

## Treatment of complicated bacterial pneumonia in children

Tratamento de pneumonia bacteriana complicada em crianças

Tratamiento de la neumonía bacteriana complicada en niños

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### Abstract

**Introduction:** Community-acquired pneumonia (CAP) is one of the most common infectious diseases in pediatrics, and may be related to the direct occurrence of local complications such as empyema, necrotizing pneumonia, lung abscess or pleural effusion, which are directly related to worsening of the clinical aspect and prolongation of the hospitalization period. **Methodology:** A narrative review of the literature was carried out in the PUBMED database, using the following keywords: “Bacterial pneumonia in children”, “Complicated Pneumonia” and “Treatment”, with the time filter for the last 5 years (2019-2023). **Results:** From the research carried out, 408 articles were identified, of which, after applying inclusion and exclusion criteria, 12 were selected for analysis. **Discussion:** The main complications are related to specific complementary exams and assertive surgical or antimicrobial therapies that seek to avoid mortality, exacerbation of other complications and reduce hospitalization time and associated morbidities. **Conclusion:** Knowledge about the complications of community-acquired pneumonia, particularly its course of development and its propaedeutic approach, helps to alleviate the difficulties of the clinical context and provide more security to the doctor in his/her healthcare assistance to the patient.

**Keywords:** Bacterial pneumonia; Therapeutics; Pediatrics; Necrotizing pneumonia.

### Resumo

**Introdução:** A pneumonia adquirida na comunidade (PAC) é uma das doenças infecciosas mais comuns da faixa pediátrica, podendo estar relacionada a ocorrência direta de complicações locais como empiema, pneumonia necrosante, abscesso pulmonar ou derrame pleural, os quais estão diretamente relacionados com piora do aspecto clínico e prolongamento do período de internamento. **Metodologia:** Foi realizada uma revisão narrativa da literatura na base de dados PUBMED, utilizando como palavras chaves: “Bacterial pneumonia in children”, “Complicated Pneumonia” e “Treatment”, com o filtro de tempo para os últimos 5 anos (2019-2023). **Resultados:** A partir da pesquisa realizada identificaram-se 408 artigos, dos quais, após a aplicação de critérios de inclusão e exclusão, 12 foram selecionados para análise. **Discussão:** As principais complicações estão relacionadas a condutas específicas de exames complementares e terapêuticas cirúrgicas ou antimicrobianas assertivas que busquem evitar a mortalidade, a

agudização de outras complicações e diminuir o tempo de internamento e suas morbidades associadas. Conclusão: O conhecimento acerca das complicações da pneumonia adquirida na comunidade, destacadamente, seu curso de desenvolvimento e sua abordagem propedêutica, auxilia a atenuar as dificuldades do contexto clínico e dar mais segurança ao médico na sua assistência em saúde ao paciente.

**Palavras-chave:** Pneumonia bacteriana; Terapêutica; Pediatria; Pneumonia necrosante.

### Resumen

**Introducción:** La neumonía adquirida en la comunidad (NAC) es una de las enfermedades infecciosas más comunes en pediatría, y puede estar relacionada con la aparición directa de complicaciones locales como empiema, neumonía necrotizante, absceso pulmonar o derrame pleural, que se relacionan directamente con el empeoramiento de la enfermedad. del aspecto clínico y prolongación del período de hospitalización. **Metodología:** Se realizó una revisión narrativa de la literatura en la base de datos PUBMED, utilizando las siguientes palabras clave: “Neumonía bacteriana en niños”, “Neumonía complicada” y “Tratamiento”, con el filtro de tiempo de los últimos 5 años (2019-2023). **Resultados:** De la investigación realizada se identificaron 408 artículos, de los cuales, luego de aplicar criterios de inclusión y exclusión, se seleccionaron 12 para el análisis. **Discusión:** Las principales complicaciones están relacionadas con exámenes complementarios específicos y terapias quirúrgicas o antimicrobianas asertivas que buscan evitar la mortalidad, la exacerbación de otras complicaciones y reducir el tiempo de hospitalización y morbilidad asociada. **Conclusión:** El conocimiento sobre las complicaciones de la neumonía adquirida en la comunidad, particularmente su curso de desarrollo y su abordaje propedéutico, ayuda a aliviar las dificultades del contexto clínico y brindar mayor seguridad al médico en su asistencia al paciente.

