treatment of CAP. [**Evidence level II; Grade B+**]
- Antibiotics administered orally are safe and effective for children presenting with severe CAP. [**Evidence level Ia; Grade A+**]
- Intravenous antibiotics should be used in the treatment of pneumonia in children when the child is unable to tolerate oral fluids or absorb oral antibiotics (e.g. because of vomiting) or presents with signs of septicaemia or complicated pneumonia. [**Evidence level IVa; Grade C**]
- Recommended intravenous antibiotics for severe pneumonia include penicillin, ampicillin, and cefuroxime, in combination with IM/IV gentamicin. Recommended dosing is as tabulated below. Empiric antibiotic therapy must be rationalized in response to a microbiological diagnosis. [**Evidence level IVa; Grade C**]
- Second line alternative therapy may include IV ceftriaxone or IV cefotaxime. [**Evidence level IVa; Grade C**]
- For CLWH, in addition to the above treatment high dose TMP/SMX, dosed as per the table below, should be included if *Pneumocystis jirovecii* pneumonia (PJP) is suspected. [**Evidence level IVa; Grade C**]
- Children with Sickle cell disease (SCD) with non-severe CAP, should receive high dose oral amoxicillin (90 mg/kg/day in 2 divided doses for at least 5 days). [**Evidence level II; Grade B+**]
- For alternative antibiotic treatment, this has been provided in the relevant table within the text.
- Children with SCD with severe pneumonia requiring hospitalization should be given IV ampicillin (150 mg/kg/day in 3 divided doses) OR IV cefuroxime (150 mg/kg/day in 3 divided doses) AND IV/IM gentamicin (5-7.5 mg/kg once daily) PLUS oral erythromycin (60-100 mg/kg/day in 4 divided doses) for at least 5 days. [**Evidence level IVa; Grade C**]
- In a patient who is receiving intravenous antibiotic therapy for the treatment of CAP, oral treatment should be considered if there is clear evidence of clinical improvement. [**Evidence level IVa; Grade C**]

#### *Prevention*

- ART should be commenced as soon as a diagnosis of HIV infection is confirmed. [**Evidence level Ia; Grade A+**]
- Co-trimoxazole preventive therapy (CPT) should be commenced for CLWH
- as soon as the HIV diagnosis is confirmed, as well

as for severely immune-compromised children, and continued until the child has shown consistent improvement in the immunological status and suppression of the HIV viral load.

- TB preventive therapy (TPT) should be used in CLWH of any age, or in immune-competent children <5 years, with a household contact with tuberculosis. [Evidence level II; Grade B+]
- TPT is indicated for any CLWH who is TST (Mantoux) positive, provided that active TB has been excluded.

### Introduction

With the background of the subsisting high childhood mortality indices in Nigeria, *vis-a-vis* the global efforts to stem the tide, there has been a corresponding need to address the common causes of deaths among under-five children. In Nigeria, as is the case in many countries in sub-Saharan Africa, pneumonia remains a common cause of under-five mortality, accounting for 17% of deaths in this age-group.<sup>1,2</sup> It has been estimated that globally, a child dies from pneumonia every 20 seconds.<sup>1</sup> With these in mind, and indeed the laudable goal of achieving a national under-five mortality rate of 25 per 1000 live births or lower by the year 2030,<sup>2</sup> prompt recognition and management of pneumonia has become imperative. This was the logic that informed the current initiative of the Paediatric Association of Nigeria, aimed at formulating helpful policies for diagnosis, treatment and control with respect to paediatric community acquired pneumonia (CAP). This document is targeted primarily at health care providers working in Nigeria in centres with limited facilities as well as those working in tertiary hospitals.

### Why an update?

The PAN initiated the development of the first edition of a professional guideline for management of childhood pneumonia in response to the poor health indices in Nigeria and other sub-Saharan countries contributed largely by morbidity and mortality from infectious diseases, especially pneumonia among under-five children, and also in line with Global effort to support and ensure availability of prompt, standard and quality care. The decision to revise the guidelines was informed by PAN's concern about the continuing prominence of pneumonia as a leading cause of infectious disease morbidity and mortality amongst children, and by a desire to align with global pneumonia control efforts to support healthcare workers in the provision of prompt, standard and quality care at all levels.

It is hoped that this professional guideline would assist care providers to properly initiate pre-referral management for pneumonia in the community, especially in situations where caregivers are unable or reluctant to promptly present their children to health facilities. Commencement of treatment at an early stage of pneumonia is key to successful outcomes, making it imperative to

support healthcare workers with guidelines and job aides that promote the application of quality information and evidence-based recommendations and standards of care. A professional guideline would assist caregivers to properly manage pneumonia both in the community and health facilities. When the disease is acquired in the community, most caregivers are reluctant to promptly present their children to health facilities. Since commencement of treatment at an early stage of pneumonia is key to successful outcome, it has become imperative therefore, to promote the practice of instituting prompt and correct treatment to ensure favourable outcomes. The presence of a guideline would no doubt serve the function of providing accurate, appropriate, and quality information to healthcare providers in facilities where the caregiver may present with severe cases of pneumonia during which only prompt commencement of appropriate and genuine antibiotics will ensure good outcome of such cases.

The First Edition of this Guideline<sup>3</sup> was developed and published in June 2015 through the laudable efforts of the contributors under the leadership of the PAN Executive Committee led by Dr. Adebisi Olowu, the then PAN President. However, since the publication of the First Edition, considerable changes have occurred, especially affecting the epidemiological indices of pneumonia in children, following the introduction of vaccines, specifically for *Strep. pneumoniae* and *H. influenzae type B*, as well as the evolution of management strategies for pneumonia in the context of HIV/AIDS, and tuberculosis. Changes in the living standards of families have led to higher prevalence of malnutrition, while environmental pollution resulting from cooking with firewood continues to expose children in their households to smoke, thereby increasing their vulnerability to acute respiratory infection.

More recently, the emergence of increasing populations of internally displaced persons living in deplorable camps/situations and in other congregate settings in Nigeria, where individuals and families displaced as a result of banditry, insurgency and communal clashes, are likely to have worsened the picture by increasing the transmission of CAP in children through overcrowding and poor environmental conditions on a background of vulnerabilities such as malnutrition. Most recent is the scourge of COVID-19 pandemic, a disease that shares similar mode of transmission and clinical manifestations with CAP, further making it necessary for such an update in the light of new available information and evidence for identification and management. Furthermore, the lingering trends in the emergence and re-emergence of drug resistance to potent therapeutic agents used in the management of pneumonia of infectious aetiology has necessitated a continuous vigilance for antimicrobial susceptibility as well as development of novel efficacious products, the use of which would require professional guidance through evidence-based recommendations

This review process was preceded by a critical appraisal of the First Edition of the Guideline, consultation of the most recently available evidence in peer-reviewed literature and use of standard tools for grading evidence as recommended by the WHO, which helped to decide which areas to review. The draft of this new revised Guideline has been further evaluated using similar standard tools and the findings show that the major flaws in the First Edition of 2015 have been largely addressed. It is expected that the revised 2021 Guideline will assist healthcare providers improve the standard and quality of treatment of community-acquired pneumonia in Nigeria.

### Method of guideline development

#### Scope of this Guideline

The PAN Guideline is developed to address management of CAP in infants, children and adolescents. The recommendations are applicable to the management of children both in the community and in the hospital. The recommendations will be useful to all cadre of health workers (doctors, house officers, nurses and community health extension workers (CHEWS)).

Procedure for Developing the Guideline (Including identification of evidence and literature search)

The development of this guideline entailed a revision of the first Edition of the Pneumonia Guideline of the Paediatric Association of Nigeria published in 2015.<sup>3</sup> The recommendations were revised, informed by recent evidence available in randomized controlled-trials (RCTs) and systematic reviews (Table 1). This guideline update also involved adaptation of the recommendations of other evidence-based clinical practice guidelines in accordance with the process described in the ADAPTE Framework.<sup>4</sup> In summary, the process included: 1) a set-up phase, 2) an adaptation phase, and 3) a finalisation phase (Figure 1).

**Table 1:** Brief description of the generic levels of evidence and guideline stated grades

Evidence Level	Definition	Guideline statement grade
Ia	A good recent systematic review of studies designed to answer the question of interest	A+
Ib	One or more rigorous studies designed to answer the question, but not formally combined	A-
II	One or more prospective clinical studies which illuminate, but do not rigorously answer the question.	B+
III	One or more retrospective clinical studies which illuminate, but do not rigorously answer the question	B-
IVa	Formal combination of expert views	C
IVb	Other information	D

**Fig 1:** Guideline adaptation process



A systematic search of literature was conducted to identify the most recent international guidelines on the subject to support adaptation. Electronic searches were conducted on the web and on specific repositories for most recent guidelines, RCTs and systematic reviews available. The Revision Group perused guidelines of the British Thoracic Society,<sup>5</sup> the South African Thoracic Society,<sup>6</sup> and the Pediatric Infectious Diseases Society/ Infectious Diseases Society of America,<sup>7</sup> to consider some of the recommendations for adaptation, taking into account the strength of evidence and their applicability to the Nigerian context.

These guidelines were chosen based on their high quality and applicability to our patient population. Original recommendations were adapted, rejected or rephrased considering consistency, currency, quality and applicability of the recommendations. Each individual recommendation based on international and local recommendations was accepted by the committee based on simple majority of the committee members.

#### i. Future Review of the Guideline

The Guideline is recommended for review every 5 years, to facilitate inclusion of new published evidence.

#### ii. External Peer Review

The draft guideline was sent to two independent external assessors before final revision for publication.

#### iii. External Peer Reviewers

1. Samuel Ibhanebor, Consultant Neonatologist, UK.
2. David P Moore, Associate Professor, Paediatric Infectious Diseases, Department of Paediatrics & Child Health, Chris Hani Baragwanath Academic Hospital, University of the Witwatersrand, South Africa.

#### 1. Definition

Pneumonia is the inflammation of lung parenchyma due to pathogenic micro-organisms such as bacteria, viruses and fungi.<sup>3,8</sup> Clinically, it is also defined as a condition typically associated with fever, respiratory symptoms, and evidence of lung parenchymal involvement, either by physical examination or the presence of infiltrates on chest radiograph.<sup>3,8</sup> In order to facilitate early recognition, prompt treatment and referral of children with

pneumonia, the World Health Organization (WHO) definition of pneumonia relies on simple clinical signs, such as tachypnoea and lower chest in-drawing.

## 2. Types of pneumonia

*Pneumonia can be classified using several parameters:*<sup>3</sup>  
8-10

### a. Source of infection:

- i. Community-acquired pneumonia (CAP). CAP is defined as pneumonia in a previously healthy child who acquired the infection outside a health facility or develops the illness within 48 hours of admission into a health facility.
- ii. Hospital-acquired pneumonia (HAP): this is nosocomial pneumonia, where there is an acute infection of lung tissue in a non-intubated patient that develops after 48 hours of hospitalization. It may include the subset of acute infection of lung tissue that develops after 48 hours of hospitalization. HAP includes the subset of acute infection of lung tissue that may occur 48 hours or longer after endotracheal intubation for mechanical ventilation; It is also known as ventilator associated pneumonia (VAP).

**b. Duration of Diseases:** Pneumonia can be classified as "acute" (less than two weeks' duration) and "chronic". Chronic pneumonias tend to have either a mycobacterial (usually tuberculosis) or fungal cause. A microbiological classification involves knowledge of the aetiological agents.

**c. Severity of Disease:** WHO classifies children with "cough or difficulty breathing" using simple clinical signs such as fast breathing, chest in drawing and general danger signs into three categories – severe pneumonia, pneumonia or no pneumonia [Evidence level Ia; Grade A+]

**d. Anatomical area(s) of involvement:** Usually recognized based on chest radiographic and physical examination findings:

**I. Lobar pneumonia:** characterized by the presence of a smooth, dense homogenous opacity of a single lobe, or a segment of a lobe, of a lung. The aetiological agent is often *S. pneumoniae*. Multilobar pneumonia involves more than one lobe, often causing a more severe illness.

