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REVIEW article

A review on pneumonia in children: Clear insights

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Abstract: In developing nations, pneumonia is the leading cause of death for young children; however, mortality can be effectively decreased with early diagnosis and care. The objectives of the review are to evaluate the significance of clinical signs and symptoms in diagnosing pneumonia, and treatment in children under the age of five, as well as to examine the precision of WHO criteria in diagnosing clinical pneumonia in general people. According to the World Health Organization's definition and the Integrated Management of Childhood Illness (IMCI) initiative, pneumonia is clinically characterized by an acute cough, with or without fever, accompanied by dyspnea or tachypnea. Acute infections of the gut and gastroenteritis can be effectively controlled and treated. Acute respiratory infections, particularly pneumonia, are increasingly regarded as the leading infectious cause of mortality among children in developing nations. The diagnosis of pneumonia is primarily clinical and categorized into four domains: clinical assessment, epidemiological factors, radiographic imaging, and standard laboratory results. Pneumonia can be classified into three categories: bacterial, viral, and acute pneumonia. In every instance, a potential diagnosis should be made and the appropriate course of therapy should be administered based on the features of that pneumonia. Preventing and lowering the death and morbidity of this significant disease in children can be greatly aided by physicians having precise and accurate information on how to identify and treat it without incurring additional expenses.

Introduction

Pneumonia is the leading cause of death for children under five in underdeveloped nations. Reducing mortality requires treating patients with pneumonia as soon as possible after diagnosis. It is difficult to determine who of the many children arriving with respiratory symptoms have a case of pneumonia that requires antibiotic therapy because cough is a common symptom in two-thirds of children who visit outpatient clinics in low-income nations [1, 2]. The most commonly used method for diagnosing pneumonia today, a chest radiograph, is unavailable in settings with limited resources where the illness burden is highest [3]. Chest radiographs, even when available, cannot be performed for every child who coughs due to the extremely high incidence of this complaint and the possible long-term effects of X-ray exposure. Thus, children who require an antibiotic or a chest scan for examination are determined using clinical predictors. Since the late 1980s, the World Health Organization (WHO) has recommended that cough, rapid breathing, and chest tightness be present to diagnose pneumonia in developing nations [4, 5]. This recommendation was substantiated by a supplementary study conducted in the 1990s and was founded on studies published in the late 1980s. Since then, no significant

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advancements have been achieved in diagnosing pneumonia, and there is still no reliable point-of-care test to help identify kids who would benefit from antibiotics. Concerns about the over-prescription of antibiotics, arising from the insufficient precision of the WHO criteria for identifying acute respiratory infections, are increasing due to the swift global proliferation of antibiotic resistance [6, 7].

Acute respiratory infections (ARI) account for 1.4 million deaths globally each year, with acute pneumonia accounting for about 90% of these cases, according to WHO estimates from 2000. The same figures show that 1.9 million of them are youngsters under the age of five and that most are connected to underdeveloped nations since hunger is an underlying cause [8-9]. Acute lower respiratory infections, particularly pneumonia, cause over 20% of pediatric fatalities. Therefore, 12 to 20 children under the age of five pass away from pneumonia for every 1000 infants in underdeveloped nations. As a result, it appears that children have a significant burden of disease from acute respiratory infections, particularly pneumonia [10-12]. Pneumonitis is the term used to describe inflammation of the lung parenchyma; pneumonia is used when the cause of the inflammation is a microbiological agent. Bacterial, viral, or even parasitic agents might be considered microbial agents. Pneumonia, according to the criteria established by the World Health Organization and the Integrated Management of Childhood Illness (IMCI) project, is characterized by an acute cough, regardless of a fever, accompanied by dyspnea or respiratory distress. Naturally, there is not much of a difference in this definition between the two significant acute lower respiratory infections that are not considered, namely pneumonia and bronchiolitis. Tachypnea is extremely sensitive in diagnosing acute lower respiratory infections, especially pneumonia. Fever and tachypnea have low specificity and high sensitivity. In diagnosing pneumonia, auscultating for pulmonary rales or assessing pleural pain has good specificity but low sensitivity [13, 14].

