American Journal of Pediatrics
2026, Vol. 12, No. 3, pp. 87–102
https://doi.org/10.11648/j.ajp.20261203.11

Research Article

Current Evidence and Clinical Controversies in the Management of Complicated Pneumonia in Children

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Abstract

Background: Parapneumonic effusion (PPE) and empyema remain serious complications of childhood pneumonia associated with significant morbidity despite advances in antimicrobial therapy and surgical techniques. Accurate disease staging and timely stage-directed intervention are fundamental to optimal outcomes. Objective: To provide a current, evidence-based synthesis of the definition, etiology, diagnosis, and management of complicated pneumonia in children, with particular focus on areas of ongoing clinical controversy. Methods: A narrative review incorporating randomized controlled trials, systematic reviews, meta-analyses, Cochrane reviews, and international clinical guidelines published between 2016 and 2026 was conducted. PubMed was searched through May 2026 using terms including pneumonia, complicated pneumonia, parapneumonic effusion, empyema, VATS, fibrinolysis, decortication, and pediatric. Results: Chest radiography remains the initial imaging modality for suspected complicated pneumonia, with lateral decubitus views needed to assess pleural fluid mobility. However, chest ultrasonography is the preferred imaging modality for evaluating parapneumonic effusions and empyema because of its superior diagnostic accuracy, ability to characterize pleural collections, and absence of ionizing radiation. Management is stage-dependent, combining targeted antibiotic therapy with procedural intervention when indicated. Image-guided pigtail catheter drainage with intrapleural fibrinolytic therapy is effective for most patients. VATS demonstrates particular utility during the fibrinopurulent stage. No single fibrinolytic agent has demonstrated clear superiority; however, tissue plasminogen activator is most widely employed. Open decortication remains reserved for refractory or advanced-stage disease. Conclusion: Early diagnosis, appropriate antibiotics, and prompt intervention or surgery are all important for optimal care. The optimal outcomes require a multidisciplinary, individualized, stage-directed approach. Interventional radiology is appropriate for single loculations, while early VATS is favored for thick pleural rind or multiple loculations. Further high-quality prospective research is needed to establish definitive treatment algorithms.

Keywords

Parapneumonic Effusion, Empyema, Complicated Pneumonia, Children, Video Assisted Thoracoscopy (VATS), Fibrinolysis, Chest Ultrasonography, Pediatric Pleural Infection

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Received: 15 June 2026; **Accepted:** 27 June 2026; **Published:** 22 July 2026

1. Introduction

Complicated pneumonia in children—particularly when accompanied by parapneumonic effusion (PPE) or empyema thoracis—represents a significant source of pediatric morbidity and healthcare resource use across developed healthcare systems [1]. The term encompasses a broad clinical spectrum, including pleural effusion, empyema, lung abscess, necrotizing pneumonia, bronchopleural fistula, and severe pneumonia with systemic complications such as sepsis or multiorgan dysfunction.

Despite widespread implementation of pneumococcal conjugate vaccines, improved antibiotic availability, and advances in pediatric supportive care, the incidence of pleural infection in children has remained persistently elevated in both North America and Europe [2, 3]. This epidemiological trend reflects, in part, ongoing shifts in bacterial ecology—including the emergence of non-vaccine pneumococcal serotypes—and heightened diagnostic vigilance and improved imaging capabilities [4].

Parapneumonic effusions span a well-characterized pathophysiological continuum, ranging from simple, free-flowing transudative fluid to complex, loculated fibrinopurulent collections and organized empyema. This progression through exudative, fibrinopurulent, and organizing stages has direct implications for treatment selection and clinical outcomes [5]. Recognizing disease stage at presentation is therefore critical, as uncomplicated early-stage effusions may resolve with antimicrobial therapy alone, whereas advanced-stage disease frequently requires procedural drainage and active measures to restore pulmonary expansion [6, 7].

Diagnostic evaluation has evolved substantially, with chest ultrasonography now firmly established as the first-line imaging modality, offering real-time assessment, high sensitivity for characterizing effusions, and no radiation exposure [8]. Computed tomography is reserved for diagnostically uncertain cases or suspected complications, such as necrotizing pneumonia [9]. Inflammatory biomarkers and pleural fluid analysis provide useful diagnostic information but are insufficient to determine disease stage on their own [10, 11].

Contemporary treatment strategies follow a stepwise algorithm that includes targeted antibiotic therapy, image-guided catheter drainage, intrapleural fibrinolysis, and surgical intervention when conservative measures fail [12]. Less invasive approaches—notably small-bore pigtail catheter drainage and VATS—have largely replaced open surgical procedures in suitable candidates [12, 13]. Nevertheless, unresolved questions remain about the optimal timing of escalation to surgery, the comparative merits of fibrinolytic therapy versus early VATS, and the preferred fibrinolytic agent [12, 14].

Given this evolving landscape and the ongoing accumulation of new evidence, a comprehensive, up-to-date synthesis is warranted. This review summarizes the best available evidence published between 2016 and 2026, addresses existing controversies, and offers practical clinical guidance for managing children with complicated pneumonia.

2. Methods

A systematic literature search was conducted in PubMed through May 2026 using the following Medical Subject Headings and keywords: pneumonia, complicated pneumonia, parapneumonic effusion, empyema, management, video-assisted thoracoscopic surgery (VATS), decortication, fibrinolysis, pediatric, and guidelines. Inclusion was limited to peer-reviewed studies published from January 2016 to May 2026 that involved patients younger than 18 years.

Studies were selected based on study design hierarchy, sample size, and contribution to the evidence base. Included study designs comprised randomized controlled trials, prospective and retrospective clinical studies, meta-analyses, systematic reviews, and narrative reviews. International guidelines from recognized North American and European professional societies were systematically reviewed. Given the inherent challenges of generating high-quality pediatric evidence for this condition, particular emphasis was placed on Cochrane Collaboration recommendations and updated societal guidelines [1, 2].