**II. Bronchopneumonia:** there are patchy changes in the lung around the bronchi or bronchioles.

Interstitial pneumonia: this involves the areas in between the alveoli. It is more likely to be caused by viruses or by atypical bacteria.

**III. Microbiological classification:** This is based on the organism(s) isolated/identified, and may include viral, bacterial, fungal, mycoplasmal and chlamydial pneumonia.

## Epidemiology

Pneumonia is the leading cause of death in children under five years of age around the world, accounting for 15% of all-cause mortality of children globally. It kills more children under 5 years of age globally than HIV/AIDS, malaria, diarrhoea, and measles combined at rate of approximately 2500 per day.<sup>3</sup> Indeed, 138 million

new episodes of clinical pneumonia occur in children under 5 years of age annually with 1.7 million of these being of sufficient severity to be life-threatening requiring hospitalization.<sup>3</sup> In sub-Sahara Africa different regions show a variable burden of childhood pneumonias. Nigeria's position has shifted from 5th to first position as the country with highest mortality due to pneumonia in the world with 162,000 child deaths annually in 2018. In Nigeria, in 2018 about 3% of children under the age of 5 years were reported with symptoms of acute respiratory infection.<sup>11-18</sup>

The burden of disease is mainly in the younger age groups. Furthermore, while 81% of deaths from pneumonia occur in children younger than 2 years,<sup>14</sup> disease incidence has been shown to fall less rapidly with age than does mortality from the disease. Pneumonia incidence and mortality are related to the knowledge and health seeking behaviour of the caregivers. Among children with acute respiratory infections in Africa, health seeking behaviour varies from 10% to 80%. The Nigeria Demographic Health Survey (NDHS) of 2018 reported an incidence rate of 73% for children with acute respiratory infections. Treatments were sought from informal health facilities such as patent medicine vendors. The implication of this is that the children with pneumonia will be faced with poor treatment due to lack of access to appropriate health care. Children in sub-Saharan Africa and other areas of the world with low-income are faced with numerous factors that sustain pneumonia-associated morbidity and mortality.<sup>14-18</sup> Poorly functioning health systems engender high rates of morbidity and mortality due to communicable diseases such as pneumonia, malaria, and diarrhoea. This is equally sustained by poverty, malnutrition and other co-morbidities.<sup>18-22</sup>

In a recent systemic review and meta-analysis conducted to assess the magnitude of pneumonia and its associated factors among under-five children in East Africa that included 34 studies (twenty-two of which reported the prevalence of pneumonia), the pooled prevalence of pneumonia was 34% with 95% CI of (23.8–44.21%).<sup>17</sup> This rate is higher than that reported in Dibrugarh, India where a prevalence of 16.34% was found.<sup>18</sup> This might be due to regional socioeconomic and seasonal discrepancies. In Nigeria a prevalence of pneumonia in under-five children was to be 31.6%,<sup>11</sup> similar to the findings of the systematic review in East Africa.<sup>17</sup>

In Nigeria as in other low-income countries the poor health system and other prevailing adverse factors contribute in a complex interplay to sustain the high level of pneumonia morbidity and mortality. Pneumonia has been described as a disease of poverty, especially as factors patently related to poor socio-economic conditions sustain its incidence. Although there have been improvements in health indices in the last decade the associated risk factors related to pneumonia since the preceding decade (WHO report 2008) are still prevalent.<sup>14</sup> Individual and environmental risk factors have also been classified by the WHO (2008).<sup>13,14</sup>

### Predisposing/Risk Factors

#### Exposure to Household Smoke

In a prevalence study of pneumonia and its associated factors among under-five children in East Africa (a systematic review and meta-analysis), use of firewood as fuel source was found to be a risk factor for the development of pneumonia among under-five children.<sup>11</sup> Of these, the highest risk among those that used firewood for cooking revealed AOR = 7.41 (95% CI: 2.75, 19.95), and lowest risk with AOR = 1.15 (0.47, 1.88), compared to those who use non wood items as a source of fuel.<sup>5</sup>

**Table 2:** Risk factors for CAP\*

Definite Risk Factors	Likely Risk Factors	Possible Risk Factors	Risk Factors for Neonate
Malnutrition (WAZ score <-2)	Parental smoking	Mother's education	Premature rupture of membranes
Low birth weight	Zinc deficiency	Day care attendance	Low birth weight
Non-exclusive breastfeeding	Mother's experience as a caregiver	Outdoor air pollution	Preterm delivery
Lack of measles immunization	Concomitant disease, e.g., heart disease, sickle cell disease, immunodeficiency states		Lack of exclusive breast-feeding
Household air pollution overcrowding			Concomitant disease, e.g., heart disease

\*Risk Categories of Community Acquired Pneumonia (modified from Rudan et al Bulletin WHO 2008)

In the same systemic review and meta-analysis involving six studies, significant association between cooking food in the living room and pneumonia among under five children was found (Adjusted Odds Ratio=3.27 (95% CI: 1.4, 7.9)).<sup>11</sup> Similarly, several others studies reported this same association.<sup>12-14</sup>

In the meta-analysis referred to above, seven studies found significant association between putting a child at the back during cooking and pneumonia among under five children. Of these the highest risk factors, AOR = 11.76(4.6, 30.08) and lowest risk factor AOR= 1.37 (0.24,7.83) compared to those who didn't put their babies at their back.<sup>5</sup> The results of the sensitivity analysis showed that the findings were not dependent on a single study.<sup>5</sup> This association between putting a child at the back and increased incidence of pneumonia was also reported by other co-workers.<sup>18-22</sup>

#### Lack of Vaccination

The meta-analysis reported from East Africa,<sup>11</sup> on the prevalence of pneumonia and its associated risk factors among under-five children revealed that seven studies found significant association between being unvaccinated and the occurrence of pneumonia among under

five children.<sup>11</sup>

#### Lack of Exclusive Breastfeeding

Eleven studies in the meta-analysis reported from East Africa found significant association between non-exclusive breastfeeding and pneumonia among under five children.<sup>11</sup> This association was similar to what was found in reports from other studies.<sup>18-22</sup>

#### History of Acute Respiratory Infection

An association between history of acute respiratory tract infection within 2 weeks before presentation and coming down with pneumonia.<sup>11</sup> This was similar to findings from several other studies.<sup>23-31</sup>

### Aetiological agents of childhood pneumonia in Nigeria

Several aetiologic agents have been implicated as causes of CAP in Nigerian children in consonance with the global pattern.<sup>23-31</sup> Bacterial causes include *S. pneumoniae*, *H. influenzae* type b, *Staphylococcus aureus* and *Klebsiella pneumoniae*, non-typhoidal *Salmonella* spp, and non-typeable *H. influenzae*. Atypical bacterial causes include *Mycoplasma pneumoniae* and *Chlamydo-philum pneumoniae*. *Bordetella pertussis* is an important cause of severe lower respiratory tract infection, particularly in unvaccinated infants. Viruses which commonly cause pneumonia include respiratory syncytial virus (RSV), influenza A, B and C virus, parainfluenza viruses 1, 2, 3 and 4, adenovirus (ADV), human metapneumovirus (HMPV), and human rhinovirus. Measles virus is an important cause of severe pneumonia in malnourished, unvaccinated children.<sup>23-31</sup> Other aetiologic agents include *Mycobacterium* spp, human cytomegalovirus (CMV) and *Pneumocystis jirovecii* which are important, particularly in immunocompromised children. The pattern of pneumonia aetiology may have changed since the epidemics of HIV/AIDS, optimization of access to antiretroviral therapy (ART), for HIV-infected children, and introduction of pneumococcal conjugate vaccine (PCV) and *H. influenzae* type b vaccine (Hib vaccine). In South Africa, similar to other countries, RSV was the most common pathogen among children who are uninfected with HIV, and *P. jirovecii*, non typeable *H. influenzae* and *S. aureus* were detected in children with HIV.<sup>11,12,30-32</sup>

The aetiological agents for CAP are dependent on environment and age. In adults, *S. pneumoniae* is the most common aetiologic agent, while in children it varies with the age group. In the newborn period it is related to maternal genital flora and the setting of the delivery facility. Those children younger than five years of age have a different spectrum of organisms causing the disease from those that cause pneumonia in the newborn and school aged children. In severely malnourished children, *K. pneumoniae*, *S. aureus*, *S. pneumoniae*, *E. coli*, and *H. influenzae* are the major aetiological agents.

There is growing evidence of the importance of the role of respiratory viruses and *M. tuberculosis* in the causal pathway of childhood pneumonia.<sup>33-36</sup> Pathogens implicated in under-five CAP in Nigeria are shown in the table 3 below.

**Table 3:** Aetiologic agents of CAP among Under-five Children in Nigeria

Studies	Isolated organisms
Abdulkarim <i>et al</i> 2013	<i>Staphylococcus aureus</i> (23.9%), <i>Klebsiella spp</i> (17.4%), coliforms and <i>coagulase negative, Staphylococcus</i> (15.2%) each; <i>micrococcus</i> and non-haemolytic <i>Streptococcus</i> (6.5%) each
Falade <i>et al</i> 2009	<i>S. pneumoniae</i> (9), <i>H. influenzae</i> type b (2), <i>Klebsiella spp</i> (14 cases), <i>Salmonella spp</i> (11), <i>Pseudomonas aeruginosa</i> (6), <i>Enterococcus faecalis</i> (2), <i>E. coli</i> (2), and possible <i>S. aureus</i> (44: only one of these cases was confirmed)
Johnson <i>et al</i> 2008	Bacteria: <i>S. aureus</i> (37.3%), <i>Klebsiella spp.</i> (15.3%), <i>S. pneumoniae</i> (5.1%), and viruses: RSV (30.4%), PIV-3 (19.5%) Flu-A (17.3%)
Ogunu <i>et al</i> 2005	<i>S. pneumoniae</i> (3), <i>S. aureus</i> (2), coliforms (2), <i>H. influenzae</i> (1), <i>Proteus mirabilis</i> (1), <i>P. aeruginosa</i> (1)

#### 4. Pathogenesis and pathophysiology of pneumonia

The respiratory tract is replete with both specific and non-specific protective mechanisms which act in concert to keep the airways and alveoli free of both particulate materials and microbes.<sup>3</sup> The non-specific defense mechanisms include the nasal hair and nasal turbinates, the vocal cords, glottis, the mucociliary escalator, the cough reflex, migratory and fixed phagocytes, nonspecific antimicrobial proteins and opsonins, and colonization with normal, relatively non-pathogenic, airway flora. Others include humidification, neutrophils, resident alveolar macrophages, airway secretions including lysozymes, iron binding proteins, defensins, complements and surfactant.<sup>1,37</sup> The specific defense system involves the coordinated activities of B and T lymphocytes resulting in activation of cytotoxic T cells and the production of specific antibodies.<sup>38</sup>

Microbes are introduced to the airway via inhalational, haematogenous, bronchogenic or lymphatic routes.<sup>3,4,38</sup> Development of pneumonia requires favourable conditions and replication of the organisms.<sup>38</sup> Favourable conditions include invasion of organisms into the lymphatic and blood circulation, in addition to the development of primary atelectasis and emphysema.<sup>38</sup> Respiratory viruses are essential in the development of acute pneumonia, with viraemia causing circulatory disorders in the pulmonary tissue, emphysematous changes, formation of atelectasis and favouring the introduction of bacterial flora.<sup>38</sup> Acute viral-bacterial pneumonia occurs mainly within the first 3-5 days from the beginning of the respiratory viral disease.<sup>38</sup>

