Pleural Effusions and Pneumothoraces

Katherine Cashen, DO,* Tara L. Petersen, MD[†]

*Department of Pediatrics, Children's Hospital of Michigan/Wayne State University School of Medicine, Detroit, MI
[†]Division of Critical Care, Department of Pediatrics, The Children's Hospital of Wisconsin/The Medical College of Wisconsin, Milwaukee, WI

Practice Gaps

1. Clinicians should be aware of the causes and clinical presentation of pleural effusions and pneumothoraces.

2. Clinicians should understand the current role of diagnostic tests, imaging modalities, and timing of minimally invasive treatments.

Objectives   After completing this article, readers should be able to:

1. Describe the pathogenesis of pleural fluid accumulation.

2. Identify the most likely causes of pleural effusion and pneumothorax.

3. Understand the basic clinical presentation, diagnostic tests, and management of pleural effusions and pneumothoraces.

4. Differentiate between transudative and exudative pleural effusions.

5. Understand the natural history of spontaneous pneumothorax.

INTRODUCTION

The pleural space is created by the parietal and visceral pleura that line the chest wall and the lung surface, respectively. Normally, only a small amount (0.3 mL/kg) of hypotonic fluid is present within the pleural space due to homeostatic balances in physiologic fluid production and absorption. Various infectious and noninfectious processes can lead to pathologic filling of the pleural space with fluid (effusion) or air (pneumothorax). Such pathologic changes create a true space that can interfere with normal lung mechanics and, in severe cases, cardiac function. Although much less common in pediatric than adult populations, pleural effusions and pneumothoraces in both groups can lead to substantial complications, resulting in significant morbidity and mortality if unrecognized or untreated.

Overall, the cause of pleural effusions and pneumothoraces differs in children compared to adults. In adults, congestive heart failure (CHF) and malignancy account for a substantial number of pleural effusions, but these are uncommon causes in children. Infectious pleural effusions in the setting of pneumonia (parapneumonic effusions) remain the most common cause of effusions in both children and adults. Unlike the adult population, children experience spontaneous pneumothoraces more often without underlying contributing pulmonary processes.

The evolving role of imaging modalities and minimally invasive treatment approaches for pleural effusions and pneumothoraces has led to ongoing debate,

ABBREVIATIONS

BTS	British Thoracic Society
CHF	congestive heart failure
CT	computed tomography
VATS	video-assisted thoracoscopic surgery

and sometimes clinical uncertainty, when selecting appropriate testing, consultation, and timing/type of therapeutic intervention. This review focuses on the epidemiology, pathogenesis, diagnosis, and management of pleural effusions and pneumothoraces. We highlight diagnostic criteria, imaging modalities, and the evidence-based role of less invasive therapeutic interventions.

PLEURAL EFFUSION

Epidemiology

Parapneumonic effusions are found in 2% to 12% of children with community-acquired pneumonia and in up to 28% of children hospitalized for community-acquired pneumonia. Despite an overall decrease in the incidence of pediatric bacterial pneumonia, the rate of complicated pneumonia cases (parapneumonic effusion or empyema) has increased. In children younger than age 2 years, hospitalizations for pneumonia complicated by empyema doubled from 3.5 cases per 100,000 admissions from 1996 through 1998 to 7 cases per 100,000 admissions from 2005 through 2007. Among children ages 2 to 4 years, the rate almost tripled. (1) Although mortality is low, parapneumonic effusion and empyema cause substantial burden to the child, family, and health-care system. Other causes of pleural effusion, including malignancy, effusions due to systemic disease, postoperative or congenital chylous effusion (lymph fluid accumulation in the pleural space), and traumatic effusions (blood accumulation in the pleural space), are much less common.

Pathogenesis

In the normal physiologic state, pleural fluid is hypotonic, with a pH of 7.6, glucose concentrations similar to those in serum, and protein concentrations of approximately 1.5 g/dL (15 g/L). Pleural fluid is filtered at the parietal pleural level, and reabsorption occurs via parietal pleural lymphatics. Movement between the vascular and pleural spaces is described by the Starling principle. To prevent excessive accumulation of pleural fluid, the flow rate in pleural lymphatics increases in response to increased pleural fluid filtration. Opposing hydrostatic and oncotic pressures act on the visceral and parietal pleural membranes to prevent passage of pleural fluid from the parietal capillaries. A pleural effusion forms when this balance is disrupted and fluid accumulates in the pleural space due to an underlying pathologic process.

Increased hydrostatic pressure (CHF), a decrease in colloid osmotic pressure (hypoalbuminemia), an increase in capillary permeability (pneumonia), increased intrapleural negative pressure (atelectasis), and decreased lymphatic drainage may all lead to pleural effusions. Blood may cause a pleural effusion related to trauma (hemothorax), and chyle may accumulate in the pleural space (chylothorax) due to disruption or obstruction of the thoracic duct. In addition, pleural inflammation from disease processes causes an influx of immune cells, leading to activation of the coagulation cascade and fibrin deposition. This contributes to the increased permeability of adjacent capillaries and further accumulation of pleural fluid.

Numerous disease processes have been associated with pleural effusions, the most common of which is pneumonia. Malignancy, renal disease, trauma, CHF, and systemic diseases remain important causes and require consideration (Table 1), although these are much less common in pediatric than in adult medicine. Parapneumonic effusions can result in multiple complications, including empyema (occurring in approximately 3% of children hospitalized with pneumonia), bronchopleural fistula, and rarely pericarditis and osteomyelitis