Of 1,229 identified articles, 825 were published within the past five years. After screening for relevance, study design quality, and publication date eligibility, 63 articles were included. The selection and appraisal process followed the PRISMA 2020 reporting principles [15].

3. Epidemiology

Pneumonia remains one of the most common infectious causes of childhood hospitalization and morbidity throughout North America and Europe [1, 3]. Pleural effusion is the most common pleural complication, and its incidence, along with that of frank empyema, has remained a significant clinical burden [3, 4].

In the United States, PPE complicates 20-40% of pediatric pneumonia admissions requiring hospitalization [3]. European surveillance data document persistently elevated rates of childhood pleural infection, with ongoing concerns about serotype replacement following universal immunization programs [4, 5]. Case-fatality rates have declined compared with historical reports, reflecting improvements in early diagnosis, advances in critical care, and the adoption of multidisciplinary management protocols [1, 6].

4. Pathophysiology

Under normal physiological conditions, the pleural space

maintains a carefully balanced equilibrium in which a small volume of fluid is continuously produced and reabsorbed. Infectious disruption triggers a well-characterized inflammatory cascade that progresses through three clinically recognizable stages (Table 1) [8, 13].

Table 1. Stages of Parapneumonic Effusion and Empyema: Pathophysiology, Characteristics, and Management Implications.

Stage	Name	Pathophysiology	Pleural Fluid Characteristics	Ultrasound Appearance	Typical Management
I	Exudative	Increased capillary permeability; protein-rich fluid accumulates; sterile or minimally contaminated	pH >7.3; glucose >3.4 mmol/L; LDH <500 IU/L; clear/straw-colored	Anechoic; freely mobile; no septations	IV antibiotics ± diagnostic thoracentesis; no routine drainage
II	Fibrinopurulent	Fibrin deposition, bacterial invasion, and neutrophil infiltration; loculation begins	pH 7.0-7.2; glucose 1.6-3.4 mmol/L; LDH 500-1,000 IU/L; turbid/purulent	Echogenic fluid; fibrinous strands; septations; partial loculation	IV antibiotics + chest tube/pigtail drainage + intrapleural fibrinolytics; VATS if complex or failing
III	Organizing	Fibroblast infiltration; collagen deposition; rigid fibrous pleural peel; trapped lung	pH <7.0; glucose <1.6 mmol/L; LDH >1,000 IU/L; thick pus/caseous	Thick hyperechoic pleural rind; dense loculations; reduced lung movement	VATS decortication (early); open thoracotomy + formal decortication (advanced/refractory)

Sources: Harris et al., 2017 [12], Principi & Esposito, 2016; [6], Shen et al., 2017 [1].

During the exudative phase, increased capillary permeability leads to the accumulation of protein-rich fluid that is typically free-flowing, sterile or minimally contaminated, and often responsive to antibiotic therapy alone. As infection intensifies, the fibrinopurulent phase is marked by fibrin deposition, bacterial invasion, neutrophil infiltration, and biochemical deterioration, reflected by declines in pleural fluid pH and glucose levels and an increase in lactate dehydrogenase levels. The final organizing phase involves fibroblast infiltration, collagen deposition, and the formation of a rigid fibrous pleural peel that encases and constrains the underlying lung, frequently necessitating surgical decortication [5].

5. Clinical Presentation and Assessment

5.1. Clinical History

Children presenting with PPE or empyema typically show features consistent with acute bacterial pneumonia, including fever, cough, tachypnea, and respiratory distress [7]. Persistent fever or progressive clinical deterioration beyond 48-72 hours despite appropriate antimicrobial therapy is a hallmark that warrants re-evaluation for pleural complications [12].

Pleuritic chest pain is common in older children and may radiate to the ipsilateral shoulder. Younger children often present with nonspecific constitutional symptoms, such as irritability, poor feeding, or abdominal pain, which can mimic an acute abdominal process [10]. Clinicians should actively inquire about prior antibiotic use, pneumococcal vaccination status, duration of illness, and predisposing conditions, including immunodeficiency, chronic pulmonary disease, and aspiration risk factors [10, 11].

5.2. Physical Examination

Clinical findings vary according to volume and stage of the pleural collection. Oxygen saturation below 92% on room air indicates significant physiological compromise warranting urgent intervention [10, 11]. Tactile fremitus is diminished over the fluid-filled region; percussion elicits stony dullness; auscultation reveals diminished breath sounds. Large effusions may produce contralateral mediastinal displacement. A pleural friction rub may be audible in early or small effusions *(Table 2)* [8, 13].

Table 2. Clinical Features of Pediatric Parapneumonic Effusion and Empyema by Age Group.

Clinical Feature	Infants (<12 months)	Toddlers/Preschool (1-5 years)	School-Age/Adolescents (>5 years)
Fever	High, persistent	High, persistent >48-72h despite antibiotics	High, persistent; often with rigors

Clinical Feature	Infants (<12 months)	Toddlers/Preschool (1-5 years)	School-Age/Adolescents (>5 years)
Respiratory symptoms	Tachypnea; grunting; poor feeding	Tachypnea; retractions; reduced activity	Tachypnea; dyspnea; pleuritic chest pain
Pain	Irritability; nonspecific distress	Abdominal pain (lower lobe); shoulder pain	Pleuritic chest pain; referred shoulder pain
Constitutional	Poor feeding; lethargy	Reduced oral intake; malaise	Malaise; anorexia; weight loss
Physical signs	Reduced chest expansion; dullness on percussion	Reduced breath sounds; dullness	Stony dullness; absent breath sounds; friction rub
Oxygen saturation	May drop precipitously	SpO_2 <92% indicates severe disease	SpO_2 <92% requires urgent intervention
Atypical features	Sepsis-like presentation; apnea	Mimics acute abdomen	Scoliosis; mediastinal shift in large effusions

Sources: Principi & Esposito, 2016 [6], Wolfler et al., 2020 [7], Krenke et al., 2017 [11].