When microbes evade the non-specific defense system, they provoke an inflammatory response in the alveoli leading to exudates of plasma, neutrophils, lymphocytes,

macrophages and inflammatory debris.<sup>3,38</sup> The inflammatory debris obstructs the airway, increasing airway resistance. The debris also causes partial or total occlusion of the smaller airways with resultant atelectasis and hyperinflation of some alveoli leading to increased work of breathing, air trapping, and wheezing. Furthermore, the increased alveolar diffusion barrier causes significant ventilation-perfusion mismatch and intrapulmonary shunt.<sup>3,37</sup>

These pathophysiological events result in:

- (1) tachypnea (increased respiratory rate)
- (2) increased work of breathing
- (3) crepitations
- (4) reduced air entry
- (5) dull percussion note
- (6) wheeze/rhonchi
- (7) fever and
- (8) hypoxaemia.<sup>3</sup>

Seeding of bacteria to the blood and other organs may occur, causing bacteraemic pneumonia and, occasionally, organ-specific manifestations (such as meningitis, septic arthritis, and acute osteomyelitis).<sup>3</sup>

Respiratory insufficiency, caused by changes in the function of external respiration and disturbance of tissue oxidation, may lead to circulatory and other end organ changes leading to the various complications that occur with pneumonia.<sup>3,38</sup>

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the causative agent of Coronavirus Infectious Disease 2019 (COVID-19) which has become a common cause of lower respiratory infection, tends to cause less severe disease in children. The predominant lung pathology in fatal COVID-19 cases is diffuse alveolar damage (DAD), based on reports from studies in adult patients and a case series of paediatric COVID-19 associated deaths from South Africa.<sup>39</sup> The reason for the lower incidence and severity in children remain speculative but the expression of Angiotensin converting enzyme (ACE2) receptor, which has been identified as a key receptor site for SARS-CoV-2 virus is believed to be much lower in children than in adults. Also, high SARS-CoV-2 viral load has been associated with severe illness and it has been speculated that lower viral loads could also account for the milder illness seen in children.<sup>40</sup>

#### 5. Clinical features

##### *i How do children with pneumonia present?*

Children with pneumonia may present in different ways, with a wide spectrum of symptoms and clinical signs. The main objective of the initial clinical assessment is to decide if the child's history and physical examination findings are suggestive of CAP.<sup>5</sup> (table 4)

It is important to start the clinical evaluation of a child that presents with cough and difficulty breathing with very relevant questions.<sup>41-44</sup>



**ii. What are the relevant history questions**

- *Host-related factors:* Age, immunization status, lack of exclusive breastfeeding, low birth weight, severe malnutrition.<sup>11, 41-47</sup>
- *Environmental factors:* household air pollution e.g., use of firewood for cooking, passive tobacco smoking, season of the year, overcrowding and poor ventilation.<sup>11, 41-47</sup>
- *Co-morbidities:* heart disease, sickle cell disease, HIV infection, gastro-esophageal reflux disease.<sup>11, 41-47</sup>

**Evidence statement**

- Children with history of acute respiratory tract infections (ARTI) in the previous 2 weeks prior to presentation have been shown to be at increased risk of CAP, the odds of pneumonia among such children are higher than that for children without history of ARTI;
- Alteration in structure and function of the respiratory tract could predispose to infection in the lower respiratory tract, including pneumonia, by increasing invasion with other microorganisms which cause secondary infection, or by progressive invasion of the LRT with the same microorganism causing the ARTI (primary infections).<sup>48,49</sup>

**Recommendations**

- History should explore information on ARTI in the previous 2-3 weeks prior to presentation.
- Appropriate intervention on potential determinants such as health education on exclusive breastfeeding, place of preparation and cooking of food, increasing vaccination coverage, and early control of respiratory tract infection are recommended to prevent those risk factors.

**iii. What are the relevant physical examination findings?**

An initial physical examination should focus on fever and signs of respiratory illness which include tachypnoea, evidence of increased work of breathing, cyanosis, auscultatory signs such as decreased breath sounds and wheezes. Other features to be looked for include evidence of other organ involvement such as heart failure (tachycardia, gallop rhythm, tender hepatomegaly), acute osteomyelitis, septic arthritis and meningitis.<sup>48,49</sup>

**Table 4:** Clinical chest examination findings in children with chest pathology

Signs	Lobar pneumonia	Broncho-pneumonia
Chest deformity	May be present in children with chronic lung disease	May be present in children with chronic lung or congenital cardiac disease
Chest movement over the consolidated lobe	Diminished or absent	Usually normal
Mediastinal shift	May be absent except there is lobar collapse, or associated pleural effusion	None
Tactile fremitus	Increased	Normal
Percussion note	Dull	Resonant
Breath sounds	Bronchial or vesicular	Vesicular
Added sound	Crepitations (crackles)	Crepitations (crackles)
Vocal resonance	Increased	Normal

**Evidence statement**

Hypoxia (oxygen saturation 92% in room air) and increased work of breathing are signs often seen in children with CAP.

Wheezing independently predicts viral infection.

The WHO danger signs of: 1) inability to drink/feed, 2) intractable vomiting, 3) convulsions, 4) lethargy, 5) central cyanosis or oxygen saturation <90%; and/or lower chest in-drawing, nasal flaring, grunting, and head nodding, are predictors of death and must be used as indicators for hospitalization.

Moderate/large pleural effusions and multilobar infiltrates on chest X-ray are predictors of severe disease.

Serum C-reactive protein 40 mg/L in the presence of lobar consolidation on chest X-ray is suggestive of bacterial CAP.

Serum procalcitonin of >0.25 ng/dL is predictive of the presence of CAP with a bacterial aetiology.

**Recommendations**

Pulse oximetry, an essential tool for decision-making and should be included in the clinical evaluation of CAP [Evidence level IVa; Grade C]

Serum procalcitonin, where available is a useful tool for decision-making and should be included in the clinical evaluation of CAP. [Evidence level II; Grade B+]

The presence of one or more of: inability to drink/feed, intractable vomiting, convulsions, lower chest in-drawing, central cyanosis, lethargy, nasal flaring, grunting, head nodding, and oxygen saturation <90% should be considered highly suggestive of severe pneumonia requiring hospitalization. [Evidence level III; Grade B-] Respiratory rates are best determined over a full 60-second period and inconsistencies require repeated observations. This is required in view of the effects of the peculiar behavioral and physiologic factors in children. [Evidence level III; Grade B-]

No single clinical finding is sufficient in determining the presence or absence of pneumonia; combinations of

clinical findings are more useful. [Evidence level II; Grade B+]

The best individual clinical findings in children less than 5 years of age are: nasal flaring (age < 12 months); oxygen saturation 90% or less in room air; age-related tachypnoea (table 5); and retractions. The absence of tachypnoea alone or of all other signs of respiratory illness is highly suggestive of the absence of pneumonia. However, among children less than 5 years, especially in neonates and those with severe malnutrition pneumonia may be present without signs of respiratory illness. [Evidence level IVa; Grade C]

**Table 5:** Respiratory Rate Cut-offs for Children According to Age Groups

Age groups	Approximate normal respiratory rates (bpm)	Tachypnoea threshold (bpm)
Less than 2 months	25 to 50	60
>2 up to 12 months	25 to 40	50
1 up to 5 years	20 to 30	40
5 years	15 to 25	30

• **Is there any relationship between clinical features and causative organisms?**

Many studies, largely retrospective and cross-sectional, have sought clinical features which may help to direct treatment options.<sup>50-53</sup> These studies have confirmed that there is no way of reliably distinguishing clinically or radiologically between aetiological agents.

However, a careful examination of the child may reveal certain features that may be useful in deciding what type of organisms may be responsible for a pneumonia episode. For instance, purulent nasal discharge may be suggestive of bacteria, whereas a clear nasal discharge may suggest viral infection.

Also, in a child presenting with carbuncles or skin abscess and features of ARI, this scenario may be highly suggestive of *Staph. aureus* as a possible cause of the CAP. Pneumonia complicating childhood illnesses such as measles, pertussis and malnutrition may also be suggestive of Staphylococcal aetiology. Many studies also emphasize the importance of history of fever and breathlessness, tachypnea, in-drawing and a toxic or unwell appearance in children with pneumococcal infections.<sup>50,51,53</sup>

• **Recommendations**

- Bacterial pneumonia should be considered when there is persistent or repetitive fever >38.5°C together with lower chest wall in-drawing and raised tachypnoea. [Evidence level IVb; Grade D]
- Staphylococcal pneumonia should be suspected in children recovering from measles, malnutrition and those with skin or soft tissue infection. [Evidence level IVb; Grade D]

**6. Severity assessment**

Children with pneumonia usually present with cough and/ or difficulty in breathing, fast breathing and fever. These children may either have severe or less severe pneumonia, as defined below. This classification forms

the basis of subsequent management:

The WHO classifies severity of pneumonia severity as follows (table 6):

- No pneumonia
- Pneumonia (non-severe) is fast breathing ± lower chest indrawing; and
- Severe pneumonia is features of pneumonia with danger signs.

**Table 6:** Classification of pneumonia by Severity (WHO)

Category	Clinical features
Severe pneumonia	Any child presenting with danger signs: Inability to drink Convulsions Abnormal sleepiness Persistent vomiting or, Oxygen saturation <90% (at altitude >1,800 m) or <92% at sea level or central cyanosis or, Infant <2 months of age with: A general danger sign Chest wall in-drawing Or, Children living with HIV, immune-compromised or, malnourished children with lower chest in-drawing
Pneumonia	Children >2 months with Lower chest wall in-drawing or, Tachypnoea ( 50 breaths/min for infants 2-11 months of age, 40 breaths/min for children 1-5 years of age) No danger signs
No pneumonia	No signs of pneumonia or severe pneumonia, i.e. upper respiratory tract infection

*Severe pneumonia*

These children will have, in addition to the features of non-severe pneumonia, at least one or more of the following:<sup>54</sup>

- Central cyanosis, or oxygen saturation <92% (at sea level) or <90% (at altitude) on pulse oximetry in room air
- Severe respiratory distress (e.g., grunting, very severe chest in-drawing)
- Chest auscultatory signs: decreased/absent breath sounds or vocal resonance (as in pleural effusion) and pleural rub.

Table 7 shows the criteria for assessment of severity of CAP

*Signs of pneumonia with a general danger sign:*<sup>3</sup>

In cases of severe pneumonia, children may present with certain signs that are called danger signs, recognition of which may alert both the mother and the healthcare givers of a child with very severe illness. Some of these signs include:<sup>3,54</sup>

- Inability to breastfeed or drink, lethargy or uncon

- unconscious, convulsions
- Presence of complications or co-morbidities: e.g., congestive heart failure, severe malnutrition or sickle cell disease.

**Table 7: Severity assessment for Pneumonia**

	Mild to moderate	Severe
Infants	Temperature <38.5°C Respiratory rate 50 breaths/min Mild recession Taking full feeds	Temperature 38.5°C Respiratory rate 70 breaths/min Moderate to severe recession Nasal flaring Cyanosis Intermittent apnoea Grunting respiration Not feeding Tachycardia* Capillary refill time 2 seconds
Older children	Temperature <38.5°C Respiratory rate <50 breaths/min Mild breathlessness with no vomiting	Temperature 38.5°C Respiratory rate 50 breaths/min Severe difficulty in breathing Nasal flaring Cyanosis Grunting respiration Signs of dehydration Tachycardia* Capillary refill time 2 seconds

\*Values to define tachycardia vary with age and with temperature.

A comprehensive assessment of clinical severity and risk factors is crucial to identify the child who is likely to require hospital admission. Only difference between infants and older children is the respiratory rate as detailed below.