TABLE 1. Causes of Pleural Effusions in Children

Infection	Pneumonia (bacterial, tuberculous, viral, fungal, parasitic)
Cardiovascular	Congestive heart failure Constrictive pericarditis Superior vena cava obstruction Postcardiac surgery
Lymphatic disorder	Chylothorax (thoracic surgery, congenital) Lymphangiectasia Lymphangiomatosis
Intra-abdominal processes	Pancreatitis Peritonitis Post abdominal surgery (liver transplant) Uremia Nephrotic syndrome Peritoneal dialysis Urinary tract obstruction
Malignancy	Lymphoma Leukemia Carcinoma
Pulmonary	Atelectasis Pulmonary infarction Extralobular pulmonary sequestration/ trapped lung Pulmonary embolism
Iatrogenic and miscellaneous	Chylothorax Extravascular central line placement Drug-induced pleuritis (angiotensin-converting enzyme inhibitors, valproic acid, amiodarone, dantrolene) Hydrops fetalis Esophageal perforation Post radiation therapy Hemothorax (trauma)

of the rib. The pathogenesis of parapneumonic effusion/empyema formation has 3 stages: exudative, fibrinopurulent, and organizational. During the exudative stage, the inflammatory process, which lasts 24 to 72 hours, causes fluid to leak into the pleural space. Over the course of the next 7 to 10 days, the fibrinopurulent stage occurs. Fibrin is deposited in the pleural space, which can result in loculated fluid collections and thickening of the parietal pleura. As the number of white blood cells increases, a thicker, more purulent fluid forms, resulting in an empyema. Finally, in the organizational stage, fibroblasts proliferate in the pleural cavity. During this phase, loculations continue to develop and mature into abscesses while the intrapleural fibrin membranes reorganize into a thick, pleural peel.

Clinical Findings

Initially, children may be asymptomatic or show signs and symptoms consistent with the underlying cause of pleural effusion formation. Rapid accumulation of pleural fluid is generally not well tolerated. The degree of impairment depends on the underlying pathology and the cardiovascular and pulmonary status of the child. Chest wall expansion and downward displacement of the diaphragm occur to accommodate the pleural fluid and preserve lung volume. Large effusions in neurologically intact children initially cause tachypnea to maintain minute ventilation in the setting of decreased tidal volumes. Children may then develop dyspnea and exhibit retractions with increased work of breathing. Finally, the resultant decreased functional residual capacity and increased dead space may lead to hypoxia and hypercapnia. These symptoms may be exacerbated in a child with low functional residual capacity and impaired thoracic volume at baseline. For example, a child with thoracic deformity causing restrictive lung disease has much lower pulmonary reserve and less tolerance of pleural fluid accumulation.

Children with parapneumonic effusions may present with initial signs and symptoms of bacterial pneumonia. The most common symptoms are fever, malaise, decreased appetite, cough, chest pain, and dyspnea. Pleuritic chest pain is usually worse with inspiration. Rarely, these patients present with severe respiratory distress and shock. Physical examination may reveal dullness to percussion, diminished or absent breath sounds, a pleural friction rub, and egophony. However, these examination findings are sometimes difficult to elicit in infants and children due to their rapid respiratory rates and inability to actively participate in the physical examination.

Laboratory Findings

Analysis of pleural fluid allows the clinician to differentiate between transudative and exudative effusions (Table 2). A transudative effusion is usually clear or straw-colored and results from fluid passage across an intact pulmonary capillary barrier caused by increased pulmonary capillary hydrostatic or decreased colloid osmotic pressure into the pulmonary interstitium and across the visceral pleura into the pleural space. An exudative effusion may be straw-colored or cloudy and results from fluid or protein passage across an altered capillary barrier in the lung, pleura, or tissues. The Light criteria, based on adult data, have been used since 1972 to differentiate between transudative and exudative effusions. In Light's study, the criteria showed very high sensitivity and specificity; subsequent meta-analysis of 8 studies revealed that other tests/criteria employed to identify exudative effusions do not significantly differ in diagnostic accuracy when compared to Light's criteria. (2) Pleural fluid appearance may help the clinician to determine the underlying cause. Purulent fluid suggests infection, thin white milky fluid suggests chyle, and blood suggests trauma or malignancy. In children, pleural biomarkers are less accurate and diagnostic thoracentesis should only be performed in select circumstances. Some indications include persistent fever despite treatment, suspected resistant organisms, and as a therapeutic intervention. Therefore, while helpful, pleural fluid analysis is not always indicated or required.

Parapneumonic effusions and empyema are exudative. The fluid may appear purulent or turbid, has a high leukocyte count with neutrophil predominance, and has a low glucose concentration. Pleural fluid sent for Gram stain and bacterial culture may show bacteria but is more often sterile because of the prior use of antibiotics. In 1 study, polymerase chain reaction detection of bacterial genes increased organism detection in cases of bacterial empyema from 18.7% by culture to 68.7% by polymerase chain reaction. (3) A complete blood cell count with differential count and serum acute-phase reactants (such as erythrocyte sedimentation rate and C-reactive protein) may provide supportive evidence of bacterial or viral pneumonia; however, these tests should only be used as adjuncts to the history and physical examination. A normal white blood cell count and low concentrations of acute-phase reactants do not exclude infectious causes. Blood cultures have been reported to be positive in only 1% to 11% of hospitalized children with pneumonia, although this yield increases to 13% to 30% in patients with a parapneumonic effusion or empyema. (4)(5)(6)(7) It is important to note that the utility of blood culture is limited when the specimen is collected after administration of antibiotics.