**Palabras clave:** Neumonía bacteriana; Terapêutica; Pediatría; Neumonía necrotizante.

## 1. Introduction

Community-acquired pneumonia (CAP) is one of the most common conditions worldwide, affecting around 5% of children every year, with approximately 1 in 10 children presenting more complex conditions, consequently requiring hospitalization (Blanco -iglesias et al., 2020; Rossin, et al., 2021). Furthermore, it causes 1.6 million deaths per year worldwide (Muro et al., 2020). The most common etiological agent is still *Streptococcus pneumoniae* (Pneumococcus), the number of cases of which has been decreasing as the vaccine becomes more widely disseminated (Blanco-Iglesias et al., 2020; Leoni et al., 2020; Erlichman et al., 2016).

Complicated community-acquired pneumonia (CAP) consists of the occurrence of local complications (empyema, necrotizing pneumonia, lung abscess or pleural effusion) or systemic complications (sepsis, multiple organ failure, acute respiratory distress syndrome, disseminated intravascular coagulation and even death) in children mainly between 28 days and 5 years of age, being the main isolated cause of morbidity and mortality in this age group, causing the death of approximately 2000 children per day (De Benedictis et al., 2020; Sharma et al., 2020; Erlichman et al., 2016).

It may be associated not only with pneumococcus, but also with *Streptococcus pyogenes* and *Staphylococcus aureus* (Alemayheu et al., 2023; Oishi, et al., 2021). The suspicion occurs in any child being treated with antibiotics for CAP who does not respond 48-72 hours after starting the medication (De Benedictis et al., 2020; Carloni, et al., 2021).

In this context, it is worth highlighting that not all patients affected by CAP develop complications, which are mainly related to the incorrect management of antibiotics in the treatment of this condition and the use of non-steroidal anti-inflammatory drugs, such as ibuprofen (Ooi et al., 2019; Kaminsky, et al., 2023). It was shown, in a study carried out in the United Kingdom between November 2016 and January 2017, that 3% of children with CAP developed complications (Esposito et al., 2022).

It is observed that approximately half of patients under 5 years old, diagnosed with CAP, develop pleural effusion, and of these, 5-10% progress to empyema (Ooi et al., 2019). However, despite being a severe disease, associated with prolonged complications, most patients manage to recover adequately (De Benedictis et al., 2020).

This review study is more likely if appropriate therapy is carried out at the appropriate time. Therefore, this present work aims to carry out a narrative review of the literature on the appropriate and updated management of complicated

community-acquired pneumonia in the pediatric age group.

## 2. Methodology

A narrative review of the literature was carried out (Rother, E.T; 2007; Snyder, H.; 2019), based on the PUBMED database, using the following keywords: “Bacterial pneumonia in children”, “Complicated Pneumonia” and “Treatment” , with the time filter for the last 5 years (2019-2023).

408 articles were analyzed, of which only 12 were included and 396 were excluded because they did not have a title directly related to the keywords, abstracts unrelated to the topic, case reports, opinion articles, letters to the editors, dissertations or comments, or articles that had online access restrictions.

## 3. Results

Through a database search, 408 articles were identified, of which, after applying inclusion and exclusion criteria, 12 were selected for analysis. Given this context, a spreadsheet was created, which includes information such as the title of the article, author, year of publication and the periodic in which the article was published (as shown in Table 1).

