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# Pleural Effusion in Children: A Review Article and Literature Review

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## Abstract

Pediatrics pleural effusion is an abnormality that frequently develops from collection of fluids in the pleural space and commonly caused by a primary phenomenon or secondary to variety of disorders such as infections. This accumulated fluid can be originated from excessive filtration or defective absorption caused by different infectious agents such as *Streptococcus pneumoniae*, which is the most common, or non-infectious factors like lymphoma or congestive heart failure. It may present a various range of complications from a self-limited one to respiratory failure. Pediatrics pleural effusion is most commonly seen in boys and younger children. The incidence and distribution of pleural effusion is increasing in most industrial countries according to the population studies. The prognosis is highly related to the underlying disorder as well as treatment approach. early drainage of fluid may dramatically reduce the rate of mortality and morbidity. Clinical manifestations are variable depended on the underlying disease, size, and location of the effusion. They range from persistent fever, cough, anorexia, malaise, tachypnea, dyspnea, and chest pain, like in infectious pneumonia, to abdominal pain, distension and vomiting. In physical examinations a pleural rub may be the only initial manifestation during the early stage of pleurisy. A large amount of fluid diminishes the chest excursion on the affected side and may shift the mediastinum and displace the trachea and cardiac apex to the contralateral side, unilaterally. Initial diagnostic test for ruling out the different causes of pleural effusion is analyzing the pleural fluid apparently and biochemically. Also imaging tests could be used such as chest radiography so as to ensure the existence of pleural effusion. Ultrasonography and computed tomography (CT) scanning are also beneficial for a more accurate assessment. In most affected cases removing underlying etiologies and also applying supportive care are sufficient to heal effusion, which can range from antibiotic therapy and using fibrinolytics to chest tube drainage. Surgical therapy in patients with pleural effusion with the failed medical management has remained controversial, though. Thus, selection of the best management approach can result in favorable outcomes and significantly reduces morbidity and mortality rates.

**Keywords:** Pleural Effusion; Pediatrics; Pleural Effusion, Diagnosis; Pleural Effusion, Therapy

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## Introduction

Pediatrics pleural effusion is an abnormality frequently develops from the collection of fluids in the pleural space commonly caused by a primary phenomenon or secondary to variety of disorders such as an infection. This accumulated fluid can be originated from excessive filtration or defective absorption. Despite asymptomatic feature in mild effusion, it may be accompanied with complications such as respiratory failure due massive fluid accumulation, septicemia, bronchopleural fistula, pneumothorax, and pleural thickening (1).

## Pathophysiology

Any conditions that may lead to fluid effusion increase into the pleural space can cause pleural effusion. In this regard, different baseline mechanisms suggested for pleural effusion include empyema, abnormal capillary permeability leading, increased hydrostatic or decreased oncotic pressure in the setting of normal capillaries, abnormal lymphatic clearance, and also hemothorax (2).

## Etiology

The etiological mechanisms of pleural effusion is considerably different in childhood and adulthood that the effusion secondary to pleural infections is the most common cause of this abnormality in children, while the most common causes in adults have been shown to be congestive heart failure and malignancies (3). Some population-based studies have shown that about half of pediatrics pleural effusion can be caused by pneumonia, followed by malignancies, renal disorders, trauma, and heart failure (4). In infectious pleural effusion, bacterial infections are the most common sources may led to serious complications such as empyema; however effusion can be less commonly occurred by viral infections that are usually asymptomatic. Among bacterial causes of pleural effusion, *Streptococcus pneumoniae* is the most common germ for this abnormality (5-6-7). In this context, among different serotypes of this pathogen, serotype 1 is dominant in children with empyema (8-12). Although Streptococcus pneumoniae is the most infectious etiology for pediatrics pleural effusion, but other less common causes for this defect include community-acquired methicillin-resistant *Staphylococcus aureus, Haemophilus influenzae type B,* coagulase-negative *staphylococcus,* and other streptococcal species as *viridans streptococcus, Group A streptococcus, alpha-hemolytic streptococcus* (13-15). Another cause of pleural effusion in children is pulmonary tuberculosis that was widely reported in 2 to 38% (16). This infection is frequently unilateral that may be occurred primarily as from direct hematogenous invasion of the pleural space or secondary to a reactivation disease such as pulmonary parenchymal disease (17).Disseminated Mycobacterium bovis also reported with complicated pneumonia (18).