*Features of severe disease in an infant include:*

- Oxygen saturation <92%, cyanosis;
- Respiratory rate 70 breaths/min;
- Significant tachycardia for level of fever (values to define tachycardia vary with age and with temperature [Evidence level II; Grade B+]);
- Prolonged central capillary refill time 2 seconds;
- Difficulty in breathing;
- Intermittent apnoea, grunting;
- Not feeding;
- Chronic conditions (e.g., congenital heart disease, chronic lung disease of prematurity, chronic respiratory conditions leading to infection such as cystic fibrosis, bronchiectasis, immune deficiency).

*Features of severe disease in an older child include:*

- Oxygen saturation <92%, cyanosis;
- Respiratory rate 50 breaths/min;

- Significant tachycardia for level of fever (values to define tachycardia vary with age and with temperature [Evidence level II; Grade B+]);
- Prolonged central capillary refill time >2 seconds;
- Difficulty in breathing;
- Grunting;
- Signs of dehydration;
- Chronic conditions (e.g., congenital heart disease, chronic lung disease of prematurity, chronic respiratory conditions leading to infection such as cystic fibrosis, bronchiectasis, immune deficiency).

#### Evidence statements

- Children with CAP could present with a range of symptoms and signs. A global assessment of clinical severity and risk factors is crucial in identifying the child likely to require hospital admission. [Evidence level IVb; Grade D]
- All children with CAP who are <2 months of age, immunosuppressed, or malnourished should be prioritized for hospital admission, even if signs of severity are lacking because they have a higher rate of mortality.

#### Recommendations

- For a child in the community, re-presentation to the general practitioner with persistent fever or parental concern about fever, after an initial consideration of malaria should prompt consideration of CAP, especially in the presence of respiratory symptoms. [Evidence level IVb; Grade D]
- Children with CAP in the community or in hospital should be reassessed if symptoms persist and/or they are not responding to treatment. [Evidence level IVb; Grade D]
- Children who have oxygen saturations <92% should be referred to hospital for assessment and management. Those already in the emergency room with saturations of <92% should be admitted into the hospital. [Evidence level II; Grade B+]
- Auscultation revealing absent breath sounds with a dull percussion note should raise the possibility of a pneumonia complicated by effusion and should trigger a referral to hospital, and for those already in the emergency room should trigger admission for inpatient care. [Evidence level II; Grade B+]
- A child in hospital should be reassessed medically if there is persistence of fever 48 hours after initiation of treatment, increased work of breathing or if the child is becoming distressed or agitated. [Evidence level IVb; Grade D]

ii. *What are the indications for referral and admission to hospital?*

#### Evidence statements

- The presence of one or more of: inability to drink/feed, intractable vomiting, convulsions, lower chest

in-drawing, central cyanosis, lethargy, nasal flaring, grunting, head nodding, and oxygen saturation <90% should be considered highly suggestive of severe pneumonia requiring hospitalization.<sup>48,54,55</sup>

### Recommendations

- Any child with a general danger sign requires hospitalization. All children <2 months of age with signs of pneumonia require hospital admission
- Children living with HIV, those with other immunosuppressive conditions and those malnourished require referral for hospital admission.

### iii. When should a child with CAP be referred to a Tertiary Centre/Getting a Specialist's Review?

A referral to a tertiary centre, possibly from a primary healthcare centre, depends on failure of improvement of the patient as indicated by the presence of certain clinical features and symptoms. For instance, a child that develops any of the danger signs or worsening of de-saturation while on treatment may indicate no-response and warrants referral. In addition to assessing severity, the decision whether to refer should take account of any underlying risk factors the child may have, together with the ability of the parents/carers to manage the illness in the community.<sup>56-58</sup> This decision may be influenced by the level of parental anxiety.

There is no single validated severity scoring system to guide the decision on when to refer a child with CAP for hospital care. An emergency care-based study assessed vital signs as a tool for identifying children at risk from a severe infection.<sup>56-58</sup>

### Recommendations

A sick child with pneumonia will require referral to a tertiary facility or highest level care available in a physician run facility if any of the following conditions is observed:

- If child's clinical state does not improve after 48 hours or worsens within this period
- When the child requires mechanical ventilation at presentation
- Evidence of de-saturation ((saturation <90% at sea level, or <92% at altitude),) or presence of cyanosis
- If blood pressure remains low
- If the child has altered mental status
- Presence of any complications

### iv. When should transfers to a Critical Care Unit be considered?

There are two main scenarios when a child is likely to need admission to an intensive care unit (ICU):

- (1) when the pneumonia is so severe that the child is developing severe respiratory failure requiring assisted ventilation; and
- (2) a pneumonia complicated by septicaemia.

Key features that suggest a child requires transfer include:

- Failure to maintain oxygen saturation >92% in fractional inspired oxygen of >0.6 [Evidence level IVb; Grade D] OR, if oxygen saturation is persistently <90% despite supplemental oxygen
- Shock, or if blood pressure remains low or the child requires inotropic agent(s) to maintain normal blood pressure; [Evidence level IVb; Grade D]
- Rising respiratory and pulse rate with clinical evidence of severe respiratory distress and exhaustion, with or without a raised arterial carbon dioxide tension; [Evidence level IVb; Grade D]
- Recurrent apnoea or slow irregular breathing. [Evidence level IVb; Grade D]
- When the child requires mechanical ventilation
- If the child has altered mental status
- Presence of other organ failure

### v. When should the sick child be reassessed

For children with CAP, reassessment is important, whether in the community or in hospital.<sup>50,52-54</sup>

If at the community, after treatment for CAP has been initiated (e.g., oral antibiotics/antipyretics/ hydration), the parents/carers should be advised on what symptoms and signs to look for when reassessing their child at home. Looking for the features in the following three areas may be useful in identifying cases where the infection is not being adequately treated and reassessment by a doctor is required:

- Fever: a high swinging or persistent fever (the temperature should start to settle within 48 hours after commencement of treatment). [Evidence level IVb; Grade D]
- Effort of breathing: the child seems to be working harder to breathe with a fast breathing rate and chest recession. [Evidence level IVb; Grade D]
- Effect of breathing: The child is agitated and distressed; or if there is a reduction in the level of consciousness. [Evidence level IVb; Grade D]

If at the hospital, all the above should also be assessed in addition to vital signs. Medical assessment should always look for signs of overwhelming infection and septicaemia, for pleural collections that may develop into empyema thoracis [Evidence level III; Grade B-] and for signs of dehydration. A prolonged fever is a useful pointer to developing empyema; [Evidence level III; Grade B-] and this may require drainage for successful management. Less common complications should also be considered.<sup>57, 59-61</sup>

### Evidence statements

- Children with CAP could present with a range of symptoms and signs. A comprehensive assessment of clinical severity and risk factors is crucial in identifying the child likely to require hospital admission. [Evidence level IVb; Grade D]

## Recommendations

- For a child in the community, re-presentation to the general practitioner must be undertaken if the child has persistent fever, or if there is parental concern about fever if malaria has been excluded, should prompt consideration of CAP. [Evidence level IVb; Grade D]
- Children with CAP in the community or in hospital should be reassessed if symptoms persist and/or they are not responding to the treatment. [Evidence level IVb; Grade D]
- Children who have oxygen saturations <90% (at sea level) or <92% (at altitude) should be referred to hospital for assessment and management. [Evidence level II; Grade B+]
- Absent breath sounds on auscultation with accompanying dull percussion note should raise the possibility of a pneumonia complicated by effusion and should trigger a referral to hospital. [Evidence level II; Grade B+] A child in hospital should be reassessed medically if there is persistence of fever 48 hours after initiation of treatment, increased work of breathing, if danger signs develop, or if the child becomes distressed or agitated. [Evidence level IVb; Grade D]

### v. When should discharge be considered?

A child that was hospitalized for treatment for severe pneumonia should be considered for discharge home when the child has shown signs of persistent clinical improvements.<sup>61</sup>

## Recommendations

- Discharge should be considered when clinical features such as fast breathing, respiratory distress, requirement for supplemental oxygen, and fever have resolved for at least 24 hours [Evidence level IVb; Grade D]
- When the child is feeding by mouth and tolerates oral medications and the caregiver is comfortable about discharge from hospital and capable of administering oral medication if required. [Evidence level IVb; Grade D]

## 6. Diagnostic evaluation/ investigations

### a. Supportive investigations

- **Are supportive investigations needed for children managed at home or community?**

Childhood CAP can be managed in the community; within the home, at health centres, or community pharmacies and patent medicine vendor's; or out-patient clinics. If treated in the ambulatory setting, emphasis must be placed on the recognition of worsening symptoms and general danger signs.<sup>62</sup> This strengthens prevention of progression to severe cases of pneumonia that would require hospitalization.<sup>62</sup> For a child with suspected CAP at the community level, investigations of any sort (microbiological or radiological) are not an immediate priority and have not been shown to impact significantly on outcome.<sup>4</sup> Caregivers and carers should

be instructed on accurate counting of the respiratory rate, recognition of danger signs, and when and how to access higher levels of care.<sup>61</sup>

### Which supportive investigations are needed for children managed in the hospital?

Within the hospital setting, the aims of management include: (1) making an aetiological diagnosis, (2) making an anatomical/pathological diagnosis, and (3) managing the disease and any consequent complications.<sup>51,63</sup> Measurement of baseline respiratory and pulse rate are essential, and assist in tracking improvement in clinical status over time.

Investigations should include:

- Pulse oximetry for oxygen saturation: The machine sensor is attached to the patient's preferred finger with no lesions or nail polish, while ensuring that the waveform is uniform with equal hills and valleys across the screen and no movement artifacts, over at least 30 seconds. The SpO<sub>2</sub> is helpful in detection of cyanosis and monitoring response to therapy. Values above >93% in room air with decreased work of breathing are acceptable for discontinuing supplemental oxygen therapy.<sup>5, 63</sup>
- Acute phase reactants such as C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and pro-calcitonin (PCT) levels have been used as a means of differentiating the aetiology and/or severity of CAP. PCT is a serum biomarker that helps distinguish bacterial infection from viral infections or from inflammation. In patients with CAP, PCT is 65 to 70 percent accurate in distinguishing bacterial from viral pathogens<sup>64-67</sup> and in some studies has helped reduce unnecessary antibiotic use. PCT rises faster than CRP levels, with consequent rapid decline once appropriate antibiotic therapy has been initiated.<sup>65-67</sup> In line with this, the BNP was found to be a marker of severity and presence of heart failure in children with pneumonia. A study in Benin, revealed that elevated levels of BNP among children with CAP actually correlated more with clinical presence of complicated pneumonia especially with CCF.<sup>68</sup>

## Recommendations

While non-specific inflammatory markers may be of clinical benefit, they should not be routinely requested<sup>54</sup> [Evidence level Ia; Grade A+]

### a. Microbiologic investigations

- **Which investigations are useful for identifying bacterial causes of CAP?**

Isolation of a microbiologic agent is desirable in children with CAP in order to avoid antibiotics misuse and development of bacterial resistance.

The gold standard for sample recovery is lung puncture aspirate from an infected region of the lung. Emphasis should be on less invasive sampling methods however.

These include:

- Blood culture: Positivity rates usually <10% in childhood CAP.
- Pleural fluid: Fluid for microscopy, culture, pneumococcal antigen detection and/or PCR where available. Pleural fluid cultures often show no growth, because most children will have received antibiotics for some time before aspiration of pleural fluid. If clinical suspicion of tuberculosis is high, consider sending pleural fluid for mycobacterial culture and/or GeneXpert MTB/Rif testing.
- Nasopharyngeal culture: bacterial isolation in the nasopharynx is not indicative of lower respiratory tract infection. Normal bacterial flora, as well as bacteria known to cause CAP, are often identified.
- Sputum culture (sputum can be obtained by sputum induction in children <5 years of age, using 5% hypertonic saline nebulisation).<sup>69,70</sup> The utility of sputum culture in children with pneumonia is very limited, as the specimen may be contaminated by upper airway colonizing bacteria. Older children, including adolescents with established chronic lung disease, can cooperate in producing an expectorated sputum specimen, culture results of which are likely to reflect the infecting organism in children with intercurrent pneumonia.
- Nasopharyngeal secretions and nasal swabs for viral detection using PCR or immunofluorescence. PCR is preferred over immunofluorescent antibody tests, because of their substantially greater sensitivity.