**Table 1** - Article, author, periodic was published and year.

No	Autores	Título	Periódico	Ano
1	GELILA ALEMAYHEU et al.	Children hospitalized with community-acquired pneumonia complicated by effusion: a single-centre retrospective cohort study	BMC Pediatrics	2023
2	ESPOSITO, S. et al.	Complications in community acquired pneumonia: magnitude of problem, risk factors, and management in pediatric age	Expert Review of Anti-Infective Therapy	2021
3	DE BENEDICTIS, F. M. et al.	Complicated pneumonia in children	The Lancet	2020
4	SHARMA, P. K. et al.	Severe Necrotizing Pneumonia in Children: A Challenge to Intensive Care Specialist	Journal of Tropical Pediatrics	2020
5	BLANCO-IGLESIAS, E. et al.	Retrospective Study in Children with Necrotizing Pneumonia: Nine Years of Intensive Care Experience	The Pediatric Infectious Disease Journal	2020
6	MARIA CHIARA LEONI et al.	Stratégie antibiotique dans les pleurésies en pédiatrie : consensus par méthode DELPHI	Revue des Maladies Respiratoires	2020
7	MURO, R. P. et al.	Predictors and outcome of first line treatment failure among under-five children with community acquired severe pneumonia at Bugando Medical Centre, Mwanza, Tanzania: A prospective cohort study	PLOS ONE	2020
8	DÍAZ-CONRADI, A. et al.	Complicated pneumococcal pneumonia with pleural effusion or empyema in the 13-valent pneumococcal conjugate vaccine era	Pediatric Pulmonology	2019
9	KUSHNER, L. E. et al.	Oral Antibiotics for Treating Children With Community-Acquired Pneumonia Complicated by Empyema	Clinical Pediatrics	2019
10	OOI, J. M. et al.	Predictive risk factors for complicated pneumonia in Malaysian children	Journal of Paediatrics and Child Health	2018
11	MAFFEY, A. et al.	Clinical, functional, and radiological outcome in children with pleural empyema	Pediatric Pulmonology	2018
12	OSOWICKI, J.; STEER, A. C.	International survey of paediatric infectious diseases consultants on the management of community-acquired pneumonia complicated by pleural empyema	Journal of Paediatrics and Child Health	2018

Sources: By the authors.

## 4. Discussion

From a thorough reading of the selected articles, the discussion was divided into three thematic axes, each related to a specific complication of community-acquired pneumonia in the pediatric age group: Necrotizing Pneumonia, lung abscess, pleural effusion and pleural empyema.

### 4.1 Necrotizing pneumonia

Necrotizing Pneumonia (NP) is a complication of Community-Acquired Pneumonia (CAP) characterized by liquefaction, cavitation and necrosis that destroy the lung parenchyma. It was reported for the first time in children in 1994. It has an incidence of 7% of CAP cases in children and generally affects children under 5 years of age without any previous illness. It has a rapid progression in healthy children, being associated with higher mortality in pediatric patients with chronic diseases, despite having low mortality in developed countries. Its main etiological agents are *Streptococcus pneumoniae*, *Staphylococcus aureus* and *Mycoplasma pneumoniae* (De Benedictis et al., 2020; Blanco-iglesias et al., 2020; Spencer, Tomaz, 2014).

NP still has an uncertain pathophysiology, but it is believed that there is a decrease in blood flow in affected vessels, leading to a reduction in the concentration of antibiotics in these locations. Due to this, the infection tends to persist, causing damage and liquefaction of the lung tissue and, therefore, the loss of the architecture of the lung parenchyma with necrosis. Generally located in a single lung lobe, with the formation of pneumatoceles or cavitations. Furthermore, it is related to a higher risk of complications such as pleural empyema, pneumothorax, septic shock, hemolytic uremic syndrome (HUS), parapneumonic effusion and bronchopleural fistula (De Benedictis et al., 2020; Sharma et al., 2020; Spencer & Tomaz, 2014).

The most common clinical findings include fever, cough, tachypnea, chest pain, dyspnea, decreased breath sounds, fatigue, abdominal pain and vomiting. Such findings do not differ from findings in uncomplicated pneumonia, making diagnosis more difficult and time-consuming. Laboratory changes in necrotizing pneumonia include anemia, hypoalbuminemia, and elevation of inflammatory markers. Furthermore, it is important to collect blood cultures to guide treatment. The sputum test is difficult to obtain in pediatric patients and is unreliable due to the growth of common pathogens of oral flora (De Benedictis et al., 2020; Krenke, et al. 2014).