Among non-infectious causes of pleural effusion, congestive heart failure is a less common cause secondary to elevated left atrial or pulmonary capillary wedge pressure (19). Lymphoma is another cause of pleural effusion that usually results from direct pleural invasion by the tumor, obstruction of the lymphatic pathway, pneumonia or atelectasis (20). Another rare cause of pleural effusion is chylothorax that can be occurred congenitally or acquired raised from the leakage of chyle into the pleural space as a result of damage to the thoracic duct by rupture, laceration, tear, or compression (21, 22). Other rare causes of pleural effusion in children include hemothorax, hypoalbuminemia, nephrosis, hepatic cirrhosis, and iatrogenic causes. (23)

**Epidemiology**

Pediatrics pleural effusion is more common in boys than in girls (17) and also in younger children in comparison with older ones. The incidence of pleural effusion in children is directly depended on the type of underlying disease. Massive pleural effusion led to empyema can be appeared in about 0.6-2% of children with bacterial pneumonia (24). Tuberculosis pleural effusion commonly occurs in adolescents and is uncommon in the preschool-aged child (25). The distribution of pleural effusion according to the population studies is now increasing in most industrial countries. As, in the United States, the empyema-associated hospitalization rate has increased from 2.2 per 100,000 in 1997 to 3.7 per 100,000 children in 2006 (26, 27). In a study on Spanish population, the incidence of infectious pleural effusion in children younger than age 5 years increased from 1.7 per 100,000 in 1999 to 8.5 per 100,000 in 2004 (28). In France, the incidence of empyema increased from 0.5 per 100,000 in 1995 to 13 per 100,000 in 2003 (29).

**Prognosis**

The prognosis of pleural effusion in children is directly depended on the features of underlying disorders as well as considered treatment approach. In this regard, infection-based effusion can be successfully resolved by using appropriate anti-infection agents, meanwhile, most viral and mycoplasmal pleural effusions usually resolve spontaneously. Generally, in untreated cases with pleural effusion, serious complications of empyema are expected especially in younger children. On the other hand, by early drainage of effusion, rates of mortality and morbidity can be considerably reduced. Moreover, the type of employed treatment regimens can also affect the prognosis of pleural effusion in children so that a higher mortality rate for children treated with antibiotics and chest tubes compared with those treated with fibrinolytic therapy, video-assisted thoracoscopic surgery (VATS), or thoracotomy has been reported (30).

**History and Clinical Manifestations**

The clinical picture and presenting symptoms of pleural effusion depend on the underlying disease and the size and location of the effusion. In this regard, the recent history of upper respiratory tract infection, bronchitis, or pneumonia is expected in effusion due to infectious pneumonia that can be manifested by persistent fever, cough, anorexia, malaise, tachypnea, dyspnea, and chest pain. The most common manifestations of Pleural effusion with tuberculosis basis include cough, pleuritic chest pain, dyspnea, night sweats, fever, hemoptysis, and even weight loss. In malignancies, some patients maybe asymptomatic that manifested only by cough and low grade fever, however in higher stages, respiratory distress or mediastinal mass can be observed (31). In pleural effusion due to congestive heart failure or nephrotic syndrome, the symptoms range from asymptomatic status to diseases specific manifestations (28).

Regardless of the etiology of pleural effusion, the symptoms severity depends to the amount of accumulated fluid and also location of the pleural effusion. A large collection of fluid leads to dyspnea, respiratory distress, dull pain, and cough. These symptoms may vary with an alteration in body position. Also, sub-pulmonic fluid collection can be associated with vomiting, abdominal pain, and abdominal distention caused by partial paralytic ileus.

**Physical Examination**

In physical examination, the patient may look dyspneic and anxious because of pain, discomfort, or hypoxemia. A pleural rub may be the only initial manifestation during the early stage of pleurisy. The rub disappears as fluid accumulates between the pleural surfaces. A large fluid collection causes fullness of the intercostal spaces and diminished chest excursion on the affected side. Excessive unilateral fluid accumulation shifts the mediastinum and displaces the trachea and cardiac apex to the contralateral side.

**Proving the existence of pleural effusion**

Chest radiography is the first simplest imaging strategy to etiological assesses of pleural effusion in children. This tool is the least expensive method to confirm existence of pleural effusion. In this way, all frontal, lateral, and decubitus radiographs are used to detect a pleural effusion (32). In this imaging technique, free-flowing pleural fluid collects in the most dependent part of the pleural space on an upright chest radiograph. Also, blunting of the costophrenic recess is the earliest sign of pleural fluid accumulation. Meniscus sign as well as opacification of the hemithorax with mediastinal shift can be also appeared in larger size of effusion (33). Next step to correct assessment of pleural effusion in children is ultrasonography that easily permits characteristics of effusion (34). This tool can easily distinguish free from loculated pleural effusion and also differentiate effusion from thickening and solid masses (35-37). For more accurately assessment of effusion, computed tomography (CT) scanning was applied to determine other parenchymal abnormalities (38-40). This tool seems to be very useful in complicated cases especially with empyema. Furthermore, CT scan is very useful in interventions in which effusions are difficult to access (41-44).