**b. Are there investigations that may be useful in identifying atypical or viral causes of CAP?**

- Acute and convalescent serology for respiratory viruses, *M. pneumoniae* and *Chlamydomphila pneumoniae*. Paired serum specimens with rising titers in antibody complement fixation tests remains the mainstay for diagnosing *M. pneumoniae* and *C. pneumoniae* infections, although they have limited clinical application as the repeat serum test should only be done 4 weeks after the acute pneumonia episode. Serology therefore does not impact on acute management of patients, but assists in epidemiologic studies of these atypical organisms.
- PCR is also useful in identifying atypical bacterial infections.
- Viral aetiology can be determined using viral culture, antigen detection, serology and PCR; however, PCR is the preferred method in view of the excellent sensitivity and specificity of test performance.

**Evidence statements<sup>68</sup>**

- Blood culture positivity is low in children with CAP. [Evidence level Ib; Grade A-]
- Microbiological investigations should not be considered routinely in those with milder dis-

ease, especially those treated in the community. [Evidence level IVa; Grade C]

- Microbiological diagnosis should be attempted in children with severe pneumonia sufficient to require paediatric intensive care admission, or those with complications of CAP. [Evidence level IVa; Grade C]
- Microbiological methods used should include:
  - Blood culture. [Evidence level IVa; Grade C]
  - Nasopharyngeal secretions and/or nasal swabs for viral detection by PCR. [Evidence level IVa; Grade C]
  - Acute and convalescent serology for respiratory viruses, *M. pneumoniae* and *C. pneumoniae*. However, paired serology will not impact on acute patient management. [Evidence level II; Grade B+]If present, pleural fluid should be sent for microscopy, culture, pneumococcal antigen detection and/or PCR, where available. [Evidence level IVa; Grade C]

**c. Diagnostic Imaging**

A diagnosis of CAP is commonly achieved by carefully considering the symptoms and signs. In the majority of cases, further radiological investigations are not indicated, especially in resource-poor countries.

1. Plain chest radiograph: This is the commonest ancillary radiological investigation for confirmation of CAP. Its main value is in the identification of opacities which may indicate bacterial, viral or mixed infection in the lung parenchyma. Radiographic pneumonia is defined as confluent opacification. Children with symptoms and signs suggesting pneumonia who are not admitted to hospital should not routinely have a chest x-ray.

**• When should a chest x-ray be done for CAP?**

In general, CAP requiring hospitalization is an indication for requesting a chest radiograph. There is controversy regarding the timing and the specific views of the chest radiograph required. The majority of clinicians request a chest radiograph for children with features of severe pneumonia. Follow-up chest radiographs may not be indicated in children who recover without CAP complications.<sup>61,71</sup>

**Indications for chest radiographs in CAP include:**

- a. Severe pneumonia as evidenced by the presence of significant chest retractions.
- b. Failure to respond to the initial course of antibiotic therapy at 48 hours.
- c. Suspected CAP with complications, e.g., pleural effusion, pneumothorax.
- d. Progressive symptoms, despite antibiotic therapy.

Possible chest radiographic findings indicative of CAP include: lobar infiltrates, interstitial infiltrates (bacterial, viral, atypical organisms), lobar consolidation, atelecta

atelectasis, nodular infiltration, hilar adenopathy, pneumatoceles, peripheral rather than central opacification, and pleural effusion. Radiographic findings can be classified as alveolar and/or interstitial pneumonia, hyperaeration, hilar enlargement, or atelectasis. The radiographic location may be in one or both lungs.

Although chest radiography is generally considered the first-line standard-of-care imaging modality to investigate suspected pneumonia, some of the limitations of chest radiography include:

Interpretation of the chest radiographs in pneumonia varies between clinicians, and upon review of the same chest radiograph by the same clinician

Poor agreement between radiologists on the presence or absence of infiltrates on paediatric chest radiographs even when standard reporting formats are used.

Chest radiographs predict the post-mortem diagnosis of pneumonia in severely malnourished children with 100% specificity but only 50% sensitivity.<sup>3</sup>

Access to chest radiography is limited in many health facilities in developing countries.

### Any need for a lateral film

Commonly, an anteroposterior (AP) view is requested as the standard. Simultaneous AP and lateral views are required to assess the hilum, paratracheal and paravertebral structures e.g., in cases of pulmonary tuberculosis or complicated pneumonia. Where massive pleural effusion is suspected, lateral views should also be obtained, especially following substantial drainage of the effusion.<sup>72,73</sup>

### Evidence statements<sup>61</sup>

- Chest radiography is not able to establish whether CAP is of viral or bacterial aetiology.

### Recommendations<sup>61</sup>

- Chest radiography should not be requested routinely in children with CAP. [Evidence level Ia; Grade A+]
- Children with signs and symptoms of pneumonia who are not admitted to hospital should not have a chest radiograph performed. [Evidence level Ia; Grade A+]
- A lateral chest radiograph should not be performed routinely. [Evidence level II; Grade B+]
- Follow-up radiography is not required in those who were previously healthy and who are recovering well, but should be considered in those with a round pneumonia, volume loss on initial chest radiograph, or persisting symptoms. [Evidence level II; Grade B+]

### The role of chest ultrasound in CAP

Due to the potentially harmful effects of radiation exposure, some clinical guidelines advise against the routine use of chest radiography in uncomplicated acute lower

respiratory infections in childhood populations with high vaccination cover for *Haemophilus influenzae* type b and pneumococcus.<sup>73-76</sup> When performed by adequately trained clinicians a structured lung US examination can detect lung consolidation and other features suggestive of pneumonia in children with the similar accuracy and reliability as chest radiographs, but with the added benefits of no exposure to ionizing radiation and potential savings in cost and time.

Some suggestive ultrasound findings in CAP include a distinct increase in the amount and density of B-lines which is considered pathological; three or more separate B-lines visualized at once in any view (Fig. 2), or when they become confluent (also known as compact B-lines), which points to thickening of the interlobular septae due to increased interstitial fluid or infiltration. Presence of white echo poor areas beneath the pleura also suggests consolidations within the lung. Lung ultrasound also facilitates the visualization of the visceral pleura sliding over the parietal layer during respiration, known as lung sliding, which gives the pleural line a shimmering appearance. When lung sliding is absent, a pneumothorax should be suspected.

In a systematic review and meta-analysis that included eight studies (n=795 children with median age of 0.03–5.6 years), both expert and novice clinician-sonographers achieved high rates of diagnostic accuracy, with sensitivity and specificity above 90% for identifying CAP on lung ultrasound.<sup>73</sup>

### Evidence statements<sup>61,75</sup>

Despite evidence of diagnostic accuracy and reliability compatible or better than chest radiography for detecting lung consolidation, the uptake of lung ultrasound into clinical practice has been slow. Lung ultrasound is not yet included in many clinical management guidelines for community-acquired pneumonia in children.

### Recommendations<sup>61,75</sup>

- In settings where chest radiography is not available, lung ultrasound may fill an important diagnostic gap for children presenting with suspected pneumonia.
- Lung ultrasound may be considered a substitute to chest radiography in children with suspected pneumonia, and preserves the option of chest radiography based on clinical judgement.
- In a setting where both modalities are available as diagnostic options, lung ultrasound holds the potential to decrease the use of chest radiographs, both in the diagnosis and follow-up of children with pneumonia.

## 6. Management of a child with cap

### 11.1 general supportive measures

#### a. In the Community<sup>61,77-84</sup>

The general management of a child who does not require hospital referral comprises advising parents and carers

about:

- **Prompt management of fever**
  - Use of antipyretics such as paracetamol at 10 mg per kilogram per dose (maximum of 4 doses in 24 hours). Caregiver must seek medical attention immediately if fever persists, or if there are signs of deterioration.
  - Tepid sponging can be applied in conjunction with antipyretic therapy, provided that this does not cause discomfort to the child (evidence level I).<sup>77</sup>
- Preventing dehydration by giving liberal oral fluids, and continuing breast feeding in children less than 2 years old.
- Identifying signs of deterioration.
- Identifying signs of other serious illness.
- How to access further healthcare (providing a 'safety net').

The 'safety net' should be one or more of the following:

- *Provide the parent or carer with verbal and/or written information on warning symptoms and how further healthcare can be accessed;*
- *Arrange a follow-up appointment at a certain time and place – the WHO recommends follow-up within 3 days, or sooner if the child's clinical status is deteriorating;*
- *Liaise with other healthcare professionals, including out-of-hours providers, to ensure the parent/carer has direct access to further assessment for their child, if warranted.*

### Recommendation

- Families of children who are well enough to be cared for at home should be given information on management of fever, prevention of dehydration and identification of any signs of deterioration. [Evidence level IVb; Grade D]

#### *b. In the Hospital*

- Clear the airway using gentle suction as needed, always mouth before nose.
- Patients whose oxygen saturation is  $\geq 92\%$  in room air should be treated with oxygen given by nasal cannula, a high flow delivery device, head box or face mask to maintain oxygen saturations  $>92\%$ . [Evidence level II; Grade B+]<sup>61,78</sup> Oxygen saturations lower than 90–92% are associated with an increased risk of death in children with pneumonia.<sup>79</sup>
- Oxygen should be administered via nasal prongs or nasal catheters: 0.5–1L/min for children 0–2months, 2–3L/min for children 3months to 5 years; maximum of 4L/min for older children);
- Supplemental oxygen should be administered in special situations including: SpO<sub>2</sub>  $<94\%$  if severe anaemia, severe heart failure, septic shock, and acute neurological illness. These children are less able to withstand moderately low oxygen levels than children with only lung disease.

- If pulse oximetry is not available, give oxygen if signs of respiratory distress and/ or cyanosis are present.
- Allow small frequent feeds/fluids if tolerated; feeding may also be done using appropriate size nasogastric tube. However, nasogastric tubes may compromise breathing and should, therefore, be avoided in severely ill children, especially in infants with small nasal passages. If the use of nasogastric tubes cannot be avoided, the smallest calibre tube should be passed down the narrowest nostril. [Evidence level IVb; Grade D]<sup>61</sup>
- If feeds are not tolerated, give intravenous isotonic fluid at  $<80\%$  of maintenance with monitoring of sodium levels. Ensure that the intravenous solution contains at least 5% glucose (e.g., 5% dextrose in 0.9% saline, or Ringer's Lactate with added glucose) [Evidence level II; Grade B+].<sup>61,78</sup>
- For high grade fever (temperature  $\geq 39^{\circ}\text{C}$ ) or chest pain, give paracetamol 10–15 mg/kg 4–6 hourly, or ibuprofen 10 mg/kg 8 hourly if required. Children with fever or chest pain should be treated with appropriate antipyretics or analgesics [Evidence level IVb; Grade D]<sup>61,78</sup>
- If widespread wheezes are present (high-pitch continuous sounds during expiration only, or during both phases of respiration) give a trial dose of short acting bronchodilator such as salbutamol or albuterol and re-assess. Repeated doses of bronchodilator therapy may precipitate tachyarrhythmias in infants, and should be used with caution in this age group.
- Vitamin A is effective for measles-associated pneumonia, or for those with features of vitamin A deficiency [Evidence level Ib; Grade A-]<sup>61,78</sup>
- Zinc supplementation given as an adjunct significantly reduces mortality. [Evidence level Ib; Grade A-]<sup>79</sup>
- Children who are haemodynamically stable should not be transfused if their Hb is  $\geq 7$  g/dL [Evidence level II; Grade B+]<sup>78</sup>
- Nursing care should be provided at least every 3 hours: check vital signs, including blood pressure, pulse rate, respiratory rate, temperature and oxygen saturation.
- Review by the attending physician should be done at least twice daily and PRN where the need arises.
- Vaccination status should be reviewed and catch-up provided, including booster immunisation, as indicated [Evidence level IVb; Grade D]<sup>78–80</sup>

#### **Drugs to Avoid in the Management of Pneumonia**

- Cough syrups containing antihistamines or opioids such as codeine or hydrocodeine, should be avoided because they add little to the management of pneumonia and may be toxic in some children [Evidence level Ia; Grade A+]<sup>61,78</sup>
- Routine use of corticosteroids for childhood CAP is discouraged [Evidence level Ib; Grade A-]<sup>61</sup>



For *Pneumocystis jirovecii pneumoniae* (PJP) in HIV infected infants, early use of steroids in addition to conventional trimethoprim-sulfamethoxazole (TMP/SMX) therapy significantly reduces mortality in hospital and 6 months after discharge.<sup>6,81</sup> It should be received within 48 hours of hospitalization.