Therefore, imaging tests are essential to identify necrotizing pneumonia earlier. Chest radiography shows the presence of fluid-containing cavities, which are difficult to differentiate from uncomplicated consolidations in the early stages. Because of this, radiography is an exam with little accuracy, diagnosing around 40% of children with PN (Sharma et al., 2020; Esposito et al., 2022).

Computed tomography (CT) is a more sensitive exam and is indicated when the patient does not improve after at least 72 hours of treatment. It is possible to demonstrate, through CT, cavitory lesions with multiple walls containing liquid that merge to form a single larger cavitation, contributing to the differentiation with lung abscess, which contains a single cavitory wall filled with purulent secretion. Ultrasonography is the most effective exam to detect the presence of parenchymal lesions, pleural effusion and pleural thickening, associated with a low cost and less exposure to radiation, in addition to enabling early identification of complications (De Benedictis et al., 2020; Sharma et al., 2020; Esposito et al., 2022).

The treatment of necrotizing pneumonia depends on the area of necrosis and whether or not it is associated with empyema. Patients with an area of necrosis that is not very extensive and not associated with empyema should undergo clinical treatment with coverage for *Staphylococcus* and *Pneumococcus*, with ceftriaxone being the recommended antibiotic. Upon suspicion of community-acquired MRSA (methicillin-resistant *Staphylococcus aureus*) or positive culture, specific antibiotics should be used, with vancomycin being the most commonly used (Blanco-Iglesias et al., 2020; Leoni et al., 2020).

In the case of patients with NP associated with empyema, the association with antibiotics such as clindamycin and linezolid is indicated. Furthermore, a pleural drain must be inserted to remove fluid from the cavity. The assessment is carried out every 24 hours, checking the amount of liquid drained. The drain should only be removed after treatment has been completed. In patients who do not improve with drainage and in patients with necrosis of a large area, video-assisted thoracoscopy (VTCA) should be performed, enabling direct visualization of the pleura and allowing cleaning of the cavity. In patients who do not improve after VTCA, segmentectomy or lobectomy is recommended (Dalponte, et al., 2020). The surgical approach should also be taken into consideration in patients with bronchopleural fistula. (Blanco-Iglesias et al., 2020; De Benedictis et al., 2020; Leoni et al., 2020).

#### **4.2 Lung abscess**

A lung abscess consists of a cavity with thick walls and purulent material, generally single and resulting from necrosis or suppuration of the lung parenchyma. The progression of its formation is slow and is not commonly seen in patients with CAP. There are some factors that favor its development, such as immunodeficiency or the presence of a congenital cystic pulmonary malformation (De Benedictis et al., 2020).

The pathogens most commonly associated with lung abscess formation in children are: *S. aureus*, *S pneumoniae*, *S pyogenes*, *Klebsiella pneumoniae*, and anaerobic bacteria (such as *Peptostreptococcus* spp and *Fusobacterium* spp). Furthermore, usually commensal bacteria belonging to the anginosus group, which includes *Streptococcus anginosus*, *Streptococcus constellatus* and *Streptococcus intermedius*, can also be etiological agents of this complication, with the last 2 having greater potential for development (De Benedictis et al., 2020; Kushner et al., 2020).

The clinical picture of children with this complication includes prolonged fever with low temperatures and productive cough, as well as chest pain, dyspnea and, more rarely, hemoptysis. On physical examination, they normally do not present significant changes. In some cases, lung abscess can lead to the appearance of other complications, such as lung compression, pneumothorax, bronchopleural fistula and mediastinal shift with consequent respiratory discomfort (Maffey et al., 2019).

The diagnosis is made through a chest x-ray, which demonstrates the presence of a single, rounded image, with a liquid level and thickened walls. However, this exam is not always able to make this diagnosis due to the similarity, in some cases, with congenital thoracic abnormalities or consolidations. Ultrasound can be used to differentiate a peripheral lung abscess from an empyema. On the other hand, computed tomography can be useful in differentiating between necrotizing pneumonia and lung abscess. As these conditions have different treatments, this differentiation is of paramount importance. In some cases, image-guided percutaneous aspiration and drainage are also used for diagnosis (Osowicki; Steer, 2018).

