Chylothorax and Other Pleural Effusions in Neonates

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Abstract

Pleural effusion is a general term for the accumulation of fluid in the pleural space. Chylothorax results from the accumulation of lymphatic fluid within the pleural space and may occur spontaneously, traumatic, iatrogenic, or as malignant infiltration. Whether congenital or acquired, chylothorax frequently resolves with nonoperative measures aimed at optimizing ventilation and maintenance of nutrition. Surgical options such as pleuroperitoneal...
shunting, thoracic duct ligation, pleurodesis, pleurectomy, and intrapleural fibrin glue can be chosen for severe and persistent cases.

Keywords
Congenital chylothorax · Acquired chylothorax · Pleural effusion · Hydrothorax · Hemothorax · Empyema

Introduction

Pleural effusions are the general designation for the accumulation of fluid in the pleural space. Although rare, chylothorax is a well-established clinical entity and the most common cause of pleural effusion in the fetus and neonates (Vain et al. 1980; Van Aerde et al. 1984; Curci and Debbins 1980), resulting from the leakage of chyle from the thoracic duct into the pleural cavity. It may occur spontaneously or may be a complication of a thoracic surgical procedure, non-iatrogenic trauma, or malignant infiltration (Beghetti et al. 2000). Whether congenital or acquired, chylothorax frequently resolves with nonoperative measures aimed at optimizing ventilation and maintenance of nutrition. For more than a decade, pharmacologic agents (e.g., somatostatin and its analogue octreotide) have successfully been added to the nonoperative therapeutic armamentarium (Roehr et al. 2006; Lim et al. 2005; Chan et al. 2006; Das and Shah 2010; Rosti et al. 2002, 2005; Caverly et al. 2010; Cheung et al. 2001). When nonoperative measures fail to effect spontaneous healing, operative management becomes imperative. For patients in whom resolution does not occur, persistent chylothorax can become a life-threatening disorder with profound respiratory, nutritional, and immunologic consequences. Although early diagnosis, aggressive initiation of nonoperative management options, and a number of alternative surgical procedures have significantly decreased the mortality rate from 50% before the 1950s (Schackelford and Fisher 1938; Lampson 1948) to more recent estimates of less than 10% (Beghetti et al. 2000; Chan et al. 2006), significant morbidity continues. This chapter provides a basic foundation for understanding the anatomy and embryology of the lymphatic system and subsequently presents an overview of the pathophysiology, clinical characteristic, diagnosis, and management of chylothorax and other less common pleural effusions in neonates and children.

Anatomy and Embryology of the Lymphatic System

Lymph is a fluid which originates in the interstitial spaces of the body and is collected in the cisterna chyli, located between the aorta and the vena cava in front of the first lumbar vertebral bodies. The lymph then reaches the thoracic duct that ascends in the posterior right mediastinum between the aorta and the azygos vein, then crosses to the left behind the aortic arch, and finally opens itself into the major circulation at the level of the left subclavian and jugular veins. In the thorax it receives lymph from the parietal pleura of both sides via several collecting trunks. Lymphatic branches from structures in the posterior mediastinum and from the left lung and its pleura join to form the left bronchomediastinal trunk; this trunk opens into the thoracic duct or directly into the great veins. There are also several potential lymphovenous communications that may function when the main duct is traumatized or blocked (Fig. 1).

The lymphatic system, a diffuse network of endothelial channels, appears during the sixth week of development. The growth of this system is a phenomenon of consecutive centrifugal budding from original lymph sacs. In the early 1900s, Sabin (1916) demonstrated that these sacs originate from the endothelium of the adjacent veins, establishing venous endothelium as the primordial structure of the lining of the lymphatic system. She further recognized that all lymphatic channels are developed as outgrowths of the venous endothelium in six original lymph spaces: two jugular lymph sacs, two iliac sacs, a single retroperitoneal
sac, and the cisterna chyli. These sacs invade the tissues by continuous growth and branching. The lymphatic system arises by confluence of peri-venous mesenchymal spaces to form larger spaces. These in turn join to form continuous vessels that eventually drain into the venous system.