6. Diagnosis

6.1. Laboratory Investigations

Routine investigations should include a complete blood count with differential, C-reactive protein, erythrocyte sedimentation rate, procalcitonin, serum electrolytes, renal function, and blood cultures before initiating antibiotics [10, 11]. Leukocytosis with neutrophil predominance and elevated acute-phase reactants are consistently observed but lack specificity [11]. Blood cultures identify a causative pathogen in only 10-20% of cases but remain the standard of care [15]. Others: Interleukin-6 (IL-6) correlates with disease severity but is not widely used clinically [24-28]. Ferritin may reflect hyperinflammatory states in severe infections [29, 30]. D-dimer is occasionally elevated in severe pneumonia but is nonspecific [31, 32]. Inflammatory markers should be interpreted cautiously because they cannot reliably distinguish bacterial from viral etiologies [33]. Sputum examination can provide supportive microbiological information for children with complicated pneumonia; however, its clinical utility is often limited, particularly in younger patients who cannot expectorate effectively [34, 35]. When obtainable, sputum should be sent for Gram stain and culture to help identify causative organisms and guide targeted antimicrobial therapy [36]. Induced sputum with hypertonic saline may be considered in selected cases, although concerns remain about contamination with upper airway flora and variable diagnostic yield [37, 38]. Overall, sputum results should be interpreted cautiously and in conjunction with clinical findings and other microbiological data, as they do not always reliably reflect pathogens present in the pleural space [39] (Tables 3 and 4).

Table 3. *Diagnostic Investigations in Pediatric Complicated Pneumonia: Indications, Findings, and Clinical Utility.*

Investigation	Indication	Key Findings Suggesting Complicated PPE	Sensitivity/Specificity	Clinical Utility	Limitations
Complete blood count	All patients	WBC >15×10^9/L; neutrophilia; elevated bands	Moderate	Baseline assessment; treatment monitoring	Nonspecific; may be normal in early disease
C-reactive protein	All patients	CRP >60-100 mg/L	Moderate-High	Distinguishes bacterial vs viral; monitors response	Nonspecific; elevated in any inflammation
Procalcitonin	All patients	PCT >0.5-2.0 ng/mL suggests bacterial etiology	Moderate	Antibiotic stewardship guidance	Limited stage-specific utility
Blood cultures	All patients before antibiotics	Positive in 10-20% of cases	Low-Moderate	Directs targeted therapy; identifies bacteremia	Low yield; often negative with prior antibiotics
Chest X-ray (AP/Lateral)	Initial imaging all patients	Blunted costophrenic angle; homogeneous opacity; mediastinal shift	Moderate	Confirms effusion presence; baseline	Cannot characterize fluid; misses small

Investigation	Indication	Key Findings Suggesting Complicated PPE	Sensitivity/Specificity	Clinical Utility	Limitations
					effusions
Chest ultrasound	First-line for all suspected PPE	Anechoic/echogenic fluid; septations; pleural thickening; guides drainage	High (>90% for effusion)	Stage characterization; drainage guidance; no radiation	Operator-dependent
CT thorax	Suspected NP; lung abscess; BPF; failure to improve	Necrotizing foci; abscess; complex loculations; peel thickness	Very High	Surgical planning defines anatomy	Radiation exposure; requires sedation in young children
Pleural fluid pH	At time of drainage	pH <7.2 indicates drainage required	High	Determines need for drainage	Requires anaerobic sample; affected by air contamination
Pleural fluid glucose	At time of drainage	Glucose <2.2 mmol/L indicates drainage	Moderate-High	Complements pH and LDH	Less reliable in isolation
Pleural fluid LDH	At time of drainage	LDH >1,000 IU/L indicates complicated PPE	Moderate	Staging tool	Overlap between stages
Pleural fluid culture	All drained fluid	Positive in 30-50% of empyemas	Low-Moderate	Guides antibiotic rationalization	Markedly reduced with prior antibiotics
16S rRNA PCR	Culture-negative empyema	Identifies pathogen DNA	Higher than culture	Improves etiological diagnosis	Limited availability; cost

Sources: Birkbak et al., 2016 [8], Krenke et al., 2017 [11], Mistry et al., 2019 [15], Bhatt & Everard, 2018 [19].

Table 4. *Pleural Fluid Analysis: Light's Criteria Adapted for Pediatric Parapneumonic Effusion Classification.*

Parameter	Transudate (Simple PPE Stage I)	Exudate (Complex PPE Stage II)	Empyema (Stage II-III)	Frank Empyema (Stage III)
Appearance	Clear/straw-colored	Turbid/yellow	Turbid/purulent	Thick pus; frank empyema
pH	>7.3	7.2-7.3	7.0-7.2	<7.0
Glucose (mmol/L)	>3.4	2.2-3.4	1.6-2.2	<1.6
LDH (IU/L)	<500	500-700	700-1,000	>1,000
Protein (pleural/serum ratio)	<0.5	>0.5	>0.5	>0.5
WBC (cells/mm^3)	<1,000	1,000-5,000	5,000-50,000	>50,000
Predominant cell type	Mononuclear	Mixed	Neutrophil predominant	Neutrophil predominant
Gram stain/Culture	Negative	Usually, negative	Often positive	Positive or visibly purulent
Management implication	Antibiotics ± observation	Antibiotics + monitor closely	Drainage + fibrinolytics	Drainage + fibrinolytics / VATS

Sources: Shen et al., 2017 [1], Harris et al., 2017 [12], Bhatt & Everard, 2018 [19].

6.2. Imaging

Chest Radiography: Chest radiography remains the primary and most accessible method for detecting suspected pleural effusions. It visualizes fluid accumulation and assesses lung involvement. [40] Early signs include blurring or loss of the costophrenic angle, with a meniscus sign appearing as fluid volume increases. [41] Large effusions can produce uniform opacity of the affected hemithorax and may shift the mediastinum to the opposite side. [40, 42, 43] In the supine position, pleural fluid tends to layer posteriorly, creating diffuse haziness that complicates interpretation. A lateral decubitus view helps assess fluid movement and volume. [40, 43, 44] Fluid

layers greater than 10 mm typically indicate a significant effusion, often requiring drainage. Lack of movement suggests loculation or increased viscosity. [45] Although chest X-ray is useful for early detection, it has limited ability to distinguish simple from complicated effusions and may underestimate loculations [42, 44].