When faced with a child with a lung abscess, the use of antibiotics for long periods has been shown to be efficient. In addition to standard treatment for CAP, patients with this complication require the addition of antibiotics with anaerobic coverage, such as metronidazole, if the aspirated fluid is suspicious. If the patient proves resistant to antibiotics, image-guided cavitation drainage through a pigtail catheter may be chosen in association with antimicrobials (De Benedictis et al., 2020).

#### **4.3 Pleural effusion**

Pleural Effusion (PE) is the formation of an abnormal fluid collection in the pleural space, located between the parietal pleural and the visceral pleura. PE can be an exudate, movement of liquid through the bloodstream with effusion into the pleural space, or a transudate, resulting from an imbalance between oncotic and hydrostatic pressures. In the present study, Parapneumonic Pleural Effusion (PPE) will be discussed, an exudate-type effusion that occurs during the clinical course of pneumonia, most commonly caused by *Streptococcus pneumoniae*, but other etiological agents can cause PPE, such as



*Staphylococcus aureus*, *Haemophilus influenzae*, *Mycoplasma pneumoniae*, *Klebsiella* spp and *Pseudomonas aeruginosa* (Ooi et al., 2019; De Benedictis et al., 2020).

The clinical picture of PPE, in most cases, overlaps with that of CAP due to the similar manifestations. The patient usually presents with a drop in general condition, fever, cough and tachypnea, which is expected in more than 90% of children, progressing to dyspnea as the stroke progresses. Pleuritic pain and respiratory discomfort are findings that should alert to the presence of PPE, as well as the lack of therapeutic response in the first 72 hours of antibiotic therapy. On physical examination, the following changes are found: reduction in lung auscultation, reduction in thoraco-vocal thrill and massive sound on percussion. (De Benedictis et al., 2020; Dorman et al., 2016).

To diagnose PPD, imaging tests are necessary, with chest radiography being the first imaging modality for investigation, however, it does not confirm the diagnosis as it does not differentiate effusion from pleural empyema. Ultrasonography is the most sensitive test for evaluating the pleural space, being able to confirm the presence of effusion, show components such as loculations and the existence of fibrin, and determine the amount of pleural fluid, the latter being an important tool for deciding on management. Computed tomography is not indicated in the initial investigation and is necessary in complicated cases. The microbiological study of pleural fluid can be used as a complementary exam with the aim of identifying the etiological agent. It is recommended to perform Gram staining, acid-fast bacilli staining and culture, also analyzing characteristics such as pH, glucose levels, LDH and liquid leukocyte count (Díaz-Conradi et al., 2019; De Benedictis et al., 2020).

Currently, the importance of targeted treatment according to the most likely microbiota of a certain population is known. However, there are still significant disagreements about the recommended initial treatment, especially when discussing empyema (Leoni et al., 2020). Treatment should always include the use of antibiotics, respiratory and hemodynamic support. Antibiotic therapy is introduced empirically due to the urgency of starting treatment, using broad-spectrum options that cover the bacteria most commonly found in clinical practice. Although there is no consensus, 3rd generation cephalosporins such as cefotaxime or ceftriaxone are usually indicated as the first line of empirical treatment, and clindamycin or vancomycin may be added if Methicillin-Resistant *Staphylococcus Aureus* (MRSA) is suspected. Furthermore, cefotaxime appears to be superior when compared to ceftriaxone. Furthermore, intravenous monotherapy is strongly recommended for initial treatment (De Benedictis et al., 2020; Leoni et al., 2020; Moreno-Pérez, et al., 2015).