Search strategy and selection criteria: Search terms such as complicated pneumonia, pneumonia in children, diagnosis of pneumonia, pathophysiology of pneumonia, lung abscess, bronchopleural fistula, and children are used to find articles published in English between 1995 and 2024 indexed in MEDLINE, PubMed, Scopus, Google Scholar, and the Cochrane Library. Case studies, reviews, and other clinical research types with a focus on children aged 15 and under were included in this study. Most of the research was done on publications that were released between 2010 and the end of 2023. This Review cites review articles, research, and book chapters to give readers more information and references.

Etiology: The etiologies of pneumonia include infectious agents, such as bacteria, viruses, and protozoa. Of course, in 25% to 33% of studies, the cause of the pneumonia has not been demonstrated, or in several cases, the pneumonia infection has been linked to two microbes simultaneously. This means that in about 41% of hospitalized patients, pneumonia has been linked to two or more microorganisms [15-18].

Pathophysiology: Pleural effusion is the most prevalent sign of complex pneumonia. It may be divided into three stages: the organizing phase, which includes fibroblast activity and peel development, exudative (simple parapneumonic effusion), and fibrinopurulent (complicated parapneumonic effusion). "Empyema" denotes the most extreme manifestation of the disease and, in a less formal context, a phase indicative of a complex series of occurrences. The primary cause of pleural fluid accumulation during infection is the dysregulation of hydrostatic and oncotic pressure equilibrium between the pleural space and the systemic and pulmonary circulations [19]. The buildup of the effusion is further facilitated by debris and thick pleural fluid obstructing lymphatic drainage [20]. The widespread disintegration and liquefaction of lung tissue is the hallmark of necrotizing pneumonia, which can still happen even in patients receiving the appropriate medications. The etiology of necrotizing pneumonia is unknown. Vascular thrombosis has been shown by Hsieh and colleagues in pathological material from a child who died of necrotizing pneumonia. Furthermore, investigations utilizing an ultrasonic Doppler have revealed a lack of blood flow in the necrotic regions of the lungs in kids suffering from complex pneumonia and parapneumonic effusion, signifying a significant blockage of blood vessels [21,

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22]. Another theory is that necrotizing pneumonia may have a hereditary tendency [22]. According to WHO recommendations, children who have a cough or breathing difficulties can be categorized into three groups depending on their clinical signs: severe pneumonia, pneumonia, or no pneumonia [23] (**Figure 1**).

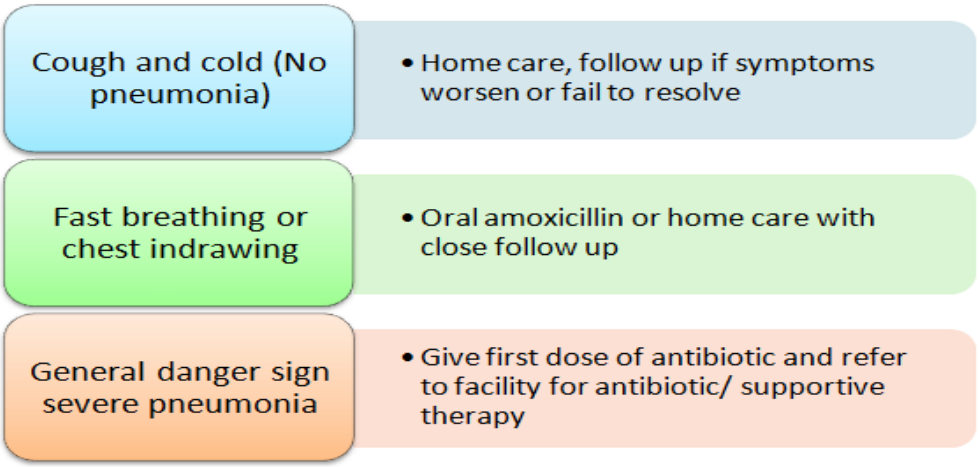

Figure 1: Updated WHO guidelines for diagnosing and treating pediatric pneumonia in hospitals