Although the thoracic duct is usually a singular structure, its embryology underscores the potential for anatomic variations and congenital anomalies. It may develop in different anatomic patterns with several lymphaticovenous anastomoses. Variation in lymphatic pathways and the presence of accessory lymphatic channels can account for chyloous effusions resulting from surgical procedures that do not expose the main thoracic duct. Trauma to the duct in the posterior mediastinum can produce a unilateral or bilateral chylothorax. Increased intraductal tension leads to drainage of chyle into the thorax. A lesion to the thoracic duct below the level of the fifth lumbar vertebra will result in a right-sided chylothorax; a left-sided chylothorax occurs with lesions above this level.

**Pathophysiology of Chyle**

Chyle has three primary functions: (1) the transportation of lipids and lip-soluble vitamins absorbed from the small bowel via lymphatic capillaries, (2) the collection of excess fluid and extravasated proteins from the interstitial space, and (3) the return of lymphocytes to the systemic circulation (Zuluaga 2012).

At birth, chyle is clear and straw colored. Soon after milk feeding begins, chylomicrons (emulsified fat globules) render it milky white. Depending on the amount of milk ingested, the fat content of the fluid varies from 0.4 to 5.0 g/dl, with a triglyceride content of >110 mg/dl (Rocha 2007). Although the protein and electrolyte contents of chyle are similar to those in plasma, chyle
is rich in T-cell lymphocytes, with a lymphocyte count of 80–100%. The volume of chyle loss per day can exceed 1.7 times the patient’s blood volume, resulting in a serious state of depletion characterized by hyponatremia, hypoproteinemia, metabolic acidosis, and lymphocytopenia (Curci and Debbins 1980).

Etiology and Presentation of Chylothorax

Congenital Chylothorax

Congenital chylothorax is an accumulation of chyle within the pleural space, and may be detected prenatally or within the neonatal period. It is estimated to occur in 1 in 10,000 live births and is the most common cause of pleural effusion in the newborn (Bellini 2013; Attar and Donn. 2017). Males are affected twice as frequently as females, and 60% of cases involve the right side of the chest (Yancy and Spock 1967). The occurrence of chylothorax in the absence of other demonstrable disease suggests the existence of congenital malformations of the lymphatic system. Congenital atresia of the thoracic duct or congenital fistulae due to failure of peripheral lymphatic channels to communicate with the major lymphatic network have moreover been assumed on the basis of diffuse chyle leakages seen during surgery (Van Aerde et al. 1984).

Congenital defects of the lymphatic system that may become evident with chylothorax are well documented in the literature, presenting clinically as generalized lymphangiomatosis (Yeager et al. 2008; Chen et al. 2013; Thomas et al. 1990; Dutheil et al. 1998) or congenital pulmonary lymphangiectasis (Moerman et al. 1993; Stevenson et al. 2006; Lee et al. 2002; Bellini et al. 2004). Congenital chylothorax is also associated with hydrops fetalis (Deurloo et al. 2007; Mussat et al. 1995; Aguirre et al. 1995; Ahmad et al. 1996; Laberge et al. 1991) and various syndromes, such as trisomy 21 (Yoss and Lipsitz 1977; Hamada et al. 1992; Foote and Vickers 1986), Turner syndrome, and Noonan syndrome (Fisher et al. 1982; Goens et al. 1992; Van Aerde et al. 1984). The occurrence of chylothorax in combination with other uncommon disorders, such as autosomal recessive lymphatic anomalies, mediastinal neuroblastoma in neonates, and neonatal thyrotoxicosis, also has been documented (Williams and Josephson 1997; Easa et al. 1991; Ibrahim et al. 1999). A genetic abnormality in the ITGA9 allele may be associated with more severe fetal chylothorax and hydrops (Yeang et al. 2012).

Acquired Chylothorax

Acquired chylothorax occurs due to trauma to lymphatic vessels and can occur after any thoracic procedure. Several studies have reported prevalence of postoperative chylothorax ranging from 2.5–4.7% (Beghetti et al. 2000; Chan et al. 2005; Be et al. 2004). Recently, Costa and Saxena (Costa and Saxena et al. 2018) performed a systematic review of postoperative chylothorax in neonates found that the type of surgery that resulted in postoperative chylothorax in 107 neonates included congenital diaphragmatic hernia repair in 71%, correction of cardiac malformations in 23.4%, esophageal atresia repair in 4.6% and pulmonary sequestration in 1%. Acquired chylothorax also manifests as a complication of both subclavian and internal jugular venous cannulation and/or obstruction, superior vena caval obstruction secondary to central venous catheters, or elevated central venous pressures (Adiotomre et al. 1994; Dhande et al. 1983; Ruggiero and Caruso 1985; Seguin 1992; Kramer et al. 1981; Blalock et al. 1936; Liote et al. 1990), chest tube insertion (Kumar and Belik 1984), and traumatic delivery (Wilson-Storey and MacKinlay 1987). Additionally, it may be caused by a blunt blow to abdomen associated with child abuse. Chylothorax/chylopericardium is a rare complication, occurring primarily following surgery for congenital heart diseases (Nguyen et al. 1995) or extensive mediastinal/pulmonary lymphatic malformations.
Clinical Features of Chylothorax