**Diagnosis**

The main goal of employing different diagnostic approaches is to differentiate different causes for pleural effusion such as ruling out immune dysfunction or other underlying systemic or local pulmonary disorders.

**Initial diagnostic approaches**

In those conditions with sufficient effusion size, thoracentesis is recommended. This diagnostic approach is more indicated among patients suspected to massive empyema, those with malignancy, or in newborn; however

is not indicated for those patients with small size of effusion, or other benign and non-complicated conditions.

The initial diagnostic test for the aim of diagnosis is analysis of the pleural fluid (25). This fluid is primarily assessed based on its appearance and color so that grossly purulent fluid indicates an empyema; a putrid odor suggests an anaerobic empyema; clear and pale yellow fluid suggests a transudate; milky fluid is consistent with a chylothorax; bloody pleural fluid is seen with trauma, malignancy, tuberculosis, uremia, and empyema due to group A *Streptococcus*; and *Aspergillus nigrans* infection produces a black pleural fluid (31). Also, the chemical components of the fluid can be very helpful to differentiate pleural effusion causes so that changes in the level of pleural fluid triglyceride, amylase, or pleural fluid hematocrit can be specified to chylothorax, pancreatitis, and hemothorax, respectively. For assessing the presence of infectious effusion, raised white blood cell count and positive C-reactive protein and blood culture can be diagnostic (45-48). Sputum or gastric aspirates for acid fast bacilli and a purified protein derivative (PPD) test should be performed in suspicion to tuberculosis.

Another approach in patients with unexplained inflammatory effusion, suspected tuberculosis, or malignancy is pleural biopsy; however it is an invasive method with some potential complications such as bleeding and pneumothorax.

**Therapeutic approaches**

In most affected cases with pleural effusion, removing underlying etiologies and also applying supportive cares is sufficient to heal effusion. Also, the sterilization of pleural fluid, re-expansion of the lung, and restoration of normal lung function are considered as the main treatment goal in these patients, especially in those who complicated with empyema. In some cases with infectious-based effusion with or without empyema complication, considering antibiotic therapy in combination with thoracocentesis, chest tube drainage with or without instillation of fibrinolytic agents is the choice approach. However, in some rare cases, surgical interventions may be indicated (49).

In patients suffering from parapneumonic effusion, the selection of antibiotic is performed based on patient's age and the known organism which is sensitive to antibiotic. In this regard, the first line antibiotics used are penicillins, cephalosporins, aztreonam, clindamycin, and ciprofloxacin (50). The antibiotic therapy should be orally or intravenously (in hospitalized patients) at least 48 hours after the patient is afebrile and the chest drain is removed. Thereafter, oral antibiotics may be continued for 2-4 weeks. Despite recent development in appropriate managing antibiotic therapy to minimize bacterial resistance to these drugs, but a marked increase in resistance to antibiotics has been revealed in pneumococcal disease (51-53) and thus hospitalization rate due to empyema has been also increased (54). Pleural effusions following viral infections are usually asymptomatic and self-limited and not required treatment.

Chest tube drainage maybe indicated in patients with enlarged effusions. In various studies, the main indications for acquiring chest tube placement have been pointed as frank pus on thoracentesis, a positive pleural fluid Gram stain and culture finding, a pleural fluid pH level of less than 7, a glucose concentration of less than 40 mg/dL, or an LDH level of more than 1000 IU (20).