Aerobic pathogens cause most bacterial parapneumonic effusions. The predominant organisms in children vary, based on region, immunization status, laboratory techniques, and pretreatment with antibiotics. Historically, with the advent of antibiotics, *Staphylococcus aureus* was the predominant organism causing parapneumonic effusion in children younger

TABLE 2. Characteristics of Exudative and Transudative Effusions

EXUDATIVE EFFUSION	
Pleural Fluid Protein/Serum Protein Ratio	>0.5
Pleural Fluid LDH/Serum LDH Ratio	>0.6
Pleural Fluid LDH	>2/3 upper limit of normal for serum LDH
pH	<7.3 (depending on the cause)
Glucose	<60 mg/dL (3.33 mmol/L) (malignancy, rheumatoid disease, empyema, tuberculosis)
TRANSUDATIVE EFFUSION	
Pleural Fluid Protein/Serum Protein Ratio	<0.5
Pleural Fluid LDH/Serum LDH Ratio	<0.6
Pleural Fluid LDH	<2/3 upper limit of normal for serum LDH
pH	>7.4

LDH=lactate dehydrogenase.

than age 6 months. *Streptococcus pneumoniae* and *Haemophilus influenzae* caused most of the infections in children ages 7 to 24 months. Today, *H influenzae* type b rarely causes infection because of the widespread vaccination of children. *S pneumoniae* is the most common pathogen causing parapneumonic effusion in children. Despite pneumococcal conjugate vaccination, complicated parapneumonic effusions from *S pneumoniae* are still prevalent. In fact, empyemas are increasing in frequency. Multiple other bacterial pathogens cause parapneumonic effusions, including anaerobes *(Bacteroides, Fusobacterium),* coagulase-negative *Staphylococcus, Streptococcus viridans,* group A *Streptococcus,* and *Actinomyces.* Parapneumonic effusions have been reported less frequently with *Mycoplasma pneumoniae.* Overall, *S pneumoniae* and *S aureus* are responsible for most complicated parapneumonic effusions in children.

Radiologic Findings

Radiographs (anteroposterior or posteroanterior and lateral) aid in the diagnosis of pleural effusions. Lateral decubitus chest radiographs can show whether an effusion layers in a dependent manner. The earliest radiographic feature of pleural effusion is blunting of the costophrenic angle, as shown in Fig 1 (in adults, approximately 200 mL of fluid must be present for this finding). However, when there is complete opacification of the lung, it is not always possible to differentiate atelectasis, consolidation, or tumor from a large effusion.

Ultrasonography can be used to evaluate the size of an effusion and to differentiate simple from complicated effusions. Effusions may appear anechoic or echoic with floating pinpoint echoes. Fibrin deposition may be identified by fibrinous strands attached to a pleural surface, septations, or pleural thickening. Loculation may be identified when the fluid does not move freely and can be seen more clearly by scanning the patient in the supine followed by the seated position. Ultrasonography can be used to guide thoracentesis or chest tube placement. The benefits of ultrasonography use include: patient tolerance, absence of radiation exposure, superiority to computed tomography (CT) scan in detecting early loculations, and increasing availability, including at the bedside. (8)
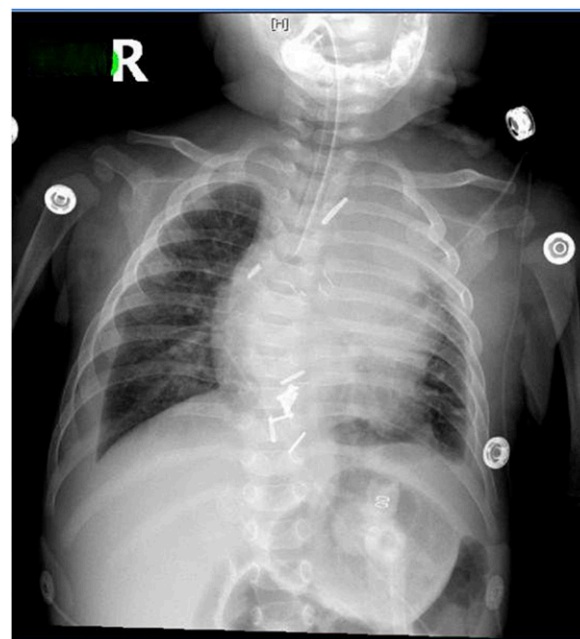

Figure 1. Pleural effusion on chest radiograph.

Chest CT scan can be used to evaluate pleural fluid but should not be performed routinely due to radiation exposure and cost. In addition, studies suggest that CT scanning does not aid in characterization of pleural fluid more than ultrasonography and does not routinely affect management decisions. Intravenous contrast material aids in the identification of the pleura. Pleural enhancement and thickening, increased density of the extrapleural subcostal fat, and internally convex pleural collections are consistent with empyema on CT scan. In most cases, the radiation exposure of a CT scan may outweigh the benefit of the study. However, findings on CT scan may aid in management decisions in complicated cases and may be useful to surgeons before operative procedures.

Treatment

Initial treatment of pleural effusion is supportive and should be directed toward the underlying disease process. If infectious pleural effusion is suspected, systemic antibiotics should be chosen empirically based on the suspected pathogen, local sensitivity patterns, patient age, clinical scenario, and presence of underlying medical conditions. The initial choice of antibiotic should provide coverage against *S pneumoniae,* community-acquired methicillin-resistant *S aureus,* and group A *Streptococcus.* Vancomycin should not be started empirically in all children with parapneumonic effusions. However, the addition of vancomycin to empirical cephalosporins is warranted when *S pneumoniae* infection is suspected in critically ill children who have severe pneumonia with hypoxia, empyema, or septic shock. Antimicrobial therapy should be tailored and unnecessary antibiotics discontinued when antimicrobial susceptibility test results are available and demonstrate effective alternative agents. When an atypical organism is suspected, macrolides are the preferred agent for the treatment of pneumonia in school-age children who have moderate-to-severe infection.

Most uncomplicated parapneumonic effusions do not require drainage and respond to antibiotic therapy. The decision to drain a pleural effusion is clinical and based on the cardiorespiratory status of the child. Radiograph size classification-based drainage alone is not recommended in children. Consultation may aid the general pediatrician if there is uncertainty about whether an effusion should be drained. In most pediatric institutions, pediatric surgeons, pediatric intensivists, or interventional radiologists place thoracostomy tubes if indicated. Unlike in adults, routine thoracentesis is not recommended and often requires sedation or anesthesia in young children. Pediatric pulmonologists typically do not perform the therapeutic procedures performed by adult pulmonologists, such as thoracentesis, placement of thoracostomy tubes, and thoracoscopy with pleurodesis, a procedure

that causes the membranes around the lungs to adhere and prevents the buildup of fluid or air in the pleural space. Therefore, pulmonology consultation may be warranted to help determine the cause of the effusion and underlying pulmonary disease, but it is generally not indicated for therapeutic interventions. Historically, complicated parapneumonic effusions (pH <7.2, lactate dehydrogenase >1,000 U/L [16.7 μkat/L], glucose <40 mg/dL [2.22 mmol/L] or <25% of blood glucose value, positive Gram stain or culture, and loculations or septations on imaging) were routinely drained. Review of the available literature shows a low level of evidence to support interventions based on chemical analysis of the pleural fluid alone. (9) Drainage should be considered based on the clinical scenario and is most likely indicated in children with large effusions, worsening symptoms, sepsis, or a lack of improvement in symptoms despite administration of broad-spectrum antibiotics. Small-bore chest tubes should be used whenever possible, even for loculated effusions, when performing chemical debridement with fibrinolytic therapy.