Presenting Symptoms

Tachypnea, dyspnea, retraction of chest, and cyanosis mark the onset of chylothorax, with dullness and diminution of breath sounds on the affected side and displacement of the heart and mediastinum to the opposite side (Lopez-Gutierrez and Tovar 2014). In cases of congenital chylothorax, symptoms of respiratory distress may be noted shortly after birth or at any time up to 2 weeks of life. In contrast, the interval between surgery and the occurrence of acquired chylothorax can vary from 1 to 25 days. The time is shortest when there is a direct injury to the duct (5–7 days) and longest when there is high pressure or thrombosis of the vena cava (10–14 days). Chyle may accumulate in the mediastinum for several days before extravasating into the pleural space.

Consequence of Continuous Chylous Flow

The loss of large quantities of chyle over a period of time produces nutritional failure, sepsis, metabolic acidosis, and renal failure. Considerable loss of protein and large numbers of lymphocytes may result in immunodeficiencies, including hypogammaglobulinemia and abnormal cell-mediated immune responses.

Confirming the Diagnosis

X-rays of the chest typically show opacification of one or both hemithoraces, with compression of lung and displacement of mediastinal structures in unilateral chylothorax (Fig. 2). X-ray diagnosis in premature infants may, however, be difficult. Most of these infants already have significant pulmonary disease, and chest X-rays may appear to have areas of increasing consolidation rather than the more typical layering of pleural fluid seen in older children. Sonography is a reliable method of detecting chylothorax in these cases, and its use in obstetric practice as the primary method of imaging the fetal chest has led to the increasing frequency with which fetal chylothorax is being diagnosed (see section below on “Fetal Chylothorax (Hydrothorax)”). Computed tomography (CT) or magnetic resonance imaging (MRI) can also be helpful, particularly for identifying loculated pulmonary parenchymal disease in complex patients.

Diagnosis is confirmed after analysis of the pleural fluid drained by thoracentesis or chest tube placement. Initially, this fluid is serous; it turns chylous only after milk feedings have begun. Chyle is characterized by elevated total protein and albumin levels, a specific gravity of >1.012, the presence of white blood cells with a predominance of lymphocytes (80–100%) and elevated triglycerides, cholesterol, and total fat levels if the infant is milk fed (Brodman 1975). In the unfed neonate, the fat content of the chylothorax may be quite low, and the fluid does not have the characteristic milky appearance. The protein content is somewhat less than that of serum and the electrolytes approximate those of serum.

Fig. 2 Chest radiograph in a term neonate demonstrating bilateral chylothorax
Management of Chylothorax

Nonoperative Management

The goal of the treatment is to decrease the chylothorax volume to keep the pleural space clear and to allow time for injured lymphatic vessels to heal or develop enough collateral connections (Tutor 2014; Attar and Donn 2017). The treatment is typically stepwise, starting with conservative therapy, such as MCT diet, TPN, chest tube drainage or repeated aspirations, administration of octreotide, somato-statin, and/or steroids (Matsuo et al. 2013; Costa and Saxena 2018). An initial trial of nonoperative management relying on adequate drainage of chyle, coupled with nutritional supplementation via MCT-enriched diets and/or TPN, should be given in order to optimize the chance of recovery without surgery. Using this regimen, the majority of cases of congenital chylothorax and up to 77% of cases with traumatic chylothorax (postoperative) resolve spontaneously (Chan et al. 2006; Robinson 1985; Rubin et al. 1977).

Some investigators have observed no difference in MCT or TPN in regard to duration or amount of drainage (Allen et al. 1991; Nguyen et al. 1995). Others have found that for patients with superior vena caval obstruction and congenital lymphatic malformation, MCT alone is not as effective; they thus recommend the rapid administration of TPN (Le Coultre et al. 1991).