The first stage of necrotizing pneumonia is characterized by consolidation with necrosis [24]. Pneumatoceles, or cavitation, is a rapidly progressing condition that is typically peripheral and confined to a single lobe after necrosis [25]. With air-fluid levels, small cavities can combine to become giant cysts that resemble lung abscesses [26]. A bronchopleural fistula may result from a breach through to the pleural area. Differentiating between localized pneumothorax and air-containing lesions that are pneumatoceles can be challenging. Severe cases of necrotizing pneumonia have also been linked to strains of *Staphylococcus aureus* that express Panton-Valentine leukocidin, an exotoxin that generates pores in immune cells and can release proteases that damage tissue [27, 28]. *Staphylococcus aureus* strains positive for Panton-Valentine leukocidin have been observed to have a higher affinity for injured airway epithelium than strains negative for the leukocidin. Meticillin resistance is common in these bacteria [29]. A lung abscess is typically a single, thickly walled chamber that has suppuration and parenchymal necrosis inside of it, including purulent material. Although it is uncommon, people who already have a hereditary cystic lung deformation or have an immune deficit may develop a lung abscess related to complicated pneumonia. Usually, there is a sluggish development from the early involvement to the creation of an abscess. Lemierre's condition, also known as internal jugular vein thrombosis, can occasionally lead to a metastatic lung abscess [30, 31].

Significant etiological elements of childhood pneumonia: In younger children, viruses are the most common cause of pneumonia; as children get older, these infections become less common [32]. Important viruses that cause pneumonia in children include rhinoviruses, enteroviruses, parainfluenza, and RSV. Adenoviruses, parainfluenza, coronaviruses, and other viruses of a lesser degree also cause pneumonia in children. One of the major causes of viral pneumonia has recently been shown to be the human pneumovirus (HPV) [33]. Naturally, extensive immunization programs are leading to the eradication of the significant viral agent known as measles, which is recognized as one of the most significant and serious viral types of pneumonia. Pneumococcus is the most common cause of bacterial pneumonia at all stages of human life, except for infancy [34]. Although interstitial pneumonia or pneumonia with effusion are possible presentations, typical local pneumonia is the most common one caused by pneumococcus. In certain developed countries, routine use of the heptavalent pneumococcal vaccine has reduced the incidence of pneumonia caused by Pneumococcus, with a 35% reduction observed in the prevalence of radiologically proven pneumonia [35]. The other of the two major causes is bacterial pneumonia, which is more common in children under five years old and whose

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clinical symptoms can be mistaken for pneumococcal infections, ranging from mild to severe. In developed nations, the *Haemophilus influenzae* type B conjugate vaccine has significantly decreased the incidence of invasive infections, including pneumonia [36]. It typically results from an early viral infection, particularly from the influenza virus, and causes pneumonia in early infancy. Pneumonia often starts suddenly, progresses quickly, and is accompanied by scattered pneumatoceles in the lung, empyema, and the development of an abscess. In older children, its radiological and clinical history might not be any different from other bacterial causes. 75% of the first cases of this type of pneumonia are the result of a child's underlying problem; these issues are unilateral in 65% of cases and often occur in children under the age of one. The secondary kind is often bilateral and results from an infection that spreads to the lung from another location.

Pneumonia induced by this microorganism is uncommon in children. A notable trait is the widespread necrosis of the respiratory tract mucosa accompanied by edema and hemorrhage, which can extend the fever in these individuals for many days, occasionally lasting up to ten days despite appropriate therapy. Pleurisy and pneumatocele are also observed following this pneumonia [36]. Pleurisy and pneumatocele are also seen after this pneumonia [37]. Acute pneumonia is most often caused by *Mycoplasma pneumoniae*, especially in children over the age of five [38]. Typically, diffuse infiltration-which might occasionally be bilateral interstitial pneumonia-is shown in the lung image. Pneumonia is seldom observed in conjunction. Since skin, nerve, heart, and blood manifestations are the most prevalent extrapulmonary manifestations, extrapulmonary symptoms are seen by 25% of hospitalized Mycoplasma infection patients [38]. Acute pneumonia can be caused by any of the three forms of chlamydia. In babies under four months old, *Chlamydia trachomatis* is often bilateral and the primary cause of pneumonia without fever. The infection is mostly spread by the vaginal secretions of the infected mother. Another significant cause of acute pneumonia in children and adolescents is *Chlamydia pneumonia*. Like *Mycoplasma pneumoniae*, it has a very similar epidemiology and is usually asymptomatic [39]. And lastly, *Chlamydia psittaci*, which can result in a high fever, tonsillitis, and a strong headache and is typically spread by contact with birds. A hallmark of this uncommon pediatric pneumonia is an elevation of alkaline phosphatase and liver enzymes.