Chest Ultrasonography: Strongly recommended as the first-line investigation by current international guidelines [12, 16]. It provides real-time, dynamic assessment of pleural fluid volume, echogenicity, and septal architecture without radiation exposure. Ultrasonographic morphology correlates closely with disease stage and pleural fluid biochemistry [8, 16].

Computed Tomography: Reserved for suspected necrotizing pneumonia, lung abscess, bronchopleural fistula, or failure to improve after initial drainage. Use should be judicious given the associated radiation dose [9, 17]. It provides detailed visualization of the lung parenchyma, pleural surfaces, and mediastinal structures. CT is particularly useful when:

1) There is no clinical improvement despite appropriate management.
2) Drainage procedures are unsuccessful or incomplete.
3) Alternative diagnoses, such as lung abscess, necrotizing pneumonia, or malignancy, are suspected.

Pre-procedural planning is required for complex cases [46]. However, given concerns about radiation exposure and the potential need for sedation in children, its use should be limited to cases where additional diagnostic information will influence management decisions [47].

Pleural Fluid Analysis

Pleural fluid should be sent for Gram stain, aerobic and anaerobic culture, total protein, LDH, glucose, and pH [12]. Molecular diagnostic techniques, including 16S ribosomal RNA PCR, are increasingly used in culture-negative cases [15]. Accepted biochemical thresholds for complicated PPE requiring drainage: pH <7.2, glucose <2.2 mmol/L, and LDH >1,000 IU/L [11, 12]. Laboratory tests support diagnosis but should be combined with clinical and radiologic findings for comprehensive management.

6.3. Microbiology

Streptococcus pneumoniae remains the predominant pathogen in community-acquired PPE and empyema in children across North America and Europe, although the serotype distribution has shifted following conjugate vaccine implementation, with non-vaccine serotypes—particularly 3 and 19A—now accounting for an increasing proportion of complicated disease [2, 5]. *Staphylococcus aureus*, including CA-MRSA, is associated with rapidly progressive necrotizing disease and high rates of surgical intervention [15, 18]. *Streptococcus pyogenes accounts* for a clinically significant proportion of cases (*Table 5*).

Table 5. *Microbiology of Pediatric Parapneumonic Effusion and Empyema: Causative Pathogens, Clinical Features, and Antibiotic Recommendations.*

Pathogen	Frequency	Age Group	Clinical Features	Antibiotic of Choice	Alternative	Special Considerations
S. pneumoniae	Most common (40-60%)	All ages; peak 2-5 years	Acute onset; rapid progression; single loculation common	Amoxicillin-clavulanate IV; Ceftriaxone IV	Penicillin G (sensitive strains)	Serotype shift post-PCV13; non-vaccine serotypes 3, 19A increasing
S. aureus (MSSA)	10-20%	All ages; infants at risk	Rapidly progressive; necrotizing features; multiple loculations; high surgical rate	Flucloxacillin IV (UK); Nafcillin IV (US)	Cefazolin IV	Associated with necrotizing pneumonia, lung abscess; pneumatocele
S. aureus (CA-MRSA)	5-15% (regional variation)	All ages; school-age	Very severe; necrotizing pneumonia; sepsis; high VATS rate	Vancomycin IV; Clindamycin (sensitive strains)	Linezolid	Higher prevalence in North America; monitor local epidemiology
S. pyogenes	5-10%	School-age	Rapid evolution; can be fulminant	Benzylpenicillin IV + Clindamycin	Amoxicillin-clavulanate	Clindamycin added for toxin suppression
Mycoplasma pneumoniae	5-10%	School-age; adolescents	Subacute onset; bilateral infiltrates; atypical features	Azithromycin PO/IV; Clarithromycin	Doxycycline (>8 years)	PCR pleural fluid often positive; culture-negative
Gram-negative bacilli	<5% (immunocompetent); higher in immunocompromised	All ages; neonates	Nosocomial or underlying disease; severe course	Piperacillin-tazobactam IV; Meropenem (severe)	Cefotaxime + aminoglycoside	Consider in immunocompromised, neonates, aspiration

Pathogen	Frequency	Age Group	Clinical Features	Antibiotic of Choice	Alternative	Special Considerations
Anaerobes	<5%; underdiagnosed	All ages	Subacute; foul-smelling fluid; aspiration history	Amoxicillin-clavulanate; Metronidazole + beta-lactam	Clindamycin	Oral flora; aspiration pneumonia; dental disease
Culture-negative	30-50% of drained empyemas	All ages	Prior antibiotic use most common explanation	Broaden empirically; consider molecular diagnostics	—	16S rRNA PCR and multiplex PCR improve yield

Sources: Mistry et al., 2019 [15]; Buckingham et al., 2019 [18]; Elemraid et al., 2019 [4]; Rodrigues et al., 2020 [5].

7. Management

7.1. Goal of Therapy

Managing complicated pneumonia in children, especially with parapneumonic effusion or empyema, centers on key goals: controlling infection, restoring lung function, and preventing immediate and long-term complications. [48-53] These aims require a timely, stage-specific, multidisciplinary approach. [44] The primary objective is to eliminate infection by promptly initiating appropriate empirical antibiotics and then adjusting them based on microbiological results and clinical response. [36] Proper infection control prevents disease progression and systemic complications. [44] A second crucial goal is adequate drainage of pleural fluid or pus when needed. In large effusions, loculated collections, or empyema, inadequate drainage can worsen infection and the patient's condition. [47] The choice of drainage method—thoracocentesis, chest tube placement, or image-guided catheter insertion—depends on disease stage and complexity. [54] Restoring normal lung mechanics by re-expanding the affected lung is essential. Fluid buildup and fibrin deposits can limit lung expansion, impair gas exchange, and delay recovery. Prompt intervention helps prevent restrictive complications such as trapped lung. [35] Management also aims to prevent complications such as bronchopleural fistula, lung abscess, sepsis, and long-term lung problems. [55] Regular clinical monitoring and early detection of treatment failure are crucial to guide escalation, including fibrinolytic therapy or surgery if needed [56].