Chest tube drainage with and without fibrinolytic therapy and video-assisted thoracoscopic surgery (VATS) followed by chest tube drainage are interventions used to treat empyemas. Historically, surgical debridement via thoracotomy or sternotomy was the definitive procedure. However, in the last decade, minimally invasive VATS became the preferred surgical therapy. During the VATS procedure, a thoracoscope is placed through a small incision and surgical instruments are inserted into the pleural space through several small incisions. The transmitted images allow the surgeon to debride infected tissue and perform decortication if necessary without the large incision needed for an open thoracotomy or sternotomy.

More recent studies suggest that chemical debridement (chest tube with fibrinolytic therapy) is equivalent in efficacy to VATS and superior to chest tube drainage alone. Chemical debridement involves placement of a chest tube into the pleural space either via Seldinger technique or surgical cutdown approach. A fibrinolytic agent (urokinase, streptokinase, or tissue plasminogen activator) is injected into the pleural space to break down fibrin and liquefy the solid material forming septations and debris. No randomized, controlled studies have definitively identified the preferred fibrinolytic agent, number of doses to administer, or optimal dwell time. Clinical results were similar in 2 pediatric studies, even when using fewer instillations and a shorter dwell time, but no direct comparative analysis has been reported.

In a meta-analysis of 67 pediatric studies, Avansino et al (10) found an increase in hospital mortality rate, hospital length of stay, duration of antibiotics, and need for reintervention in patients with empyema treated nonoperatively compared with patients treated with a primary operative

procedure or chest tube with fibrinolysis. Intrapleural alteplase decreased parapneumonic effusion volume compared with saline irrigation without additional complications. Two prospective, randomized trials in pediatric patients compared initial VATS to chest tube placement with fibrinolysis and found no difference in complications or length of stay but fewer additional drainage procedures. However, patients with chest tube placement with fibrinolysis had decreased readmission, suggesting that chest tube placement with chemical fibrinolysis may be the more economic treatment. (11)(12) The American Pediatric Surgical Association developed a treatment algorithm based on a comprehensive literature review in 2012 recommending thoracostomy drainage and intrapleural fibrinolytics as first-line treatment and reserving VATS for refractory cases. Therapeutic intervention (thoracostomy drainage with fibrinolytic therapy or VATS) should be initiated upon diagnosis, with earlier intervention associated with decreased hospital length of stay. (9)

NONINFECTIOUS CAUSES OF PLEURAL EFFUSIONS

Chylous Effusions

Chylous effusions are caused by leakage of chyle (lymphatic fluid) into the pleural space due to damage or obstruction of the thoracic duct and lymphatic collaterals. Congenital chylothorax is among the most common causes of pleural effusion in the neonate. In children, subclavian vein thrombosis, damage to the thoracic duct from surgery, superior vena cava obstruction, Fontan surgery, malignancy, and malformations of the pulmonary or thoracic lymphatic systems (seen in Noonan, Turner, and Down syndromes) are responsible for most chylous effusions.

Pathogenesis. Chyle, containing primarily long-chain triglycerides, proteins, and lymphocytes, is transported through the thoracic duct to the bloodstream. The thoracic duct ascends to the right of the vertebral column then crosses over to the left hemithorax at the fifth thoracic vertebral body and empties into the venous circulation in the region of the left jugular and subclavian veins. Disruption of the thoracic duct at any point due to trauma (including surgery), extrinsic compression (from tumor), or spontaneous causes (coughing, vomiting, hyperextension) may cause leakage of chyle into the pleural space. In addition, abnormal lymphatic vessels and impaired venous return can cause rupture of collateral lymphatics and leakage of chyle.

Clinical Findings. Children present with signs and symptoms of pleural effusion as previously described. They may have cough, tachypnea, and decreased breath sounds on physical examination. Postoperative patients may have persistent or milky-appearing drainage from chest tubes. Chest radiograph typically shows varying degrees of unilateral opacification, although bilateral opacifications can also be seen.

Laboratory Findings. Chyle is usually milky-appearing, with a high concentration of triglycerides as chylomicrons. Pleural fluid is typically exudative but may appear serous in neonates, malnourished or fasting children, and children on a low-fat diet. The pleural fluid of a chylothorax classically has a triglyceride concentration greater than 110 mg/dL (1.24 mmol/L) with a white blood cell count of more than $1,000/\mu L$ ($1 \times 10^9/L$) and greater than 80% lymphocytes. Chyle has a high protein concentration and immunoglobulin content.

Treatment. Chylothorax treatment for children is based on small case series. The goal is to remove fluid from the pleural space and decrease lymphatic flow through the thoracic duct until spontaneous healing occurs. Drainage of chyle by thoracentesis for diagnosis and symptom relief is usually indicated. Dietary treatment includes the use of medium-chain triglycerides and avoidance of long-chain fatty acids as the major source of dietary fat to decrease lymphatic flow and to provide enteric rest. Replacement of nutrient and electrolyte losses may be necessary in patients who require enteric rest, and this may be achieved with parenteral nutrition.