Clinical features: Empyema must be considered in any child who remains febrile or unwell 48-72 hrs after initiating the prescribed antibiotic therapy. Pneumonia and pleural effusion both exhibit dullness to percussion and reduced breath sounds upon physical examination; fremitus is enhanced in consolidation but decreased in pleural effusion. Fremitus detection in children may not be as helpful as in adults and is dependent on the child's size, age, and compliance. In cases of lung consolidation, bronchial breathing is audible, but not in cases of pleural effusion [40]. It's critical to recognize the risk of meningitis, septic arthritis, and metastatic hematogenous infections in children with bacteremic pneumococcal pneumonia. A kid with necrotizing pneumonia usually looks unwell and has a high fever, cough, and tachypnea that lasts for many days. Hypoxia is common, mild anemia and hypoalbuminemia are commonplace, and physical examination often reveals pleural effusion. Children usually stay sick for several days, most likely as a result of tissue necrosis releasing inflammatory mediators. Children with necrotizing pneumonia can also sometimes experience multiorgan involvement, acute respiratory distress syndrome, septic shock, and escalating respiratory distress [41]. The signs indicating a possible deterioration include hemoptysis, an erythematous rash, influenza-like symptoms, and decreased peripheral white blood cell counts. These symptoms are often associated with strains of S aureus that produce Panton-Valentine leukocidin. In more severe situations, extracorporeal membrane oxygenation or even circulating and ventilation assistance in critical care units may be needed [42, 43]. Pediatric patients suffering from lung abscesses typically exhibit a protracted low-grade fever and cough; less frequently, they also have chest discomfort, dyspnea, sputum production, and hemoptysis. An examination of the chest may show no abnormalities or evidence of consolidation. Pneumothorax, lung compression, bronchopleural fistula, and mediastinal shift with increasing respiratory compromise are some of the outcomes [44].

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Diagnosis process of pneumonia: Most community-acquired pneumonia (CAP) cases do not need the identification of the causal agent, and pneumonia is only diagnosed under certain conditions, such as severe and complex pneumonia, certain hospital-acquired pneumonia (HAP) cases, and others. When treating patients with underlying medical conditions, progressive pneumonia cases that do not improve with early medication, or cases of empyema or lung abscess, identifying the bacteria involved is critical (e.g., infants with primary immunodeficiency or CF patients) [45]. Samples from nasopharyngeal secretions should only be prepared under certain circumstances, such as viral illnesses like RSV and influenza, as natural colonization in that location makes sample preparation unreliable for antigen assessment or microorganism culture. The etiological agent of pneumonia is typically not identified by taking samples from the oropharynx and throat [46]. In the event of pleurisy, blood or fluid production from the cavity is also beneficial. Only 15% of cases with bacterial pneumonia have a positive blood culture due to the low sensitivity of the finding that germs are present in the blood. However, this finding has a high specificity. Thus, for every kid suspected of having bacterial pneumonia, a blood culture is advised. Invasive procedures such as bronchoscopy, preparing the bronchoalveolar lavage (BAL), or an open or closed lung biopsy may occasionally be necessary for a definitive diagnosis and an appropriate course of treatment. Acute phase reactants, including white blood cell count, C-reactive protein, and erythrocyte sedimentation rate, are frequently ineffective in differentiating between viral and bacterial pneumonia in humans; however, serial assessments may aid in monitoring therapeutic response. The clinical setting is essential. Increased C-reactive protein levels can aid in identifying the bacterial etiology of community-acquired pneumonia (CAP), although they lack sufficient specificity and sensitivity to inform treatment options [47]. Percutaneous, image-guided lung abscess aspiration, and drainage may be used for diagnostic purposes. Despite prior antibiotic therapy, an organism may typically be recognized on the aspirational material culture. Still, lung aspirate culture is not a standard clinical procedure. Aspirating lung abscesses appear to carry a lower incidence of bronchopleural fistulae than aspirating necrotizing pneumonias, however, seepage into the pleural area from an abscess can happen both during and after drainage. The performance of age-related rapid breathing and chest indrawing (**Table 1**), while determining the criteria for clinical pneumonia found from research selected by WHO.