Corticosteroids should also be used with tuberculosis medication to reduce the risk of nodal compression of the airways, if there is evidence of extrinsic airways compression on chest radiographs.<sup>79</sup>

- Routine use of vitamin D supplementation is not recommended [Evidence level Ia; Grade A+] <sup>61</sup>
- Chest physiotherapy is not beneficial and should not be performed routinely in children with pneumonia. [Evidence level Ib; Grade A-] <sup>61,78</sup>
- Chest physiotherapy may be of benefit in children with lobar collapse [Evidence level Ia; Grade A+] <sup>78</sup>
- There is no evidence for the use of other micronutrients in the treatment of acute pneumonia in well-nourished children, however, nutritional support including vitamins and zinc should be given in malnourished children [Evidence level Ia; Grade A+] <sup>79</sup>

## 11.2 Antibiotic therapy for cap

### a. Introduction

Whereas the aetiology of pneumonia could be due to various organisms including non-bacterial agents, the identification of aetiological pathogen may be difficult, especially as distinguishing between viral and bacterial, and collection of respiratory specimens often yield multiple co-pathogens.<sup>11,78,86,87</sup> The pattern of clinical presentation may also not be able to distinguish between the different aetiological agents of pneumonia.<sup>88-90</sup>

### b. Management of non-severe pneumonia in infants and children

A double blind randomized clinical trial in immunocompetent under-five Malawi children with non-severe pneumonia, a 3-day course of amoxicillin twice daily (as recommended by WHO) compared with placebo, showed that amoxicillin had a significantly lower treatment failure rate on or before day 4 and placebo was significantly inferior to treatment with amoxicillin.<sup>91</sup> Fast-breathing pneumonia resolved by day 4 in 93% of children without the use of the antibiotic; there was no significant difference between groups in treatment failure or relapse by day 14, and treating 33 children with amoxicillin was necessary for 1 child to benefit. Although placebo was inferior to amoxicillin for treatment of non-severe fast-breathing pneumonia, the vast majority of children in the placebo group recovered without amoxicillin. However as in several other studies, the result of this extensive study suggested that it might be advisable to schedule a follow-up visit on day 4 for re-evaluation and treatment if necessary for low-risk children who are available for follow-up. For those whose follow-up cannot be assured (and this may be the major-

ity of children in routine settings in sub-Saharan Africa especially Nigeria), treatment with amoxicillin may be warranted for every such child that presents with symptoms suggestive of pneumonia (non-severe).<sup>79,88-94</sup> Considering 6% relapse versus the 4% treatment failure rates among children with non-severe fast-breathing pneumonia who received 3 days of amoxicillin, there may be need for a longer duration of amoxicillin instead of the 3-day duration.<sup>77,79,87-91</sup>

Considering the difficulty in distinguishing between bacterial and non-bacterial causes of pneumonia in under-fives and the need for further follow-up visits if not placed on antibiotics (with many of the caregivers not likely to present until the pneumonia is severe), routine treatment of children that will present with non-severe pneumonia is common.<sup>11,88,89,91</sup> This is in line with WHO recommendation that immune-competent under-five children with non-severe fast-breathing pneumonia should have amoxicillin. The WHO's integrated management of childhood illness (IMCI) guidelines identify non-severe pneumonia in children with cough or difficult breathing who demonstrate fast breathing without WHO danger signs.<sup>9,90,92</sup>

### c. Management of neonatal pneumonia

Neonatal pneumonia is a lung infection in a neonate. Onset may be within hours of birth and part of a generalized sepsis syndrome (early onset neonatal sepsis), or after 7 days (late onset neonatal sepsis). Signs may be limited to respiratory distress, but may be non-specific or may progress to shock and death. All infants under 2 months of age that present with features of community-acquired or congenital pneumonia warrant hospitalisation. Treatment is initially with broad-spectrum antibiotics, changed to targeted therapy if a bacterial organism is cultured from blood, urine or cerebrospinal fluid.<sup>85,95,96</sup>

### d. Antibiotic regimens for childhood community-acquired pneumonia

A meta-analysis of trials carried out to determine the most suitable antibiotic therapy for CAP examined the route, dose, combination and duration against very severe/severe/non-severe CAP by enrolling 20,593 children aged 2–59 months, all of whom were pooled from 22 studies. It was found that a combination of penicillin or ampicillin plus gentamicin was effective for very severe pneumonia, while oral amoxicillin alone was as effective as other parenteral antibiotics for both severe and non-severe CAP. The review further found that a short 3-day course of an antibiotic was as beneficial as 5-day course for non-severe pneumonia in children aged 2–59 months.<sup>77,90, 94-97</sup>

#### Evidence statements

- Evidence suggests that amoxicillin is superior to placebo for children with non-severe pneumonia. [Evidence level Ia; Grade A+] <sup>77,79,90, 92-97</sup>
- A short (3-day) course of antibiotics was as beneficial as a 5-day course. [Evidence level Ia; Grade

A+] 77,79, 92-97

**Recommendations**

- All children with a clinical diagnosis of pneumonia should receive antibiotics, as bacterial and viral pneumonia cannot be reliably distinguished from each other. [Evidence level II; Grade B+]
- High dose oral amoxicillin (90 mg/kg/day in 2

divided doses for at least 3 days) should be used in the treatment of children aged 2 months to 5 years for 5 days in areas with high HIV prevalence, and for 3 days in areas with low HIV prevalence. [Evidence level Ib; Grade A-]

- Children living with HIV should still receive oral co-trimoxazole preventive therapy alongside amoxicillin for treatment of CAP. [Evidence level II; Grade B+]

**Table 8: Summary of antibiotic recommendations**

Age range	Outpatients						Inpatients					
	First line	Evidence Grade & Ref.	R. S	Alternatives*	Evidence Grade & Ref.	R. S	First line	Evidence Grade & Ref.	R. S	Alternatives*	Evidence Grade & Ref.	R.S
<2 months	Admit and treat as neonatal sepsis	1a 13, 14	B+	-	-	-	-	-	-	-	-	-
2 months	High dose oral Amoxicillin (90mg/kg/d in 2 divided doses) for at least 5 days	1a 2,6-12,15-18	A-	Oral Amoxicillin-clavulanic acid (Amoxicillin 90mg/kg/d in 2 divided doses) OR Oral Cefpodoxime (10mg/kg/d in 2 divided doses) OR Oral Cefuroxime (20-30mg/kg/d in 2 divided doses) for at least 5 days	1a 6-12,11 5-18	B+	IV Amoxicillin (150mg/kg/day in 3 divided doses), OR IV Cefuroxime (150mg/kg/d in 3 divided doses) AND IV/IM Gentamicin (5-7.5mg/kg od) for at least 5 days	1a 6-12,15 -18	C	IV Ceftriaxone (50-100mg/kg/d every 12-24hours), OR IV Cefotaxime (100-200mg/kg/d in 4 divided doses), OR IV/IM Gentamicin (5-7.5mg/kg od for at least 5 days), AND IV Cloxacillin (100-200mg/kg in 4 divided doses)	6-12,15-18	C
Children living with HIV	High dose oral Amoxicillin (90mg/kg/d in 2 divided doses) for 10 days	1a 2,6-12,14-18	B+	Oral Amoxicillin-Clavulanic acid (Amoxicillin 90mg/kg/d in 2 divided doses) OR oral Cefpodoxime (10mg/kg/d in 2 divided doses), OR oral Cefuroxime (20-30mg/kg/d in 2 divided doses) for at least 10 days	1a 6-12,14-18	C	IV Amoxicillin (150mg/kg/d in 3 divided doses), OR IV Cefuroxime (150mg/kg/d in 3 divided doses) PLUS IV/IM Gentamicin (5-7.5mg/kg od) PLUS high dose Co-trimTMP/SMX (20mg/kg/d of trimethoprim) for at least 10 days	1a 6-12,14 -18	C	IV ceftriaxone (50-100mg/kg/d every 12-24hrs), OR IV Cefotaxime (100-200mg/kg/d in 4 divided doses) PLUS, high dose Co-trimoxazole (20mg/kg/d trimethoprim in 4 divided doses) for at least 10 days, PLUS IV/IM Gentamycin (5 – 7.5mg/kg od)	1a 6-12,14-18	C
Children with Sickle cell disease	High dose Oral Amoxicillin (90mg/kg/d in 2 divided doses) for at least 5 days	IVa 19,20,21	C	Oral Amoxicillin-clavulanic acid (Amoxicillin 90mg/kg/d in 2 divided doses), OR oral Cefpodoxime (10mg/kg/d in 2 divided doses), OR oral Cefuroxime (20-30mg/kg/d in 2 divided doses) for at least 5 days.	IVa 19,20,21	C	IV Amoxicillin (150mg/kg/d in 3 divided doses), OR IV Cefuroxime (150mg/kg/d in 3 divided doses), PLUS IV/IM Gentamicin (5-7.5mg/kg od) PLUS oral Erythromycin (60-100mg/kg/d in 4 divided doses) for at least 5 days.	IVa 19,20,21	C	IV Ceftriaxone (50-100mg/kg/d 12-24hrly), OR IV Cefotaxime (100-200mg/kg/d in 4 divided doses), OR oral azithromycin (10 mg /kg) od dose for 3 days, AND IM/IV Gentamycin (5-7.5mg/kg/od) for at least 5 days, PLUS oral Azithromycin (10mg/kg/d for 3 days).	IVa 19,20,21	C

Notes:

Step down to appropriate oral antibiotics when improvement is sustained. For instance, cefpodoxime after ceftriaxone. Pathogens targeted in CAP antibiotic regimens include *S. pneumoniae* and Hib for outpatient management; in children requiring hospital admission, additional organisms targeted in recommended antibacterial regimens include *S. aureus* and Gram-negative bacilli. The maximum dose of gentamicin should not exceed 120 mg per day – children treated with gentamicin should have their renal function monitored, as well as gentamicin drug levels (trough levels on day 3 of therapy) if these testes are available. Chloramphenicol is not included in the antibiotic protocol because of its toxicity in the face of effective alternative antibiotics.