Somatostatin and octreotide (a synthetic analog) have been used to treat chylous effusions in children. These drugs cause vasoconstriction of the splanchnic circulation and probably a reduction of lymphatic fluid production, although the mechanism is unclear. Case series have reported successful treatment with these agents using different dosing and timing of initiation, but no randomized, controlled trials have been conducted to determine the safety and efficacy of this treatment. A Cochrane review of octreotide use in neonates concluded that there was insufficient evidence to make a recommendation. (13)

Surgical procedures (pleurodesis or ligation of the thoracic duct via thoracotomy or VATS) should be considered if chylothorax persists despite drainage and dietary modifications. There are no guidelines regarding timing of surgical procedure, but most practitioners consider surgery after 2 to 4 weeks of failed medical therapy.

Cardiovascular Causes of Pleural Effusion

CHF is much less common in children than in adults. CHF can be caused by myocardial dysfunction (cardiomyopathies and myocarditis), arrhythmias, congenital heart disease, myocardial ischemia, and systemic diseases such as sepsis. Other cardiovascular causes of pleural effusions in children are restrictive pericarditis, superior vena cava obstruction, and cardiac surgery.

Pathogenesis. The accumulation of pleural fluid is primarily due to left atrial hypertension or elevated pulmonary capillary wedge pressure from left heart failure. Increased capillary hydrostatic pressure leads to fluid leaking into the pleural space. Unlike in adults, right heart failure and pulmonary artery hypertension rarely cause pleural effusion in children.

Clinical Findings. Children present with signs and symptoms of heart failure in addition to the symptoms of pleural effusion. A child who has poor cardiac reserve does not tolerate a large pleural effusion well and may experience hemodynamic collapse. Radiographic findings show opacification consistent with pleural effusion that is most often bilateral.

Laboratory Findings. Pleural fluid is typically bilateral and transudative. The protein concentration is usually low. Adult studies have shown elevated N-terminal pro-brain natriuretic peptide in the pleural fluid of adults with CHF. This test may be helpful in the setting of pleural effusion following diuresis when the pleural fluid analysis may be confusing and appear exudative.

Treatment. Pleural effusions due to CHF usually resolve with treatment of the underlying condition causing CHF and improvement in cardiac function. If patients have substantial clinical signs (dyspnea, large effusion, hemodynamic compromise), thoracentesis may improve symptoms but is not routinely recommended.

Malignancy-related Pleural Effusions

Malignancy-related effusions in children are most commonly caused by lymphoma. Leukemia and carcinoma infrequently cause pleural effusion in children.

Pathogenesis. Effusion may result from pleural invasion by the tumor, obstruction of lymphatic flow, pneumonia, or atelectasis from extrinsic compression of the tumor or lymphadenopathy.

Clinical Findings. Children with malignancy-related effusions show many of the symptoms previously described for children with pleural effusions. In addition, they may have systemic signs of lymphoma, including lymphadenopathy, cough, shortness of breath, fever, unexplained weight loss, and fatigue. Effusions may be unilateral or bilateral on imaging. The clinical signs and symptoms differ based on the type of cancer and size of effusion.

Laboratory Findings. Pleural fluid is exudative and may be bloody or chylous. Cytopathologic study documenting the presence of malignant cells is diagnostic.

Treatment. Drainage of large effusions in patients with moderate-to-severe respiratory symptoms is indicated. However, children with lymphoma may present with mediastinal masses. Therefore, the risks and benefits of surgical intervention and administration of anesthetics should be carefully considered before proceeding with intervention. Treatment of the underlying malignancy often results in improvement of the effusion.

PNEUMOTHORACES

Epidemiology

An accumulation of air in the pleural space (pneumothorax) may be spontaneous with no identifiable underlying cause or related to a variety of disease processes. Spontaneous pneumothoraces occur in 3.41 per 100,000 children younger than age 18 years. There is an increased incidence in males, with 7.4 to 18 cases per 100,000 compared to only 1.2 to 6 cases per 100,000 females. Spontaneous pneumothorax is reported in 1% to 2% of term neonates. The incidence of secondary pneumothorax in the pediatric population is not well described.

Pathogenesis

A pneumothorax occurs when air leaks through the parietal pleura into the intrapleural space and leads to either partial or total lung collapse. The pleural space is usually free of air because the pressure gradient between total gas pressure in the venous system and the pleural space favors absorption of gas into the circulation.

Spontaneous pneumothoraces occur in the absence of trauma, and both primary and secondary causes are associated with anatomic abnormalities such as blebs, bullae, and pneumatoceles. Blebs and bullae are theorized to result from lung connective tissue changes that develop slowly over time and predispose the patient to spontaneous rupture. Spontaneous pneumothoraces are more common in males than females but much less common in the pediatric population compared to adults.

Secondary pneumothoraces are most common in children with asthma, cystic fibrosis (Fig 2), and connective tissue disorders (Marfan syndrome, Ehlers-Danlos syndrome, α_1-antitrypsin deficiency). Secondary causes are believed to result directly from systemic inflammatory or local lung tissue changes associated with these disorders. Various pulmonary histologic changes have been reported in children with underlying connective tissue disorders such as Marfan syndrome, including patchy cystic changes, emphysematous changes, pulmonary bullous dysplasia, and bronchiectatic changes that increase the risk for pneumothoraces. In children with asthma, the presence of inflammation, bronchospasm, and hyperinflation likely contribute to bleb rupture and pneumothorax.

Traumatic pneumothorax occurs when air enters the pleural space from injury to the chest wall, lungs, esophagus, or tracheobronchial tree. Pneumothoraces occur in one-third of pediatric cases of thoracic trauma, with a similar rate in both blunt and penetrating trauma. Pneumothorax associated with hemothorax is more likely in penetrating than in blunt trauma, where hemothorax is rarely present. Finally, iatrogenic pneumothoraces are caused by medical procedures (central venous cannulation, thoracentesis, thoracic surgery) or mechanical ventilation. In particular, neonates may develop a pulmonary air leak due to pneumothoraces or pulmonary interstitial emphysema as a result of mechanical ventilation. Preterm neonates and pediatric patients with heterogeneous lung disease requiring mechanical ventilation have an even higher risk of pneumothorax due to uneven distribution of alveolar inflation.