Table 1: The WHO used research to determine the performance of age-related rapid breathing and chest indrawing while determining the criteria for clinical pneumonia

	Age range	Reference standard	True positive	False-negative	False-positive	True negative	Sensitivity (95% CI)	Specificity (95% CI)
Lower chest wall indrawing								
Cherian et al. [48]	< 5 year	Crepitations or chest radiograph	193	57	11	421	0.77 (0.71-0.82)	0·97 (0·95-0·99)
Campbell et al. [49]	0-4 year	Chest radiograph	15	10	117	113	0.60 (0.39-0.79)	0·39 (0·32-0·46)
Harari et al. [50]	< 6 year	Chest radiograph	18	38	16	113	0.32 (0.20-0.46)	0·88 (0·81-0·93)
Age-related fast breathing								
Cherian et al. [48]	< 5 year	Crepitations or chest radiograph	204	46	47	385	0.82 (0.76-0.86)	0.89 (0.86-0.92)
Shann et al. [51]	<5 year	Crepitations	52	15	36	97	0.78 (0.66-0.87)	0.73 (0.65-0.80)
Harari et al. [50]	< 6 year	Chest radiograph	41	15	47	82	0.73 (0.60-0.84)	0.64 (0.55-0.72)
Mulholland et al. [23, 52]	2-59 month	Pediatrician	20	6	64	201	0.77 (0.56-0.91)	0.76 (0.70-0.81)

*CI stands for confidence interval. Respiratory rate: >60 breaths per minute in infants under 2 months, >50 breaths per minute in infants between 2 and 11 months, and >40 breaths per minute in infants between 12 and 59 months

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Treatments and prevention: Based on the findings of the four examinations, the patient is evaluated for one of the three types of pneumonia: bacterial or viral, which include epidemiological outcomes, clinical findings, radiology findings, and routine laboratory results. Penicillins are still the first-choice antibiotics when the patient only has pneumonia and the infection is confined to the lungs; simply raising the dosage of these antibiotics will not cause them to fail. This is more significant than the fact that penicillin-resistant pneumococci are becoming more and more resistant to antibiotics [53]. The preferred medication is third-generation intravenous cephalosporins; if there is no first response and the pneumococcal MIC (minimum inhibitory concentration) for penicillin exceeds 4.0 μg/dl, vancomycin is included in the treatment regimen [54]. The fragile sternum, more horizontal ribs, and weaker intercostal muscles in youngsters facilitate the retraction of the intercostal muscles as a compensatory approach in response to hypoxia from pneumonia, the primary cause of which is an unbalance between ventilation and perfusion. Treatment for severe pneumonia, particularly in children, depends on avoiding hypoxia and the ensuing acidosis since this compensatory mechanism to keep the lungs from collapsing cannot function for an extended period [55]. The WHO recommends giving oxygen, ideally by a nasal probe, to any kid exhibiting cyanosis signs, as well as the inability to feed and a breathing rate of more than 60 breaths per minute [56]. Both chest indrawing pneumonia and quick breathing pneumonia can be treated with oral amoxicillin (**Table 2**).