Numerous case studies suggest that somatostatin (SST) and octreotide (OCT) exert a positive effect on persistent congenital and postoperative chylothorax (Roehr et al. 2006; Chan et al. 2006; Das and Shah 2010; Rosti et al. 2002; Cheung et al. 2001; Pessotti et al. 2011; Al-Hussaini and Butzner 2012). SST is a polypeptide with mainly inhibitory actions on the release of various hormones (e.g., growth hormone and insulin) and lymph fluid excretion (Lamberts et al. 1996; Tauber et al. 1994). OCT is a synthetic SST analog with antisecretory properties similar to those of SST. It is thought that octreotide may act directly on somatostatin receptors in the splanchnic circulation to reduce lymph fluid production (Cheung et al. 2001; Goyal et al. 2003). Thoracic duct lymphatic flow depends on splanchnic vascular tone as well as gastric motility (Nakabayashi et al. 1981). OCT decreases the volume of gastric, pancreatic, and biliary secretions, thus reducing the volume and protein content of fluid within the thoracic duct. It offers a number of advantages over SST, including a longer half-life in the circulation (1–2 h vs. 2–3 min), a higher potency, and good bioavailability after subcutaneous administration (Al-Hussaini and Butzner 2012). In view of these advantages, OCT has largely supplanted SST as an adjunctive pharmacologic agent for chylothorax. Moreover, published data indicate that it shortens the duration of TPN and hospital stay and avoids the need for surgical intervention (Al-Hussaini and Butzner 2012; Rosti et al. 2002; Cheung et al. 2001; Goyal et al. 2003). OCT is well tolerated at dosing ranges of 40–100 μg/kg per day for 3–6 weeks, and the earlier use of higher doses may be preferable to gradual upward tapering of the dose (Helin et al. 2006). A recent review reported that octreotide is a relatively effective and safe treatment option in neonates with chylothorax especially for the congenital forms. Potential adverse effects include cholelithiasis, liver impairment, renal impairment, transient glucose intolerance (Rimensberger et al. 1998; Tibballs et al. 2004), hypothyroidism (Maayan-Metzger et al. 2005), and necrotizing enterocolitis (Lam et al. 2001). It is thus prudent for patients to undergo routine monitoring of liver function, blood glucose, and thyroid parameters during the course of treatment.

Costa and Saxena (Costa and Saxena 2018) reported results of treatment in 107 cases of postoperative chylothorax and found that MCT alone was effective in 27 (25.3%) cases and TPN, either as first line or second line treatment modality, resulted in the resolution of chylothorax in 42 (39.3%) cases respectively.

Operative Management

The percentage of neonates requiring surgery and the timing of surgical intervention vary widely among reported series and are dependent upon the patient population being studied, etiology, and the
clinical status of individual patients. Operative management has, however, been the mainstay of treatment for a number of clinical conditions that have a high failure rate with standard nonoperative management; these include postsurgical cases in which there is injury to the thoracic duct and massive lymph leakage, caval obstruction, or elevated central venous pressures (Nguyen et al. 1995; Le Coultre et al. 1991; Higgins and Mulder 1971; Puntis et al. 1987; Nath et al. 2009). Congenital chylothorax associated with superior vena caval thrombosis in the premature neonate is also particularly refractory to standard nonoperative therapy (Dhande et al. 1983). Since failure is associated with a high mortality rate, some investigators maintain that surgical intervention should be considered early in the management of such cases (Le Coultre et al. 1991; Nath et al. 2009; Rheuban et al. 1992; Engum et al. 1999).

Several surgical options exist, and they are often used in combination. These options include pleuroperitoneal shunting, thoracic duct ligation (open thoracotomy or thoracoscopy), chemical and mechanical pleurodesis with various agents, pleurectomy, and intrapleural fibrin glue.

**Pleuroperitoneal Shunts**

Pleuroperitoneal shunts, first used by Azizkhan et al. in 1983 (Azizkhan et al. 1983) to treat five ventilator-dependent infants with persistent chylothorax, remain a viable treatment option (Rheuban et al. 1992; Engum et al. 1999; Murphy et al. 1989).

The procedure avoids the risks associated with a more complicated, open surgical procedure in high-risk infants and is considered safe, highly effective, and easy to perform. Nonetheless, it is associated with several drawbacks. These include having to manually press a pumping chamber several times a day and having the valve and pumping chamber become dysfunctional after several weeks due to an accumulation of fibrin and protein in the valve mechanism. It thus is ideal for patients who require a relatively short or stabilizing procedure.