Clinical Findings

A small pneumothorax may be asymptomatic in children. However, with increasing air accumulation and resultant compression of lung parenchyma, symptoms of respiratory distress develop. Tachypnea, accessory muscle use, cough, chest pain, and hypoxia may all be presenting signs/symptoms. On physical examination, the patient may have decreased chest excursion, hyperresonance, and diminished breath sounds. If the volume of air continues to increase in the pleural space, tension physiology may develop. Tension pneumothorax causes vascular compromise, decreased cardiac return, and tachycardia and if untreated, may progress to hypotension, bradycardia, and cardiac arrest. Additional physical examination findings of tension pneumothorax include diminished heart sounds, tracheal deviation, and

Figure 2. Pneumothorax on chest radiograph.

shifting of the apical impulse (toward the contralateral side). Tension pneumothorax is rare in spontaneous pneumothoraces; it most often occurs in the setting of trauma.

Radiologic Findings

Historically, chest CT scan has been considered the gold standard for detecting pneumothoraces. However, this investigative modality may not be practical or feasible and has the additional drawback of increased radiation exposure. Upright chest radiography shows displacement of the pleural line. Ultrasonography may be used with the patient in the supine or seated position and is more sensitive than chest radiography when used by an experienced clinician. With ultrasonography, the lack of lung sliding in the B mode and the presence of a linear, laminar pattern in the tissue superficial to the pleural line and a similar linear pattern deep to the pleural line in M mode (barcode sign) indicates absent lung sliding and suggests the presence of pneumothorax at this interspace. Finally, neonatal literature supports the use of transillumination to diagnose pneumothorax.

Treatment

The management of pneumothorax in neonates and children depends on the size and respiratory status of the child, the cause, and contributing factors. Supplemental oxygen is indicated for children with respiratory distress and hypoxia. Immediate treatment of tension physiology requires needle decompression with a large-bore needle or angiocatheter. Adult guidelines recommend observation in stable patients with small spontaneous pneumothoraces on chest radiograph and hospital admission with placement of a chest tube for stable patients with large spontaneous pneumothoraces. No pediatric-specific guidelines are available for initial management of pneumothoraces. Large-bore thoracostomy tubes are rarely necessary; pigtail catheters and small-bore catheters are safe and effective in children. Treatment is aimed at preventing recurrence of pneumothorax, allowing lung reexpansion, and treating persistent air leaks. The recurrence rate for primary spontaneous pneumothorax has been reported to be as high as 40% to 61% in children. However, the increased cost and morbidity associated with primary VATS with blebectomy and pleurodesis in children makes this approach controversial. (14) Surgical therapy includes VATS and pleurodesis and is generally reserved for patients with persistent air leak or recurrent pneumothoraces.

No pediatric consensus guidelines have been developed regarding discharge and follow-up management. Recommendations are extrapolated from pediatric case series, the British Thoracic Society (BTS) guidelines, and the American College of Chest Physicians consensus statement on management

of spontaneous pneumothorax. (15)(16) In general, patients should be advised to return to the hospital if they develop increasing breathlessness. The risk of recurrent pneumothorax lasts up to 1 year after the initial event. Commercial air travel should be avoided until full resolution of the pneumothorax. The BTS guidelines recommend delaying air travel for 1 week after radiographic resolution of pneumothorax and preferably a 2-week delay for traumatic pneumothorax. For patients who develop signs and symptoms of pneumothorax in flight, supplemental oxygen should be provided and emergency landing at the nearest airport should be advised. In-flight makeshift chest tubes and needle decompression to decompress tension pneumothoraces have been reported in the literature. The optimal time to wait after resolution of a pneumothorax before air travel or travel to remote regions without access to medical care is not known. Individual decisions regarding travel should be made, taking into consideration the risk of recurrence and presence of underlying lung disease. Scuba diving should be permanently avoided unless a patient has undergone bilateral surgical pleurectomy and has normal lung function and normal findings on chest CT scan postoperatively. For patients who were managed by observation alone or needle aspiration, a follow-up chest radiograph should be performed in 2 to 4 weeks to monitor for resolution. Patients may resume normal physical activities once all symptoms have resolved, but it is reasonable to avoid sports that involve extreme exertion and physical contact until complete resolution of pneumothorax.

PNEUMOMEDIASTINUM/PNEUMOPERICARDIUM

Epidemiology

Air or gas in the mediastinum (pneumomediastinum) and pericardium (pneumopericardium) can be spontaneous or due to infection, esophageal disruption, surgery, or trauma. It is usually associated with other air leaks such as pneumothoraces and pneumomediastinum. Similar to pneumothoraces, pneumomediastinum has been categorized as primary (no risk factors or underlying lung disease) or secondary (known lung disease such as asthma or cystic fibrosis). Pneumomediastinum is rare in pediatric patients. In newborns, the incidence is 1.7 to 2.5 per 1,000 infants and is associated with shoulder dystocia. In the pediatric population, the incidence of spontaneous pneumomediastinum has been reported to be 1 in 8,000 to 1 in 15,000 children consulting the emergency department.

Pathogenesis

Traumatic pneumomediastinum and pneumopericardium are caused by blunt or penetrating trauma to the chest, tracheobronchial tree injury, or iatrogenic injury during procedures or surgery. Spontaneous pneumomediastinum occurs when a sudden increase in intrathoracic pressure causes an increase in intra-alveolar pressure, resulting in alveolar rupture with leaking of air into the interstitium, bronchoalveolar tissue, and mediastinum. Air from the upper respiratory tract, intrathoracic airways, and gastrointestinal tract may contribute to pneumomediastinum. Air moves along vascular sheaths into the mediastinum, through subcutaneous tissues of the thorax and neck, and can even enter the pericardium. Rarely, pneumopericardium occurs spontaneously.