7.2. Suppurative Care

All children require supplemental oxygen targeting saturation >92-95%, adequate fluid resuscitation, analgesia for pleuritic pain, and nutritional support [7, 12]. Children with hemodynamic compromise or respiratory failure require intensive care-level monitoring [7].

7.3. Stage-Directed Management Algorithm

Management follows a stepwise stage-directed algorithm *(Table 6, Figure 1)*:

Table 6. *Evidence-Based Management Algorithm for Pediatric Parapneumonic Effusion and Empyema.*

Clinical Scenario	Stage	First-Line Management	Second-Line (if no improvement 48-72h)	Third-Line (refractory)	Evidence Level
Small free-flowing PPE; child clinically stable; SpO_2 >95%	I Exudative	IV antibiotics; close monitoring; repeat US at 48-72h	Add diagnostic thoracentesis; consider drainage if increasing	Chest tube + fibrinolytics	Grade B; Expert consensus
Moderate-large PPE; child unwell; SpO_2 <95%; pH 7.2-7.3	I-II Transitional	IV antibiotics + pigtail catheter drainage under US guidance	Add intrapleural fibrinolytics (tPA)	VATS if failing or loculating	Grade A; RCT/Meta-analysis
Complex/loculated PPE; multiple septations on US; pH <7.2	II Fibrinopurulent	IV antibiotics + pigtail/chest tube + intrapleural tPA	VATS (primary or rescue within 72h)	Open decortication (rare)	Grade A; RCT/Meta-analysis
Thick pleural rind on US/CT; multiple dense loculations	II-III Early organizing	IV antibiotics + early VATS	Open thoracotomy if VATS incomplete	Formal decortication	Grade B; Cohort studies

Clinical Scenario	Stage	First-Line Management	Second-Line (if no improvement 48-72h)	Third-Line (refractory)	Evidence Level
Established fibrous pleural peel; trapped lung; failed VATS	III Organizing	Open thoracotomy + formal surgical decortication	Prolonged IV antibiotics post-operatively	—	Grade C; Expert consensus
Necrotizing pneumonia with PPE	II-III	IV antibiotics (include MRSA coverage) + drainage; CT for assessment	VATS; avoid early decortication of necrotic lung	Lobectomy (rare; last resort)	Grade C; Cohort series
Suspected bronchopleural fistula	II-III	IV antibiotics + chest tube; CT to confirm; thoracic surgery consultation	VATS repair; water-seal monitoring	Open repair	Grade C; Expert consensus

Sources: Harris et al., 2017 [12], Shen et al., 2017 [1], Ricciardi et al., 2022 [13], Bhatt & Everard, 2018 [19].

Stage I — Exudative (Simple PPE): Intravenous antibiotics with close clinical and radiological monitoring. Thoracentesis is performed if diagnostic clarification is required. Procedural drainage is not routinely indicated [6, 12].

Stage II — Fibrinopurulent (Complex PPE/Empyema): Chest tube or pigtail catheter drainage under ultrasound guidance combined with intrapleural fibrinolytic therapy. VATS in cases with multiple loculations, thick peel, or failure of fibrinolysis within 48-72 hours [12, 13, 19].

Stage III — Organizing (Chronic Empyema): VATS decortication for early organized empyema; open thoracotomy with formal decortication for advanced or refractory disease with established fibrous rind [12, 13].

7.4. Antibiotic Therapy

Empirical antibiotic selection is guided by local epidemiology, the likely pathogen, vaccination status, and individual risk factors [1, 12]. For immunocompetent children with community-acquired disease, intravenous amoxicillin-clavulanate or a third-generation cephalosporin combined with a macrolide is appropriate. In settings with documented CA-MRSA prevalence or in cases of severe necrotizing disease, significant effusion, loculation, younger age, or a sick patient, vancomycin or clindamycin should be added empirically [1, 12, 18]. Total antibiotic duration is 2-4 weeks, with transition to oral therapy once clinically improved. Duration can be extended based on clinical, laboratory, and radiologic response (Table 5).

7.5. Chest Tube and Pigtail Catheter Drainage

Small-bore pigtail catheters (10-14 French) are as effective as larger-bore surgical chest tubes for pediatric pleural infections, with superior patient comfort and comparable drainage outcomes [19]. All drainage procedures should be performed under real-time ultrasound guidance [8, 12].

7.6. Intrapleural Fibrinolytic Therapy

Intrapleural fibrinolytic agents lyse fibrinous septations and enhance drainage of fluid from complex, loculated collections [1, 19]. The usual indications include:

1) Persistent fever, shortness of breath, and elevated inflammatory markers despite appropriate antibiotics and thoracostomy
2) Poor drainage despite the drain being in the correct position
3) Imaging evidence of septations
4) Large loculated effusions or empyema. [57-59] Fibrinolytics improve drainage by breaking down fibrin septations, reducing fluid viscosity and loculation, and promoting lung re-expansion [57, 59].

Tissue plasminogen activator (tPA) is the most widely used agent in contemporary North American and European pediatric practice. Standard protocols involve instilling tPA 4 mg in normal saline intrapleurally two to three times daily, with a dwell time of one to four hours [1, 19]. Alternatively, intrapleural alteplase is commonly administered at 0.1 mg/kg per dose (maximum 4 mg) via chest tube or pigtail, with a dwell time of 45-60 minutes, repeated according to institutional protocols for approximately 3-6 days [60-62]. The adult MIST2 trial demonstrated the superiority of combined tPA and DNase over either agent alone; dedicated pediatric trials remain an important research priority [20] (Table 7).

Table 7. Intrapleural Fibrinolytic Agents in Pediatric Empyema: Comparison of Evidence, Dosing, and Outcomes.