A postoperative chest X-ray is obtained to make certain that the pleural catheter is properly placed. During the immediate postoperative period, the pumping chamber is compressed 50–100 times per hour in order to completely clear the hemithorax of chyle. As the infant’s clinical status improves, a gradual decrease in the frequency of shunt compression is begun. Noninvasive transcutaneous oxygen saturation monitoring, arterial blood gas determination, and serial chest X-rays are used to assess shunt efficacy (Fig. 3). Manual compression of the shunt valve is discontinued when it is clear that chylothorax is resolved. This often occurs within 2–3 weeks. However, some infants require a more prolonged period of manual compression, lasting 6–8 weeks.

A high-flow externally located valve reservoir designed to avoid some of the discomfort and positioning problems associated with a subcutaneous valve reservoir is available. Once the chylous effusion clears, parents are taught the technique of pumping the chamber, and the patient is discharged from the hospital. Over the ensuing 2–3 months, the frequency of pumping is further reduced. When the chylous effusion completely resolves, the catheter is removed. This approach offers less interruption of the sleep cycle and may facilitate a shorter hospital stay. Although this approach carries an increased risk of infection, this risk has not been documented in clinical studies.

Although there has been concern that elevated right atrial pressures transmitted to the venous and
lymphatic bed of the peritoneal space may impair absorption of shunted pleural fluid, the successful use of pleuroperitoneal shunting with this patient population, even in the face of moderate elevations in right atrial pressure, has been reported (Rheuban et al. 1992). Failure to resolve chylous effusions is associated with occlusion of the shunt catheter or significant intra-abdominal chylous ascites. When the latter occurs, a pleuroperitoneal shunt and a peritoneovenous shunt combination have been successfully used in some cases.

The same principle has been applied in the management of patients with chylopericardium. Case reports indicate that pericardial–peritoneal shunting provides an easy and effective alternative to prolonged pericardial draining, thoracotomy, or thoracic duct ligation in patients with chylopericardium of various etiologies (Chan et al. 1990).

Other Surgical Alternatives
Thoracic duct ligation has historically been the most common surgical therapy and has been successfully utilized in resolving chylous leaks in many patients. However, the risk that a compromised, frail, or premature neonate must endure a major surgical procedure is not insignificant. Despite this drawback, thoracic duct ligation is currently an option when pleuroperitoneal shunting fails to resolve the chylous leak or when chylothorax is due to penetrating trauma (Zuluaga 2012; Nath et al. 2009; Matsuo et al. 2013). Giving a small bolus of “cream” through the nasogastric tube several hours before operations may help to identify the sites of leakage of the milky white fluid. Major leaks from the thoracic ducts can be closed by direct suturing or by ligating the duct above and below the leak. Pleurodesis and parietal pleurectomy have been used when there is generalized seeping of chyle from parietal pleura; however, these are extensive surgical procedures that may increase the possibility of pulmonary lymphedema, fibrosis, and further pulmonary compromise. Fibrin glue applied to the leakage site after patent ductus arteriosus ligation has been reported to successfully manage chylothorax in both a 3.5-month-old infant (Stenzl et al. 1983) and a premature infant weighing 600 g (Nguyen and Tchervenkov 1994). The choice of either an open or thoracoscopic approach to thoracic duct ligation depends on the experience of the surgeon.

Video-assisted thoracoscopic procedures (VATS) are being used with increasing frequency. These procedures offer the advantage of access to the entire hemithorax, with excellent visualization of the mediastinal structures (Beghetti et al. 2000). This approach allows application of clips to the thoracic duct at the hiatus or to the thoracic duct injuries or pleural defects. It also facilitates mechanical or chemical pleurodesis and application of fibrin glue. Despite its advantages, its use is limited by an infant’s size and pulmonary status. Also, it may be difficult to correctly visualize leaks in the presence of a massive chylous effusion.