Risk factors for pneumomediastinum and pneumopericardium include asthma, Valsalva maneuvers (related to intense activities such as weightlifting, coughing, and drug-induced exertion), vomiting, respiratory infection, foreign body ingestion, scuba diving, and inhalation of helium or inhalation drugs. Pneumopericardium may also be caused by pericardiocentesis, entrainment of air with pericardial drain placement, and infectious pericarditis with gas-producing organisms. Pneumopericardium has also been associated with preterm birth, severe respiratory distress syndrome, and mechanical ventilation.

Clinical Findings

Children with spontaneous pneumomediastinum may complain of chest pain radiating to the neck or back, cough, and shortness of breath. Typically this pain is worse with inspiration. Dysphagia has also been reported. Many affected children have subcutaneous emphysema, and if pneumomediastinum is due to underlying lung disease such as asthma, they may have clinical signs related to the disease process. In addition, cervical emphysema and facial or neck swelling, hoarseness, cough, and wheezing on auscultation have been reported. The Hamman crunch (a sound of crunching or rasping coinciding with the heart beat when auscultating the precordium) has also been described. Tachycardia and tachypnea are usually present in secondary pneumomediastinum. With a large pneumomediastinum or pneumopericardium, patients may have muffled heart sounds and tension pneumomediastinum with poor venous return, and they can develop tamponade physiology. Other children may look well and have normal vital signs and vague nonspecific symptoms.

Radiologic Findings

In pneumomediastinum, chest radiograph shows radiolucent gas outlining the mediastinal structures. Spinnaker sign, an upward and outward displacement of the thymic lobes, may be seen in infants. Mediastinal gas outlining the surface of the diaphragm and separating it from the heart is called

the continuous diaphragm sign. In addition, gas may be seen outlining the lateral margin of the descending aorta and extending laterally between the parietal pleura and the medial left hemidiaphragm. In pneumopericardium, chest radiograph shows air surrounding the heart, and the parietal pleura may project as a thin radiopaque line outlining the air. Unlike in pneumomediastinum, the air in pneumopericardium does not extend to the aorta or great vessels because of the anatomic limits of the pericardium. Associated subcutaneous emphysema, pneumothorax, and pneumoretroperitoneum may be present in both pneumomediastinum and pneumopericardium. CT scan is rarely necessary to diagnose pneumomediastinum but should be used when evaluation of underlying lung disease is necessary. Ultrasonography may identify an echogenic interface anterior to the heart that obscures the view of cardiac structures in pneumomediastinum. Pneumopericardium may appear as bright echogenic foci moving along the pericardial layer during diastole.

Treatment

Treatment is supportive, and isolated spontaneous pneumomediastinum generally resolves with a low recurrence rate. Secondary pneumomediastinum and pneumopericardium treatment is aimed at treating the underlying lung pathology, traumatic injury, or other causes for air introduction. In mechanically ventilated children, attempts to minimize airway pressures should be employed. Very rarely mediastinal or pericardial drainage must be performed for large air collections. In general, avoidance of activities with forceful inspiration or increased positive end-expiratory pressure should be avoided in the recovery period, although no guidelines to aid in timing of these recommendations have been published.

Summary

- On the basis of class C evidence and consensus, ultrasonography should be used preferentially over computed tomography scan for the diagnosis of parapneumonic effusion and empyema.

- On the basis of class C evidence and consensus, pleural fluid should be drained in patients with large effusions, loculated effusions, and moderate-sized effusions who fail to improve or have worsening symptoms.

- On the basis of class C evidence and consensus, small-bore chest tubes should be used even when chemical fibrinolytic therapy is planned.

- On the basis of class A evidence and consensus, even though prospective trials have shown equivalent efficacy of video-assisted thoracoscopic surgery and chest tube insertion with fibrinolytic therapy, chest tube with chemical fibrinolysis should be first-line therapy when resources allow due to decreased resource utilization.

- On the basis of class B evidence, definitive management with chest tube placement with fibrinolysis should be initiated when empyema is diagnosed.

- On the basis of class C evidence, primary surgical intervention should be reserved for pediatric patients with recurrent primary spontaneous pneumothoraces and those with persistent air leaks.

Additional Resources for Pediatricians

AAP Textbook of Pediatric Care, 2nd Edition
- Chapter 368: Pneumothorax and Pneumomediastinum - https://pediatriccare.solutions.aap.org/chapter.aspx?sectionId=137951738&bookId=1626

Point-of-Care Quick Reference
- Pneumothorax and Pneumomediastinum - https://pediatriccare.solutions.aap.org/content.aspx?gbosid=165601

PIR Quiz

1. A 2-year-old girl is admitted to the hospital with right middle lobe pneumonia and hypoxia. She has an unremarkable past medical history and is up-to-date on her immunizations. The patient is started on oxygen and intravenous antibiotics, with some improvement in her fever and oxygen need. On hospital day 7, she starts having recurrence of her temperature spikes, increased work of breathing, and worsening hypoxia. Physical examination is significant for an ill-appearing child in moderate respiratory distress. Lung examination shows diffuse crackles and distant breath sounds on the right compared to the left. Blood culture obtained on admission (prior to antibiotics) is negative. Which of the following is the best next step in management of this patient?

   A. CBC with differential count.
   B. Chest ultrasonography.
   C. C-reactive protein measurement.
   D. Nasopharyngeal wash for viruses.
   E. Repeat blood culture.

2. Bedside ultrasonography shows a multiloculated hyperechoic pleural effusion of moderate size on the right, with septation and pleural thickening consistent with empyema. The patient looks clinically worse despite broadening the spectrum of antibiotic coverage in the past 24 hours. Which of the following is the most appropriate next step in management for this patient?

   A. Addition of antifungal coverage to the antimicrobial regimen.
   B. Chest tube with fibrinolytic therapy.
   C. Computed tomography scan of the chest.
   D. Needle aspiration of fluid sample for Gram-stain and culture.
   E. Watchful waiting.