Agent	Mechanism	Pediatric Dosing (Typical)	Dwell Time	Frequency	Evidence Base	Success Rate	Advantages	Limitations
Tissue Plasminogen Activator (tPA / Alteplase)	Converts plasminogen to plasmin; lyses fibrin clots and septations	4 mg in 40 mL normal saline (weight-based: 0.1 mg/kg, max 4 mg)	1-4 hours	2-3× daily for 3 days	Most widely used in pediatric practice; multiple case series; extrapolation from adult MIST2 trial	70-85% avoid surgery	Most evidence base; widely available; rapid action	Hemorrhagic risk; chest pain during instillation; limited dedicated pediatric RCT data
Urokinase	Directly activates plasminogen; lyses fibrin	40,000 IU in 40 mL normal saline (weight-based protocols vary: 10,000-40,000 IU)	4 hours	Once or twice daily for 3-5 days	Multiple pediatric RCTs including MIST1 equivalent pediatric studies; Cochrane reviews	65-80% avoid surgery	Established safety profile in children; lower cost	Less potent fibrin lysis than tPA; no longer available in some countries
Streptokinase	Binds plasminogen forming activator complex; indirect fibrinolysis	15,000-25,000 IU/kg in 50 mL normal saline	4 hours	Once or twice daily for 3-5 days	Older RCT evidence; largely superseded	60-75% avoid surgery	Low cost; widely available in low-resource settings	Allergic reactions; limited use in streptococcal infection; largely replaced by tPA
tPA + DNase (combined)	tPA lyses fibrin; DNase degrades DNA, reducing fluid viscosity	tPA 4 mg + DNase 5 mg alternating doses	1-4 hours	Alternating doses twice daily	MIST2 trial (adults; N=210); pediatric data limited to case reports and small series	Adult data: superior to either alone	Theoretically superior combined mechanism; adult evidence strong	No dedicated pediatric RCT; cost; DNase availability variable

Sources: Piccolo et al., 2021 [20], Bhatt & Everard, 2018 [19], Shen et al., 2017 [1].

7.7. Role of Dornase Alfa (DNase)

Dornase alfa (DNase) has an adjunctive role in children with complicated parapneumonic effusion or empyema, particularly when the pleural fluid is thick and loculated. It enzymatically degrades extracellular DNA released by neutrophils and bacteria, thereby reducing pleural fluid viscosity and improving drainage. [59] Role of dornase alfa in complicated pneumonia/empyema.

1) Reduces the viscosity of purulent pleural fluid
2) Enhances chest tube drainage
3) May improve lung re-expansion
4) Commonly used in combination with intrapleural tPA
5) It may reduce the need for surgical intervention. It is not yet universally standard in children, but it is emerging as an adjunct therapy in selected cases. in selected cases [60, 61].

7.8. Video-Assisted Thoracoscopic Surgery

VATS is the preferred surgical intervention for pediatric PPE and empyema failing antibiotic therapy and catheter drainage, or for patients presenting with established fibrinopurulent or early organized empyema [13, 21]. VATS allows direct visualization, complete evacuation of purulent material, systematic debridement of loculations, early decortication, and drain placement under direct vision [13].

Contemporary meta-analyses demonstrate that VATS results in shorter hospital stays, faster resolution of fever, lower treatment failure rates, and comparable or superior clinical outcomes compared with non-surgical management for fibrinopurulent empyema [13, 21] (Table 8).

7.9. Open Decortication

Reserved for failure of less invasive approaches or presentation in the advanced organizing phase with an established fibrous pleural rind [12, 13]. Provides definitive management with complete pleural rind removal and full re-expansion of the entrapped lung. Associated with the longest recovery, but low mortality and excellent long-term pulmonary outcomes in children [13].

Table 8. Comparative Outcomes: VATS versus Fibrinolytic Therapy versus Open Decortication in Pediatric Empyema.

Outcome Measure	VATS	Fibrinolytic Therapy + Drain	Open Decortication	Statistical Significance	Evidence Quality
Hospital length of stay (days)	7-12	10-18	14-21	VATS significantly shorter vs fibrinolytics (MD −3.2 days; 95% CI −5.1 to −1.3; p<0.001)	Meta-analysis; RCTs
Duration of fever post-procedure (days)	2-4	4-7	4-8	VATS significantly shorter (MD −2.1 days; p=0.002)	Meta-analysis
Treatment failure rate	5-10%	15-30%	<5% (definitive)	VATS superior to fibrinolytics (RR 0.42; 95% CI 0.26-0.68)	Meta-analysis
Requirement for further intervention	5-8%	20-35% (require escalation to VATS)	<5%	Fibrinolytics significantly higher escalation rate	RCT/Cohort data
Surgical complications	3-8% (air leak; wound infection; port site complications)	2-5% (hemorrhage; drain displacement)	8-15% (prolonged air leak; wound complications; longer ICU stay)	Open decortication highest complication rate	Cohort studies
Mortality	<1%	<1%	<2%	No significant difference across groups	Meta-analysis
Time to radiological resolution (months)	1-3	2-4	2-5	VATS fastest; open decortication longest	Cohort studies
Long-term pulmonary function	Normal or near-normal in >90% at 6 months	Normal or near-normal in >85% at 6 months	Normal or near-normal in >85% at 12 months	No significant difference at 12 months	Prospective cohort
Cost (relative)	High (OR time; equipment)	Moderate	Highest (prolonged hospitalization; OR time)	Context and setting dependent	Economic analyses
Patient/family preference	Favoured for shorter stay	Favoured for less invasive initial approach	Least preferred; reserved for refractory disease	—	Survey/qualitative data

Sources: Ricciardi et al., 2022 [13], Sola et al., 2022 [21], Bhatt & Everard, 2018 [19].

8. Outcomes and Follow-up

The long-term pulmonary prognosis is generally favorable, with most children achieving full or near-complete radiographic and functional lung recovery within three to six months after treatment [14, 22]. Residual pleural thickening or minor restrictive defects may persist in a small proportion of cases, particularly after prolonged severe infection or open decortication [22].