General Management Principles
The general principles of management for chylothorax include the following:

- Thoracentesis is performed to provide immediate relief of respiratory failure and to confirm the diagnosis through chemical analysis of pleural fluid specimen.
- Supportive ventilation is instituted as required.
- Thoracostomy tube drainage is carried out if pleural fluid reaccumulates after one or two thoracenteses. (Repeating this procedure carries a risk of producing pneumothorax and introducing infection; chest tube drainage keeps the lungs fully expanded, which is necessary for sealing chyle leakage.)
- Nutritional losses are replaced through a high protein diet, rich in MCTs that are absorbed directly into the portal venous system.
- Parenteral feeding is instituted. (When superior vena caval thrombosis is present with chylothorax, TPN may need to be delivered via a peripheral vein.)
- The albumin, gamma globulin, and fibrinogen that are contained in chyle, as well as fat-soluble vitamins, are adequately replaced.
- Full expansion of the lungs is maintained by continuous chest tube drainage of chyle. (These tubes may become obstructed and require replacement as necessary.)
Prophylactic antibiotics are given when chest tubes are in place, since many of these infants have an acquired immune deficiency caused by lymphocytopenia. Some infants may also need salt restriction, diuretics, and digoxin.

- Octreotide may be used for cases recalcitrant to other medical therapies or as an adjunct to standard medical therapy.
- Surgical intervention is warranted when medical therapies fail to significantly diminish chylous drainage for more than 14 days or if there is obvious deterioration in the patient prior to that period of time (Fig. 4).

**Fetal Chylothorax (Hydrothorax)**

As mentioned earlier in this chapter, primary fetal chylothorax (also known as hydrothorax) is the most common fetal pleural effusion, occurring in
10,000–15,000 pregnancies (Nygaard et al. 2007). Owing to the growth of routine prenatal ultrasonography over the past several decades, it has been diagnosed with increasing frequency from as early as 16 weeks’ gestation to an average of 30 weeks’ gestation (Nygaard et al. 2007). In contrast to chylothorax diagnosed at birth, fetal chylothorax is associated with an overall mortality rate as high as 50% (Longaker et al. 1989). Nevertheless, its clinical course is highly variable, ranging from complete spontaneous resolution (10–20%) to progression into hydrops fetalis and/or lung hypoplasia and perinatal death (Weber and Philipson 1992; Aubard et al. 1998; Devine and Malone 2000). Survival depends on multiple factors, including the presence of associated anomalies and the gestational age at which diagnosis is first made. In fetuses with isolated pleural effusions and low gestational age, spontaneous resolution rates are reportedly as high as 50% (Nygaard et al. 2007; Aubard et al. 1998; Klam et al. 2005). Prognosis is poor when effusion is associated with chromosomal aberrations, multiple malformations, and fetal hydrops (Yinon et al. 2008).

The management of fetal chylothorax has been controversial, and the optimal treatment approach remains unclear. Dissension is primarily focused on the following issues: (Vain et al. 1980) whether treatment should be attempted in utero or the infant should be delivered and treated after birth, (Van Aerde et al. 1984) under what clinical circumstances antenatal intervention should be carried out, and (Curci and Debbins 1980) whether pleurocentesis or pleuroamniotic shunting should be used for thoracic decompression.

Despite the dissension, there is a general consensus that fetal chylothorax with rapid progression warrants intervention. Although reports of successful management with pleurocentesis or pleuroamniotic shunting have appeared in the literature (Longaker et al. 1989; Klam et al. 2005; Yinon et al. 2008; Rodeck et al. 1988; Roberts et al. 1986; Blott et al. 1988; Mandelbrot and Dommergues 1992), pleurocentesis has been associated with rapid reaccumulation of the effusion and is therefore unlikely to be advantageous (Weber and Philipson 1992; Aubard et al. 1998; Klam et al. 2005; Yinon et al. 2008). Thoracoamniotic shunting has been effective in selected patients with progressive pleural effusions, especially when there is evidence of intrathoracic hypertension (Yamamoto et al. 2007). Most commonly, a Harrison double-pigtail catheter is used. Both techniques are associated with serious pregnancy risks, including preterm labor, prerupture of the membranes, intrauterine infection, bleeding, and maternal or fetal organ trauma. Additionally, technical failures such as shunt displacement and blockage are common (Longaker et al. 1989; Weber and Philipson 1992; Klam et al. 2005; Yinon et al. 2008; Picone et al. 2004). Several case reports emanating from Europe and Japan have documented the successful use of intrapleural injection of OK-432 for the treatment of severe fetal chylothorax associated with pronounced hydrops (Jorgensen et al. 2003; Tanemura et al. 2001; Okawa et al. 2001).