\*Alternatives: Consider alternatives when first line drugs are not available or applicable, or if the child has not responded to the first line drugs R.S. = Recommendation strength; Ref = references

**e. Which antibiotics should be used and how should these be administered to a child on admission for severe and very severe CAP?**

In the 2005 WHO CAP guidelines, very severe pneumonia and severe pneumonia were likely to be treated in hospital. Children with severe pneumonia presented with cough, difficulty breathing and lower chest wall indrawing; very severe pneumonia was associated with at least one danger sign, including: convulsions, lethargy or reduced level of consciousness, inability to feed, vomiting everything, central cyanosis, head bobbing or grunting.<sup>90-92</sup>

The 2014 WHO guideline for the management of pneumonia reclassified the management into three categories: severe pneumonia, pneumonia and not pneumonia. The new approach was designed to simplify the management of pneumonia at the outpatient level, reduce the number of referrals for hospitalisation and achieve better treatment outcomes.<sup>90-92</sup>

The 2014 revision preferred oral amoxicillin to oral TMP/SMX for the treatment of fast-breathing pneumonia, as amoxicillin was equivalent to injectable penicillin/ampicillin in cases of chest-indrawing pneumonia. Since both fast-breathing and chest-indrawing pneumonia are now best treated with amoxicillin, classifications were also revised. The new classification was revised to include only two categories of pneumonia: 'pneumonia' with fast breathing and/or chest indrawing, which requires home therapy with oral amoxicillin, and 'severe pneumonia', pneumonia with any general danger sign, which requires referral and injectable antibiotic therapy.<sup>90-93</sup> This is in line with several other recommendations.<sup>41, 61, 77, 79, 87, 94-98</sup>

**Recommendations**

- Antibiotics administered orally are safe and effective for children presenting with severe CAP. **[Evidence level Ia; Grade A+]**
- Intravenous antibiotics should be used in the treatment of pneumonia in children when the child is unable to tolerate oral fluids or absorb oral antibiotics (e.g., because of vomiting) or presents with signs of septicaemia or complicated pneumonia. **[Evidence level IVa; Grade C]**
- Recommended intravenous antibiotics for severe pneumonia include penicillin, ampicillin, and cefuroxime, in combination with IM/IV gentamicin. Recommended dosing is as tabulated above. Empiric antibiotic therapy must be rationalized in response to a microbiological diagnosis. **[Evidence level IVa; Grade C]**
- Second line alternative therapy may include IV ceftriaxone or IV cefotaxime. **[Evidence level IVa; Grade C]**
- For children living with HIV, in addition to the above treatment, high dose TMP/SMX, (table 8), should be included if PJP is suspected. **[Evidence level IVa; Grade C]**

**f. Which Antibiotic should be used for treatment of CAP in children with sickle cell disease?**

As a consequence of their condition, children with sickle cell disease (SCD) are at high risk of developing CAP, caused by a variety of bacterial organisms. There is a need to identify the efficacy and safety of different antibiotic treatment approaches for children with sickle cell disease suffering from CAP.<sup>99-102</sup>

Generally, clinicians agree that special attention should be given to children with chronic illnesses, as these will alter the choice of antibiotics. Suggested antibiotics for children with sickle cell anaemia include penicillin V, ampicillin, cefuroxime, cefixime, cefaclor, ceftriaxone, cefotaxime, azithromycin, and clarithromycin.<sup>100</sup>

However, a systematic review of the Cochrane Database published in 2016, did not find randomized controlled trials (RCTs) of antibiotics for treating CAP in children with SCD. Therefore, it was not possible to determine the efficacy and safety of the antibiotic treatment approaches (monotherapy or combined) for children with SCD suffering from CAP.<sup>100</sup>

**Evidence Statement**

- No randomized controlled trials (RCTs) available as yet supporting the use of antibiotics for treating CAP in children with SCD.
- Recommendations on this are based on expert clinical opinion.

**Recommendations**

- Children with SCD with non-severe CAP, should receive high dose oral amoxicillin (90 mg/kg/day in 2 divided doses for at least 5 days). **[Evidence level II; Grade B+]**
- For alternative treatment, see Table 8.
- Children with SCD with severe pneumonia requiring hospitalization should be given IV ampicillin (150 mg/kg/day in 3 divided doses) OR IV cefuroxime (150 mg/kg/day in 3 divided doses) AND IV/IM gentamicin (5-7.5 mg/kg once daily) PLUS oral erythromycin (60-100 mg/kg/day in 4 divided doses) for at least 5 days. **[Evidence level IVa; Grade C]**
- For alternative antibiotic management, see Table 8.

**g. When should we switch from parenteral to oral antibiotics?**

No RCTs were identified that addressed the issue of when it is safe and effective to transfer from intravenous to oral antibiotic therapy. There can thus be no rigid statement about the timing of transfer to oral treatment. This is an area for further investigation.

**Recommendation**

- In a patient who is receiving intravenous antibiotic therapy for the treatment of CAP, oral treatment should be considered if there is clear evidence of clinical improvement. **[Evidence level IVa; Grade C]**

## 7. Summary: step-wise approach to management of cap

A stepwise approach to management is preferred for children with a history of fever, cough, and/or difficulty breathing. This will serve as an easy guide to clinicians in the emergency rooms to ensure that no step is left out.

**Step 1:** Count the respiratory rate for one full minute when the child is awake and calm, or asleep. If the breathing is fast, consider pneumonia.

**Step 2:** Look for evidence of increased work of breathing (difficulty breathing): look specifically for indrawing of the lower chest wall when the child breathes in, and nasal flaring. Listen for grunting, wheeze or stridor in a calm child.

**Step 3:** Check for cyanosis (bluish discolouration) by looking at the tongue and buccal mucosa. Document the oxygen saturation using a pulse oximeter.

**Step 4:** Palpate for the position of the trachea.

**Step 5:** Percuss the chest for dullness, or hyper-resonance.

**Step 6:** Auscultate for bronchial breath sounds, crepitations, or wheezes.

**Step 7:** Look for complications such as heart failure (tachycardia, tender hepatomegaly), pleural effusion (stony dull percussion note, reduced/absent breath sound over the region of either or both chest regions), pneumothorax (hyper-resonance and reduced/absent breath sounds over the upper and lateral region of the involved lung field).

**Step 8:** Look for signs of other organ involvement. Ask/determine if convulsion, lethargy, inability to drink or feed or not responding to voice is present. Presence of these features or any of the complications listed above indicates severe pneumonia.

**Step 9:** Classify the severity of pneumonia (using the WHO classification).

**Step 10:** Decide whether the child you are attending to requires hospitalization. Criteria for management in the hospital are:

- Age less than 2 months
- Severe pneumonia
- Presence of complications or co-morbidities
- SpO<sub>2</sub> 90% or less in room air
- Features of malnutrition.

**Step 11:** Decide on relevant investigations:

- Chest radiography is not required in children who are stable enough to be managed in the outpatient setting.
- Do chest radiography in children with pneumonia needing hospitalization, more so in those children suspected of having complications such as parapneumonic effusion (pleural effusion, empyema) or pneumothorax.
- Routine full blood count is not required for children suspected of having pneumonia who are stable enough to be managed in the outpatient setting.

- A full blood count should be obtained for all children with severe pneumonia, or who are sick enough to be hospitalized.
- A minimum of Rapid diagnostic test screen for malaria (RDT) should be obtained as malaria is a common and important co-morbidity in this environment,
- Blood culture should be obtained in sick children requiring hospitalization. Serum electrolytes, urea and creatinine, and random blood sugar should be obtained in children with severe pneumonia.

**Step 12:** Appropriate antibiotic therapy (Table 7) must be prescribed for all children with pneumonia.

**Step 13:** Regular re-assessment of patients, including necessary investigations, should be undertaken. Children stable enough to be managed in the outpatient setting should be reviewed on day 3 or 4, or earlier if their status deteriorates.

**Step 14:** If no improvement, consider transferring to a tertiary centre or ICU (see conditions for transfer to ICU).

**Step 15:** If improving, consider discharge (see condition for discharge).

### At Discharge

- Plan to review the child two days after discharge.
- Review immunization record and make plans to catch up immunisations if vaccines have been missed. In addition, children under 2 years should get recommended doses of pneumococcal conjugate vaccine (PCV) or Hib vaccine if not already immunized.
- Instruct the caregiver to bring child to the hospital if a child with cough and catarrh develops fast breathing or danger signs.
- Instruct the caregiver to increase frequency of feeding for the next 2 weeks after treatment for pneumonia. Children with moderate to severe malnutrition should receive treatment advice according to standard guidelines.

### Drugs to Avoid in the Management of Pneumonia

Cough syrups containing antihistamines or opioids such as codeine and hydrocodeine. These preparations add little to the management of pneumonia, and may be toxic in some children.

## 8. Prevention

There are proven strategies for the prevention of CAP in children. These include:

### Recommendations

#### A. Primary prevention

- Counseling/Health Education for CAP
- Health education and guidance play important roles in the management of children with CAP. Counselling

should be ongoing from admission to discharge, with regular updates to the family on progress of management. Information on what the caregiver should observe in the child, and when to report to the health facility should be communicated.

**Such education to caregivers should include:**

1. The fact that CAP is caused by micro-organisms.
  2. Environmental factors may predispose to CAP and CAP-related deaths. Indoor air pollution including passive parental smoking, overcrowding, poor ventilation, poor personal and environmental hygiene should be optimized in the home environment to prevent pneumonia episodes in young children residing in the household. Good hand washing practices should be emphasized.
  3. Education about the presenting features of pneumonia must emphasise the need for early recognition of fast breathing.
  4. Immunization against common childhood diseases is a key preventative measure. Vaccines that protect against pneumonia such as PCV, Hib vaccine, pertussis vaccine, and measles vaccine are routinely administered as part of the Expanded Programme on Immunization (EPI), and caregivers should be encouraged to ensure that the children under their care are fully vaccinated.
  5. The importance of exclusive breastfeeding in the first 6 months of life and adequate nutrition should be explained to the caregiver.
  6. Opportunities should be given for caregivers to express his/her fears. Cultural and religious beliefs that may be detrimental to achieving optimal health and development of the child should be discussed.
  7. Caregivers should be educated to avoid over-the-counter medications, including the use of cough mixtures.
- *Measures to reduce risk factors*
    - Improved housing: improved ventilation, reduction of overcrowding and indoor air pollution.
    - Improved nutrition
    - Exclusive breastfeeding for the first 6 months.
    - Micronutrient supplementation, including vitamin A and zinc.

**B. Specific prevention**

**Evidence statements**

- Antiretroviral therapy (ART) is life-saving in children living with HIV [CLWH]. [Evidence level Ia; Grade A+]
- Co-trimoxazole preventive therapy (CPT) provides significant protection against opportunistic infections (OIs) in young CLWH, and in older, ART-naïve or severely immunosuppressed children. [Evidence level Ia; Grade A+]
- TB preventive therapy (TPT) protects against the development of TB disease in CLWH of any age, or in immune-competent children <5 years, who are household contacts of adults with active tuberculo-

sis and other children with positive Mantoux test result [Evidence level II; Grade B+]

**Recommendations**

- ART should be commenced as soon as a diagnosis of HIV infection is confirmed. [Evidence level Ia; Grade A+]
- CPT should be commenced for CLHW as soon as the HIV diagnosis is confirmed, as well as for severely immune-compromised children, and continued until the child has shown consistent improvement in the immunological status and suppression of the HIV viral load.
- TPT should be used in CLWH of any age, or in immune-competent children <5 years, with a household contact with tuberculosis. [Evidence level II; Grade B+]
- TPT is indicated for any CLWH who is TST (Mantoux) positive, as long as active TB has been excluded.

Tables 9 and 10 show the dosages and frequency of administration of CPT and TPT for children living with HIV

- *Specific Vaccines*
  - Conjugate vaccine for *S. pneumoniae*
  - Conjugate vaccine for *H. influenzae* type b
  - Influenza vaccine
- *Other vaccines*
  - Measles containing vaccine (including booster doses)
  - BCG vaccine
  - Pertussis vaccine (now in pentavalent vaccine used nationwide; including booster doses)
  - HIV prevention – prevention of mother-to-child transmission of HIV.