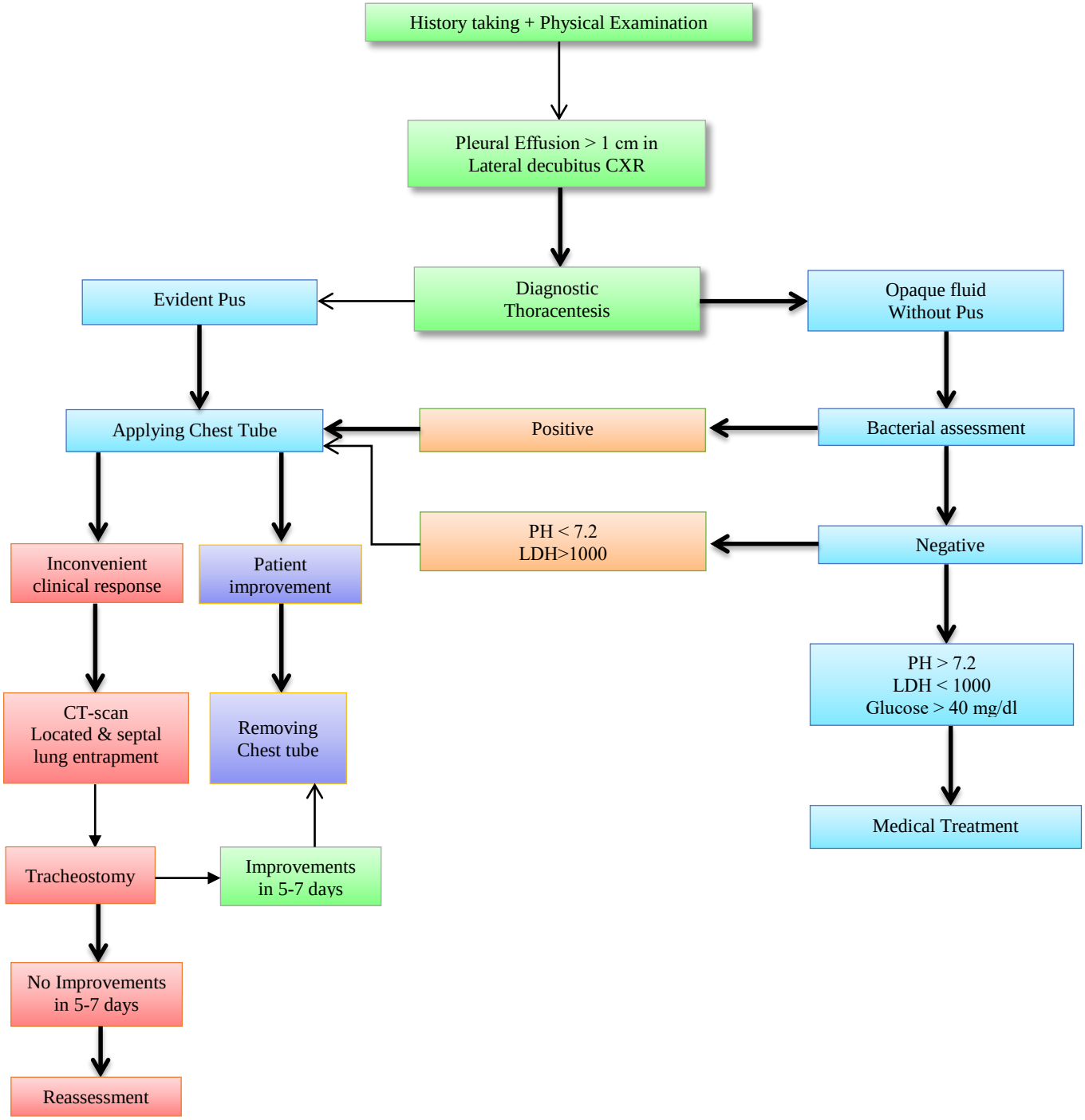
Considering surgical therapy in patients with pleural effusion with the failed medical management has remained controversial. Some authors believe that children who are affected by empyema and parapneumonic effusion who failed to improve by antibiotic therapy can successfully treated by surgery. Also, persistent sepsis, complex empyema with significant lung pathology, and bronchopleural fistula with pyopneumothorax are other indications for surgical treatment with successful results and favorable outcome (55).

## Conclusion

Although pleural effusion in children is a rare finding and is asymptomatic in most affected children, but in conditions with an excessive fluid collection, it may be complicated with empyema or other serious complications leading high rates of morbidity and even morbidity. Thus, selection of the best management approach including removal of underlying diseases, supportive cares, selection of proper antibiotics, and invasive approaches if required can result in favorable outcome.

**Table 1.** Features of Pleural Effusion Fluid and Related Diagnosis.

| Glucose | LDH | PH | Appearance | Diagnosis |
|---|---|---|---|---|
| > 40mg/dl | < 1000 IU/L | > 7.2 | Clear | Transudate |
| < 40mg/dl | >1000 IU/L | < 7.2 | Opaque | Exudate |
| | more assessments are needed | <7 | Evident Pus | Empyema |

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