From a broad perspective, antenatal diagnosis is significant not only in that it can often identify the need for potentially helpful intrauterine intervention and facilitate preparation of appropriate postnatal outcome but also in that it is a reliable predictor of fetal outcome. As such, it facilitates the communication of a more accurate prognosis to parents. Since most large pleural effusions discovered in utero lead to hydrops and pulmonary hypoplasia, such effusions have a high mortality rate. Retrospective research indicates that the absence of hydrops predicts 100% survival and that fetuses that initially present without hydrops and subsequently develop it have only a 38% survival (Laberge et al. 1991).

Other Pleural Effusions

Hemothorax

Although massive hemothorax is uncommon, accidental injury to the intercostal artery during thoracentesis or closed intercostal drainage can result in intrapleural bleeding (Haller 1986). Hemothorax has been reported as a complication of a variety of congenital malformations (e.g., sequestration, patent ductus, and vascular anomalies) and of subclavian vein catheters (Tetsuka et al. 2009; Webber and Rescorla 2012; Feliciano et al. 1979; Casado-Flores et al. 2001; Lee et al. 2010). It
is also an occasional manifestation of intrathoracic neoplasms and blood dyscrasias, as well as bleeding diatheses. Additionally, it can occur spontaneously in neonates, sometimes in association with a pneumothorax. Symptoms reveal respiratory embarrassment similar to that seen in tension pneumothorax. However, the percussion note is dull, and chest X-rays show opacification. More importantly, the infant may show signs of hypovolemic shock. Blood transfusion and urgent tube thoracostomy generally provide adequate control of bleeding. To avoid sudden circulatory collapse, transfusion should precede intercostal drainage. If massive blood loss continues, urgent thoracotomy and identification and securing of the bleeding site are required (Webber and Rescorla 2012).

**Empyema**

Empyema (purulent effusion) is a relatively uncommon condition in children thought to evolve from a parapneumonic fluid collection subsequently infected by an adjacent lung infection. Although many organisms cause pediatric empyema, the most common is *Streptococcus pneumoniae* (Krenke et al. 2016); other frequently identified organisms include *Staphylococcus aureus*, *Pneumococcus*, and *Haemophilus influenzae*. This condition can also be incurred through the introduction of skin bacteria during thoracentesis or thoracotomy and may be accompanied by anaerobic infection. Although empyema in children is less serious than empyema in adults, it nevertheless poses a considerable burden on hospitals and families and complicates the course of 2–8% of children hospitalized for pneumonia in the United States (Gates et al. 2004; Tan et al. 2002).

Symptoms include indications of respiratory distress in addition to abdominal distension, lethargy, and, at times, a septicemic state. The size of effusion typically correlates with the presence of symptoms (Bradley et al. 2011). In symptomatic patients, chest radiographs are helpful in identifying the effusion and pneumonic process. In children with suspected disease on radiographs, ultrasonography is the initial and primary imaging modality used to evaluate the pleural space. It is generally agreed that it is superior to CT in identifying pleural debris or loculations and that CT should be reserved for more complicated cases (Islam et al. 2012).

The presence of loculations typically requires intervention in addition to antibiotics (Islam et al. 2012; Calder and Owens 2009). Prior to beginning a course of antibiotic therapy, a fluid specimen taken during thoracentesis is sent for a Gram stain and aerobic and anaerobic culture. Although most cases resolve with effective intercostal tube drainage and a prolonged period of systemic administration of antibiotics, anaerobic infection tends to be multilocular and may thus require debridement. Based on a comprehensive review of evidence to date, the American Pediatric Surgical Association Outcomes and Clinical Trials Committee recommends the following management strategy: (Islam et al. 2012) (1) chemical debridement with a fibrinolytic agent (e.g., deoxyribonuclease) should be a first line of therapy; (2) if a child is persistently ill after the chest tube drainage is diminished and imaging demonstrates significant pleural space disease, VATS should be considered; (3) parenchymal abscess and lung necrosis should be managed nonoperatively; and (4) antibiotic therapy should continue for at least 10 days after resolution of fever.

**Cross-References**

- Clinical Genetics
- Embryology of Congenital Malformations
- Fetal Counseling for Congenital Malformations
- Fetal Surgery
- Lymphatic Malformations
- Principles of Minimal Invasive Surgery

**Acknowledgment** The author wishes to acknowledge the assistance of Aliza P. Cohen, MA, in the writing of this chapter.

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