A follow-up chest radiograph at 4 to 6 weeks post-discharge is recommended to confirm progressive resolution. Repeat cross-sectional imaging is reserved for children who remain symptomatic or in whom an underlying structural lung anomaly is suspected [12] (*Table 9*).

Table 9. *Summary of Key Studies on Management of Pediatric Complicated Pneumonia (2016-2026).*

Study	Year	Design	N	Population	Intervention	Key Findings	Evidence Level
Ricciardi et al. [13]	2022	Systematic review & meta-analysis	1,847	Children <18 years with empyema	VATS vs non-surgical management	VATS: shorter LOS (MD −3.2d), faster fever resolution, lower failure rate (RR 0.42)	Level I

Study	Year	Design	N	Population	Intervention	Key Findings	Evidence Level
Sola et al. [21]	2022	Prospective multicenter	312	Children with fibrinopurulent empyema	VATS vs fibrinolytics	Comparable outcomes when case-selected appropriately; VATS is superior for multiple loculations	Level II
Piccolo et al. [20]	2021	Systematic review	847	Adults and pediatric pleural infection	tPA vs tPA+DNase vs urokinase	tPA+DNase is superior in adults; pediatric data insufficient for conclusion	Level I
Bhatt & Everard. [19]	2018	Narrative review	—	Pediatric empyema	Comprehensive management review	Pigtail equivalent to large-bore tube; US guidance mandatory; tPA first-line fibrinolytic	Level III
Baranowski et al. [16]	2021	Guideline/Review	—	Pediatric pleural disease	Ultrasound guidance	US mandatory for all drainage procedures; morphological staging guides management	Level III
Buckingham et al. [18]	2019	Retrospective multicenter	423	Children with necrotizing pneumonia/empyema	CA-MRSA epidemiology	CA-MRSA accounts for 15% of necrotizing pneumonia; vancomycin empirical coverage justified	Level III
Krenke et al. [11]	2017	Prospective cohort	186	Children with PPE	Risk factors for local complications	pH <7.2, LDH >1,000, loculation on US independently predict need for procedural escalation	Level II
Krenke et al. [14]	2018	Prospective follow-up cohort	143	Children post-empyema at 12-24 months	Long-term pulmonary function	92% normal spirometry at 24 months; residual pleural thickening in 18% at 6 months	Level II
Nenna et al. [22]	2021	Prospective cohort	98	Children post-empyema	Radiological and functional outcomes	Full radiological recovery in 87% by 6 months; restrictive defects in 13% post open decortication	Level II
Mistry et al. [15]	2019	Multicenter retrospective	521	Children with culture-confirmed PPE	Microbiological trends	S. pneumoniae 52%; CA-MRSA 14%; non-vaccine serotypes in 67% of pneumococcal cases	Level III
Al-Shamrani [23]	2020	Narrative review	-	Complicated pneumonia	Comprehensive management review	US helpful Decubitus film recommended Dornase alfa is the best fibrinolytic Earlier VATS is recommended	Level III

Source:

9. Controversies and Future Directions

Several important management controversies remain unresolved:

1) Optimal timing of VATS versus fibrinolytic therapy as primary intervention for fibrinopurulent empyema.

For most children with fibrinopurulent empyema, early chest tube drainage combined with intrapleural fibrinolytic therapy is an appropriate first-line treatment. VATS should be performed promptly if fibrinolysis fails within 48-72 hours or if extensive multiloculated disease predicts a poor response to catheter-based drainage. Delaying definitive intervention beyond several days of ongoing sepsis may prolong hospitalization and increase morbidity [1, 34].

2) The role of combined tPA and DNase has been established in adult practice but has not yet been validated in dedicated pediatric trials. In the multicenter randomized DTPA trial, the addition of DNase to tPA did not improve hospital length of stay, duration of chest tube drainage, fever resolution, or need for surgical intervention compared with tPA alone. Consequently, current pediatric practice continues to favor fibrinolytic therapy alone, and routine use of DNase cannot yet be recommended outside selected refractory cases or research settings [20, 60, 63].
3) Molecular diagnostics, including multiplex PCR for pathogen identification in culture-negative empyema. Because pleural fluid cultures are often negative after antibiotic administration, multiplex PCR has emerged as a

valuable adjunctive diagnostic tool, increasing microbiological yield from approximately 20-30% with conventional cultures to more than 70% in some pediatric series, thereby improving pathogen-directed treatment strategies [49, 50].

4) Impact of continued serotype shift following higher-valency vaccine programs on microbiology and management.

Future well-designed multicenter randomized controlled trials within established North American and European pediatric research networks are essential to resolve these uncertainties.

Table 10. *Indications for Escalation of Management in Pediatric Complicated Pneumonia.*

Clinical or Laboratory Indicator	Threshold/Finding	Action Recommended	Urgency
Persistent fever despite antibiotics	>48-72 hours	Repeat US; consider drainage	Urgent
Oxygen saturation	SpO_2 <92% on room air	Supplemental O_2; assess for drainage	Immediate
Pleural fluid pH	<7.2	Drainage mandatory	Urgent
Pleural fluid glucose	<2.2 mmol/L	Drainage strongly indicated	Urgent
Pleural fluid LDH	>1,000 IU/L	Drainage strongly indicated	Urgent
Frank pus on thoracentesis	Grossly purulent	Drainage mandatory	Immediate
Positive Gram stain	Organisms on stain	Drainage mandatory; optimize antibiotics	Urgent
Ultrasound: multiple loculations	≥3 septations; dense partitioning	Consider early VATS over fibrinolytics	Urgent
Ultrasound: thick pleural rind	Peel >5 mm; fixed lung	Early VATS or open decortication	Urgent
Failure of fibrinolytic therapy	No improvement after 48-72h of tPA	Escalate to VATS	Urgent
Suspected necrotizing pneumonia	Cavitation on CT; failure to improve	CT thorax; thoracic surgery consultation; broad-spectrum antibiotics	Immediate
Hemodynamic instability/sepsis	SIRS criteria: vasopressor requirement	ICU admission; urgent source control drainage; broad-spectrum antibiotics	Emergency
Suspected bronchopleural fistula	Air leak through drain; CT confirmation	Thoracic surgery consultation; water-seal drainage	Urgent

Sources: Harris et al., 2017 [12], Shen et al., 2017 [1], Krenke et al., 2017 [11].