3. A female infant is born to a 28-year-old primigravida woman by spontaneous vaginal delivery. The mother received prenatal care. Pregnancy was complicated by suspected lung hypoplasia on prenatal ultrasonography due to an echogenic fluid-filled space-occupying lesion on the right. Apgar scores are 7 and 8 at 1 and 5 minutes, respectively. At age 24 hours, the baby is transferred to the NICU due to worsening respiratory distress. Lung examination is significant for dullness to percussion and poor air entry over the right lung field. The remainder of the physical examination findings are unremarkable. Which of the following is the most likely diagnosis in this patient?

   A. Congenital chylothorax.
   B. Congestive heart failure.
   C. Empyema.
   D. Pneumatocele.
   E. Spontaneous pneumothorax.

4. The baby undergoes thoracentesis, with improvement in respiratory distress. A milky-appearing fluid is drained and sent to the laboratory. Concentrations of which of the following laboratory markers are expected to be elevated in the fluid drained from this patient?

   A. Bilirubin.
   B. Cholesterol.
   C. Complements.
   D. Neutrophils.
   E. Triglycerides.

5. A 17-year-old previously healthy young man presents to the clinic with the acute onset of right-sided chest pain associated with shortness of breath and cough after running. There is no history of fever or rhinorrhea. The patient is known to have exercise-induced asthma and is on albuterol metered-dose inhaler (MDI) as needed. The patient used his MDI before exercise and after feeling the chest pain, with no significant relief. On physical examination, he is in mild respiratory distress. Lung examination shows decreased breath sounds over the right lung field, with no wheezes. Pulse oximetry is 93% in room air. Chest radiograph shows a sliver of translucency on the right side consistent with spontaneous pneumothorax. Which of the following is the most appropriate next step in management of this patient?

    A. Admission and chest tube placement.
    B. Inspiratory spirometry and repeat chest radiograph in 1 week.
    C. Needle aspiration and repeat chest radiograph in 3 months.
    D. Observation and repeat chest radiograph in 2 to 4 weeks.
    E. Placement on nasal continuous positive airway pressure.

Pleural Effusions and Pneumothoraces

Katherine Cashen and Tara L. Petersen

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seizures in the early neonatal period. Intraventricular hemorrhage is generally more common in preterm infants. In contrast, subarachnoid hemorrhage is more common in term infants and may be secondary to birth trauma or nonaccidental trauma once the infant goes home. Focal seizures in neonates are often caused by stroke, with the distribution of the middle cerebral artery being most commonly affected. Other important causes of seizures to recognize early are homeostatic disturbances (hypoglycemia, hypocalcemia, and hyponatremia) and IEMs (aminoacidopathies and urea cycle defects). Finally, if findings from initial laboratory and neurologic evaluations are normal, there are some familial epilepsy syndromes that can present in the neonatal period. Initial evaluation for neonatal seizures should always include serum electrolytes and a complete blood cell count. In addition, if infection is suspected, blood, urine, and cerebrospinal fluid should be cultured. Electroencephalography as well as neuroimaging with ultrasound or magnetic resonance imaging should also be performed.

Cases of HIE with seizures from fetal asphyxiation (umbilical cord prolapse, placental abruption, traumatic delivery, or fetal heart decelerations) can affect other organ systems. Kidney injury may be seen with only a mild insult, resulting in the inability to concentrate urine, but in more severe cases, acute tubular necrosis with complete loss of function can be seen. Measurement of serum creatinine levels, serum electrolytes, and urine output can help diagnose the initial injury and monitor kidney recovery. Myocardium may also become ischemic, which may result in impaired function and heart failure in some patients. Functional echocardiography has been used at the bedside to measure cardiac impairment secondary to hypoxic injury in real time. Regarding the pulmonary system, the injury may be primary or secondary due to cardiac failure. With coexisting heart failure, pulmonary edema may develop secondary to poor right-sided heart function. Persistent pulmonary hypertension and acute respiratory distress syndrome can also develop secondary to hypoxic injury with no discernible myocardial injury. Finally, feeding intolerance can develop secondary to underperfusion of the gastrointestinal tract. This can progress to necrotizing enterocolitis if the hypoxic injury is severe. Ischemic liver injury can also result in poor hepatic function, and if the synthesis of clotting factors is disrupted, bleeding disorders such as disseminated intravascular coagulation may develop.

COMMENT: The problems of neonatal lethargy, seizures, and asphyxia can be subtle in the newborn period but present with an incredibly broad differential diagnosis. The vigilant observations of the NICU staff and the parents are critical for rapid diagnosis. Physical examination findings may be subtle, but examination of the infant's level of consciousness, breathing pattern, pupillary response, and tone may provide additional cues. Although I feel that those of us in developed countries are fortunate to have at our disposal all the laboratory and neuroimaging modalities needed to make the correct diagnosis, I marvel at practitioners in developing countries where these modalities may not be available. These providers often need to treat based on clinical suspicions, enhancing the importance of reliance on observation and physical examination skills.

– Janet Serwint, MD
Assistant Editor, *In Brief*

Correction

An error was found in the April 2017 review "Pleural Effusions and Pneumothoraces" (Cashen K, Petersen TL. Pediatrics in Review. 2017;38(4):170-181, DOI: 10.1542/pir.2016-0088). On page 179, under the heading "Treatment," the first sentence should read, "Treatment is supportive, and isolated spontaneous pneumomediastinum generally resolves with a low recurrence rate." The online version of the article has been corrected; for the print edition, a correction will be published in the next available issue. The journal regrets the error.

ANSWER KEY FOR JUNE 2017 PEDIATRICS IN REVIEW
Heart Rate and Rhythm Disorders: 1. A; 2. D; 3. A; 4. E; 5. E.
Group B Streptococcal Infections: 1. D; 2. D; 3. A; 4. D; 5. E.
Environmental Risks to Children: Prioritizing Health Messages in Pediatric Practice: 1. D; 2. D; 3. C; 4. C; 5. D.

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