Table 2: Doses of amoxicillin for children 2-59 months of age with pneumonia [57]

Pneumonia types	Age/weight of child	Dosage of amoxicillin dispersible tablets (250 mg)
Rapid breathing pneumonia	From two months to twelve months (4-<10 kg)	1 tab twice a day x 5 days (10 tabs)
	From one year to five years old (11-19 kg)	2 tabs twice a day x 5 days (20 tabs)
Rapid breathing and chest Indrawing pneumonia	2 months up to 12 months (4-<10 kg)	1 tab twice a day x 5 days (10 tabs)
	12 months up to 3 years (10-<14 kg)	2 tabs twice a day x 5 days (20 tabs)
	3 years up to 5 years (14-19 kg)	3 tabs twice a day x 5 days (30 tabs)

If oral medication is selected, three to five days of treatment are enough, according to the IMCI plan. Nonetheless, it appears that the type of crime determines the appropriate oral therapy. Therefore, the course of treatment for moderate bacterial pneumonia by a timeframe of 5-7 days, and for more severe conditions, it is 10-14 days. When hospitalization and intravenous therapy are started, oral medication may be substituted for intravenous therapy if clinical symptoms worsen, fever goes away for 48-72 hrs, ESR drops by 20%, and CRP drops. The following general preventative measures, which are compiled in (**Table 3**), lessen the frequency and severity of pneumonia.

Table 3: Strategies for preventing pediatric pneumonia

General strategy	Summary
Nutrition	Children who are malnourished are more likely to die and get severe pneumonia (breastfeeding is protective).
Vitamin A	The Road to Health card schedule should be adhered to when taking vitamin A. At six months, two years, and eighteen months, the IU statistics were 100,000, 200,000, and 200,000, respectively. 200 000 IU every six months for youngsters two to five years old after 24 months
Vitamin D	Vitamin D-deficient children are at increased risk for CAP, supplement with vitamin D 400 IU daily
Zinc	The incidence of pneumonia is significantly reduced by giving older children and newborns 10 mg or 20 mg of zinc per day, respectively.
Reduction in passive smoking and indoor fuel exposure	There is a high correlation between children's lung health and environmental exposure to indoor air pollution or cigarette smoking.
Infection prevention and control and physical distancing	The burden of respiratory disease is decreased when respiratory pathogen transmission is well controlled. Keeping hands clean, coughing manners, cleaning outdoor surfaces, and wearing masks.

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The mechanisms of action and anti-inflammatory properties of corticosteroids in juvenile respiratory diseases have been reviewed. The purpose of treating robust inflammatory responses in pneumonia patients is why corticosteroids are used. A Cochrane review involving 310 patients from 17 randomized controlled trials (RCTs) found that corticosteroid treatment reduced morbidity in adults with severe CAP, but not death, and morbidity excluded mortality in adults and children with less severe CAP. Four of the RCTs involved children. Adult corticosteroid medication was linked to a greater number of side effects than placebo treatment, particularly hyperglycemia [58, 59]. Malnutrition is a significant risk factor for the morbidity and mortality of children with pneumonia. Furthermore, initiating oral feeding and maintaining appropriate hydration for a kid suffering from severe pneumonia promptly is crucial in expediting the child's recuperation. A deficit in vitamin A increases the risk of respiratory infections and pneumonia-related deaths [60]. Therefore, a patient's prognosis is greatly influenced by malnutrition and a deficiency in vitamin A. Sulfate treatment, on the other hand, lowers hospital stay length by 25% and pneumonia prevalence by 40% when done concurrently [61]. The prevalence of invasive infections, including pneumonia, caused by these two bacteria has significantly decreased after the 1990 release of the Hemophilus influenza type B vaccine and the 2000 introduction of the seven-valent pneumococcal immunization (Heptavalan) in developing countries [62]. Currently, research is being conducted on the administration of the 14-valent pneumococcal vaccination to expectant women during the latter stages of their pregnancy, to prevent pneumococcal illness in young children [63].

Conclusion: Acute respiratory infections, particularly pneumonia, are now thought to be the leading infectious cause of death for children in developing nations. The diagnosis of pneumonia is mostly a clinical diagnostic that falls into four areas: clinical, epidemiology, chest radiography, and routine laboratory findings. These categories include bacterial, viral, and acute pneumonia. In each case, a potential diagnosis is made and the appropriate course of therapy is administered depending on the features of that particular pneumonia. The cornerstone of therapy is high-dose intravenous antibiotics that are guided by traditional bacteriological expertise. A major part in preventing and lowering the death and morbidity of pneumonia in children may be played by physicians having the right and precise knowledge on how to identify and treat it without incurring additional expenses.

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