10. Conclusion

Complicated pneumonia in children requires a systematic, evidence-based, and multidisciplinary approach. Lateral decubitus chest X-ray should be encouraged, while chest ultrasonography is the cornerstone of diagnostic evaluation. Management must be individualized by disease stage, with stepwise escalation from antibiotic therapy to catheter drainage and fibrinolysis, and to surgical intervention when required. Interventional radiology is recommended for single loculations, while VATS is the procedure of choice for thick pleura, multiloculated effusions, fibrinopurulent and early-organized empyema in experienced pediatric surgical centers. Open decortication is reserved for refractory, advanced disease. If fibrinolytics are indicated, tPA is preferred. Treatment may extend over several weeks, and early involvement of pulmonology is recommended. Most patients regain full lung function within several months. Further high-quality prospective research remains essential to refine evidence-based.

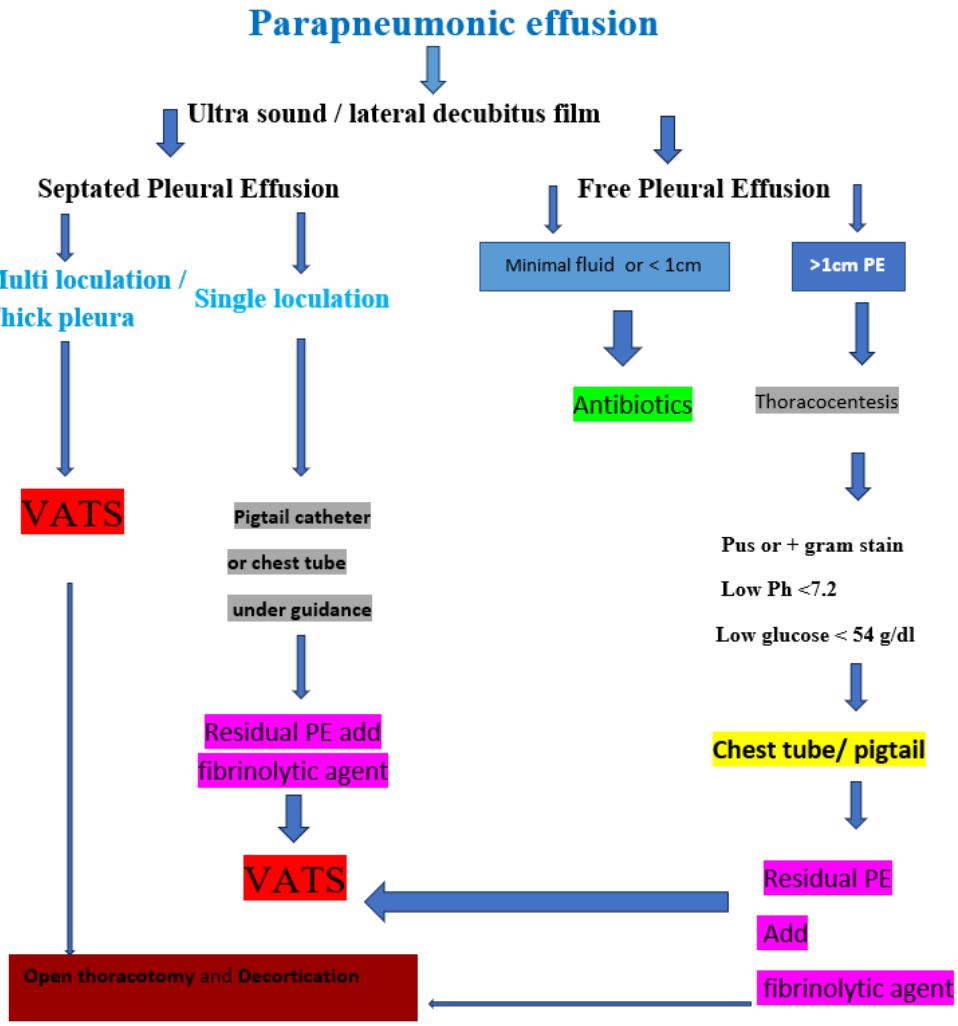

Figure 1. Proposed Clinical Management Algorithm for Pediatric Parapneumonic Effusion and Empyema.

Abbreviations

PPE	Parapneumonic Effusion
VATS	Video-assisted Thoracoscopic Surgery
PCR	Polymerase Chain Reaction
DNase	Deoxyribonuclease
tPA	Tissue Plasminogen Activator
CA-MRSA	Community-Associated Methicillin-resistant Staphylococcus Aureus
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
LDH	Lactate Dehydrogenase
rRNA	Ribosomal RNA
RNA	Ribonucleic Acid
MIST2	Second Multicenter Intrapleural Sepsis Trial
WBC	White Blood Cell Count
PCT	Procalcitonin
AP	Anteroposterior
NP	Necrotizing Pneumonia
BPF	Bronchopleural Fistula
MSSA	Methicillin-sensitive S. Aureus
PCV13	13-valent Pneumococcal Conjugate Vaccine
IV	Intravenous

PO	Oral
US	Ultrasound
CT	Computed Tomography
RCT	Randomized Controlled Trial
SpO_2	Oxygen Saturation
IU	International Units
MD	Mean Difference
CI	Confidence Interval
RR	Relative Risk
ICU	Intensive Care Unit
OR	Operating Room
LOS	Length of Stay
SIRS	Systemic Inflammatory Response Syndrome
Evidence grade A	RCT/ Meta - Analysis
Evidence grade B	Cohort/ Observational Evidence
Evidence grade C	Expert Consensus/ Case Series

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Conflicts of Interest

The authors declare no conflict of interest.

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