Depending on the result of the pleural fluid culture, bacterial coverage will be increased or decreased. It is worth mentioning that, in case of severe clinical signs or infection with an atypical germ, combined antibiotic therapy is indicated. Antibiotic selection needs to be appropriate to the patient, and in children at risk of aspiration or with dentition in poor condition, anaerobic coverage is suggested. Another treatment modality is thoracentesis, which helps as an adjuvant to antibiotic therapy, and is recommended when the amount of liquid exceeds 10 mm. (De Benedictis et al., 2020; Leoni et al., 2020).

Furthermore, it is possible that performing chest drainage in case of spills allows for a shorter period of hospital stay and facilitates the identification of the etiological agent (Alemayheu et al., 2023).

#### **4.4 Pleural empyema**

Pleural Empyema (PE) is defined by the presence of purulent fluid in the pleural space, associated with the following macroscopic findings: presence of leukocytes in the pleural fluid  $> 50,000/\mu\text{L}$  or the detection of *S. pneumoniae* in the pleural fluid, either by culture or PCR (Díaz-Conradi et al., 2019; Maffey et al., 2019). Findings of low pH, low glucose concentration and high LDH concentration are considered predictors of a more prolonged course of the disease. Empyema is commonly considered an advanced stage of parapneumonic effusion, being considered a serious complication of CCAP, associated with

significant morbidity, often due to delay in diagnosis and unclear recommendations regarding the indication, timing and method of drainage. correct pleural space (Kushner et al., 2019). The main etiological agents causing pleural empyema are: *Streptococcus pneumoniae*, *Streptococcus pyogenes*, methicillin-resistant and susceptible *Staphylococcus aureus* (MRSA) and *Haemophilus influenzae* type B (Osowicki & Steer, 2018). Furthermore, there are cases in the literature of empyema and lung abscesses caused by the *Streptococcus anginosus* group (SAG), with *S. anginosus* being the main causative pathogen (Reis-Melo et al., 2020).

In addition to the classic signs of pneumonia, patients with PE may present the following signs on physical examination: decreased chest expansibility, dullness on percussion, decreased or abolished bowel sounds on auscultation, reduced thoracovocal thrill and, in some cases, the presence of pericardial effusion with parapneumonic effusion on the left side. Imaging exams, such as chest X-rays, may show signs of parapneumonic effusion, with obliterated costophrenic sinuses, meniscus signs and varying degrees of pleural thickening. It is important to highlight that the presence of scoliosis and other causes of acute abdomen, such as appendicitis and gastroenteritis, must be ruled out (Maffey et al., 2019; De Benedictis et al., 2020).

Empyema can simulate uncomplicated pneumonia and should be suspected in any child who remains febrile and unwell 48 to 72 hours after starting antibiotics. Every child with PDE or pleural empyema needs to be hospitalized for antibiotic therapy. The recommended therapy consists of the use of penicillin or ampicillin in high doses, amoxicillin – clavulanic acid, clindamycin and second or third generation cephalosporins for a period of 3 to 4 weeks. There is no difference in treatment failure rates between children who received oral or intravenous antibiotics (Leoni et al., 2020; De Benedictis et al., 2020).

The main indication for surgery in PE is the failure of initial treatment and the persistence of an unfavorable clinical picture, in order to create the necessary conditions for the correct penetration of antibiotics into the pleural space (Maffey et al., 2019). Pleural drainage, preferably guided by ultrasound, should be performed in symptomatic patients and in those with very small loculations, as it helps in lung re-expansion, restores the mobility of the chest wall and diaphragm and helps to return normal respiratory function, as that many patients may develop restrictive ventilation disorders (Maffey et al., 2019; Leoni et al., 2020; De Benedictis et al., 2020).

## 5. Conclusion

Empyema, necrotizing pneumonia, lung abscess and pleural effusion are characterized as pulmonary and thoracic complications related to community-acquired pneumonia, with a prevalence of significant relevance within the clinical approach to respiratory infections in large hospitalization centers. Therefore, knowing its presentations, its course of development and its therapeutic approach is essential to reduce hospitalization time and other associated systemic complications.

Therefore, this article assertively elucidates the main propaedeutic information related to this clinical context, in addition to promoting the need for more clinical studies on treatments applied to the population described.

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