**Table 9:** Dosage of Co-trimoxazole for prophylaxis in CLWA

Children <14 kg	Adolescents 14 kg
Infants <6 months or < 5 kg: 120mg daily	14 years or >30 kg: 960 mg daily
Children 6 months–5 years or 5 –15 kg: 240 mg daily	
Children 6 –14 years old or 15 – 30 kg: 480 mg daily	

**Table 10:** Dosage of prophylactic regimens for TB Preventive Therapy in children

Regimen	Dosage	Maximum Dose
Isoniazid (INH) daily for 6 months (6H)	10 mg/kg/day (range:7 – 15 mg/kg/day)	300 mg/day
Weekly Rifapentine plus Isoniazid for 3 months - 12 doses (3HP)	Isoniazid: Children aged 12 years – 15 mg/kg/dose Children aged 2-11 years – 25 mg/kg/dose Rifapentine: 10.0 - 14.0 kg = 300mg 4.1 - 25.0 kg = 450mg 25.1 - 32.0 kg = 600mg 32.1 -50.0 kg = 750mg > 50 kg = 900mg	Isoniazid – 900 mg per week Rifapentine – 900 mg per week
Daily Isoniazid plus Rifampicin for 3 months (3HR)	Rifampicin: Age < 10 years = 15 mg/kg/dose (range 10–20 mg/kg/dose) Age 10 years = 10 mg/kg/dose Isoniazid Age <10 yrs = 10mg/kg/dose (range 7–15 mg/kg/dose) Age 10 yrs = 5 mg/kg/dose	Rifampicin – 600 mg/day Isoniazid – 300 mg/day
Daily Isoniazid and Rifapentine for 1 month	Age 13 years (regardless of weight) Isoniazid 300 mg/day Rifapentine 600 mg/day	Isoniazid –300 mg Rifapentine – 600 mg

### Prevention of CAP and COVID-19<sup>102-105</sup>

- Coronavirus Infectious Disease 2019 (COVID-19) is a viral respiratory illness caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), a single stranded RNA virus that most likely originated from zoonotic origin.. SARS-CoV-2 is transmitted by contact with infected individuals through contaminated hands, by inoculation into the mucosal surfaces of the eyes, nose or mouth. Respiratory droplets are produced during coughing or sneezing, and they are other source of infection, through inhalation into the respiratory tract. The incubation period is 1 – 14 days, and many of those infected remain asymptomatic or mildly symptomatic. Individuals with COVID-19 pneumonia develop changes in their lungs, including:
  - Inflammation that may be so severe as to damage the alveoli, impairing gaseous exchange, with associated fluid leak and pulmonary oedema. Respiratory symptoms of COVID-19 are similar to that of pneumonia.
  - The pathophysiologic process of the SARS-Cov-2 virus involves attachment, penetration, biosynthesis, maturation and release. Gaining access into the host cells is by the spike protein to the angiotensin converting enzyme receptor (ACE 2) on the surface of target cells through endocytosis. The viral content is then released inside the host

cell and the viral RNA enters the nucleus for replication. This initiates activation of the cell mediated response; a major part of the immune response to the presence of the virus in the host. This is usually initiated by antigen presentation i.e., dendritic cells and macrophages. Following recognition of the presented antigens, the T-cells produce pro-inflammatory cytokines such as interleukins 4, 5, 6 which are very powerful activator of B-cells leading to production of viral specific antibodies and the activated killer T-cells (CD<sub>8</sub> T-cells). This host immune response and the production of other pro-inflammatory mediators by the T-cells eventually lead to very high levels of these pro-inflammatory cytokines which is referred to as the cytokine storm. This plays a major role in lung destruction and other end organ damage.

### Management of COVID-19 in children

#### A. Supportive:

1. Fever control – exposure of patient, tepid sponging, paracetamol, dipyrrone, ibuprofen as applicable.
2. Rehydration with oral or intravenous fluid
3. Ensure adequate caloric intake - continue breastfeeding in infants and younger children.
4. Monitoring of fluid input / output.

#### B. Specific anti-viral drugs: Specific anti-viral drug for treatment of COVID-19 has been controversial.

Research is currently ongoing on manufacturing of specific effective anti-viral drug(s) against COVID-19.

#### C. Adjunct treatment

1. Azithromycin 10mg/kg on the first day followed by 4mg/kg/day for 4 days with a maximum dose of 30mg/kg or 1500mg.

OR

2. Use of amoxi-clav @50mg per kg per day; giving 12 hourly for 10 days.
3. Suspension Zinc 10mg daily for 2 weeks.
4. Suspension Vitamin D 400 IU daily for 2 weeks.
5. Suspension Vitamin C 50mg 8 hourly for 2 weeks
6. Use of corticosteroids should be considered following the pathophysiology especially the interleukin storm. Specifically, drugs like anti-IL-6 (Actema) may be more useful. Corticosteroids may be useful in reducing bronchospasm or those in septic shock.
7. The dose in the COVID-19 study stipulates that Dexamethasone should be given orally (liquid or tablets) or intravenous preparation 6 mg once daily for ten days. Dose in children should be 0.1mg/kg/day tablet/syrup given once orally for 10 days.

#### Major preventive measures include:

- Regular hand washing with water and soap.
- Make use of hand sanitizers regularly.
- Avoid touching surfaces.
- Maintain physical distance when in public spaces, and avoid overcrowded places.
- Wear a face mask, especially when around other

- people and when venturing into public spaces.
- Do not share personal care products.
- Practice good self-care by getting plenty of rest, eating regularly, and drinking lots of fluids.
- Visit a health facility if signs of illness develop.
- Adults (persons >18 years of age) are eligible to be vaccinated against COVID-19; at least two doses taken 3 months apart.

### 9. Area of future research

Although recommendations about investigations and antimicrobial therapy are given in this guideline, they are generally not supported by strong evidence, reflecting the paucity of well-conducted local and regional studies examining the problem of community-acquired pediatric pneumonia. The paucity of data on various aspects of childhood community acquired pneumonia in Nigeria makes it imperative for developing a research agenda directed at filling the knowledge gaps in areas that include:

1. Viral contribution to aetiology of CAP
2. Bacterial super-imposition following an initial viral infection
3. Seasonal variations in the contribution of various organisms to childhood community acquired pneumonia
4. Contribution of *Mycoplasma pneumoniae* to childhood CAP
5. Severity grading of childhood community acquired pneumonia
6. Antibiotic sensitivity/resistance patterns of common organisms causing CAP
7. Appropriate and relevant clinical scoring tool
8. Usefulness of procalcitonin and C-reactive protein in CAP
9. Surveillance on the prevalent pneumococcal serotypes in Nigeria
10. Surveillance on the prevalence and role of non-typeable *Haemophilus influenzae* in Nigeria.

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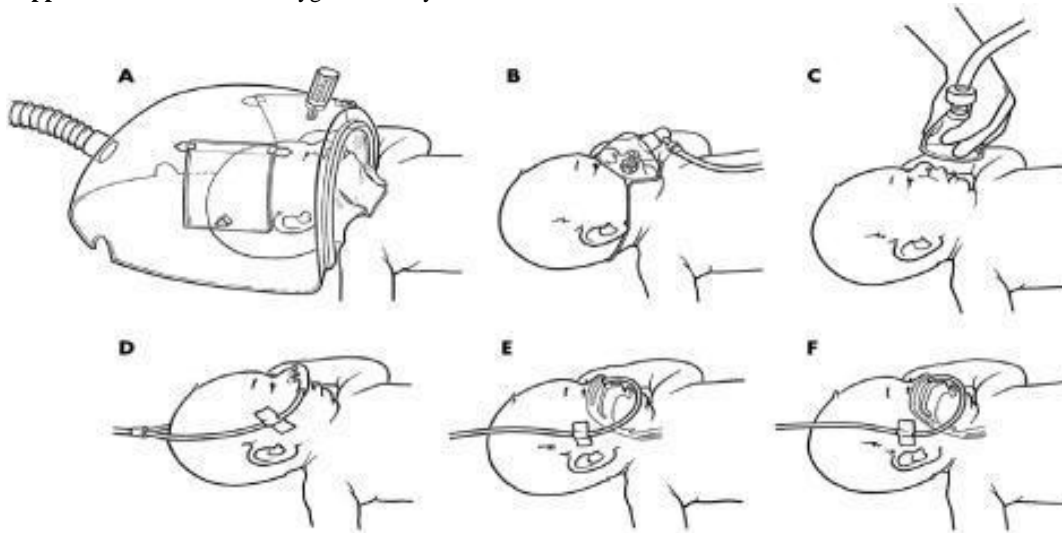
**Appendix I: Lung Sound Nomenclature**

Lung Sound Nomenclature	Description	Term
Discontinuous	Fine (high pitched, low amplitude, short duration)	Fine crackles (crepitations/Rhales)
	Coarse (low pitched, high amplitude, long duration)	Coarse crackles (crepitations/Rhales)
Continuous	Continuous, musical sound heard during	Rhonchi or wheezing

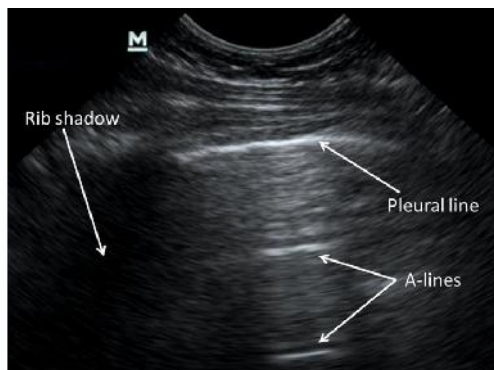
expiration only or during both phases of respiration

NB: Wheezes and Rhonchi may be heard in severe Pneumonia

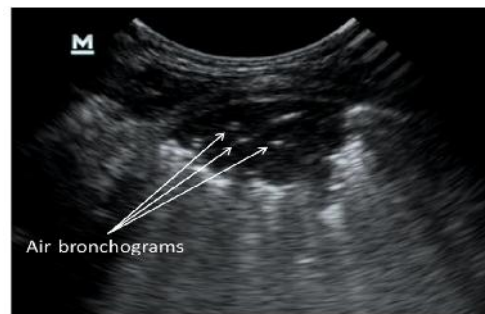
**Appendix II: Methods of Oxygen Delivery**



**Appendix III<sup>106</sup>**



**Fig. 1** An ultrasound image from the right anterior upper lung zone in a 16-month-old girl demonstrates normal lung echo pattern with a smooth, hyperechoic pleural line, A-lines and no B-lines



**Fig. 3** An ultrasound image from the right posterior upper lung zone in a 3-month-old girl hospitalised with pneumonia shows a wedge-shaped hypoechoic area of subpleural consolidation. Associated features that can be seen are air bronchograms represented by punctate hyperechoic specks within the lesion, a hypoechoic pleural line over the lesion and multiple B-lines that arise from the deep edge of the consolidation rather than from the pleura

**Appendix IV**

List of abbreviations

ACE	Angiotensin converting enzyme	RCT	Randomised-control trial
ADV	Adenovirus	RSV	Respiratory syncytial virus
AOR	Adjusted odd ratio	RR	Respiratory rate
AP	Antero-posterior	SCA	Sickle cell Anaemia
APR	Acute phase reactants	TPT	TB preventive therapy
ARI	Acute respiratory infection	VAP	Ventilator-associated pneumonia
ART	Anti-retroviral therapy	WAZ	Weight-for-age Z score
ARTI	Acute respiratory tract infection		
BCG	Baccille-Calmete Guerin	WHO	World Health Organization
BNP	Brain natriuretic protein		
CAP	Community-acquired pneumonia		
CLWH	Children living with HIV		
CI	Confidence Interval		
COVID-19	Coronavirus disease 2019		
CPT	Cotrimoxazole preventive therapy		
DAD	Diffuse alveolar damage		
HAP	Hospital-acquired infection		
HIV	Human immunodeficiency virus		
IMCI	Integrated management of childhood illnesses		
LRT	Lower respiratory tract		
NDHS	National Demographic Health Survey		
OI	Opportunistic infection		
PCV	Pneumococcal conjugate vaccine		
PCR	Polymerase chain reaction		
PCT	Pro-calcitonin		