Chylothorax in Infants and Children

abstract

Chylothorax, the accumulation of chyle in the pleural space, is a relatively rare cause of pleural effusion in children. It can cause significant respiratory morbidity, as well as lead to malnutrition and immunodeficiency. Thus, a chylothorax requires timely diagnosis and treatment. This review will first discuss the anatomy and physiology of the lymphatic system and discuss various causes that can lead to development of a chylothorax in infants and children. Then, methods of diagnosis and treatment will be reviewed. Finally, complications of chylothorax will be reviewed. Pediatrics 2014;133:722–733

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KEY WORDS
chylothorax, infants, children

www.pediatrics.org/cgi/doi/10.1542/peds.2013-2072
doi:10.1542/peds.2013-2072

Accepted for publication Oct 2, 2013

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PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).
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FINANCIAL DISCLOSURE: The author has indicated he has no financial relationships relevant to this article to disclose.

FUNDING: No external funding.

POTENTIAL CONFLICT OF INTEREST: The author has indicated he has no potential conflicts of interest to disclose.
Chylothorax, the accumulation of chyle in the pleural space, occurs after disruption of the thoracic duct. The incidence of chylothorax in children is unknown. Although a rare cause of pleural effusion in most children, it is the most common form of pleural effusion in neonates. It can result in significant respiratory morbidity and immunodeficiency in infants and children if not diagnosed and treated.

Here, the anatomy and physiology of the lymphatic system will be reviewed, as well as some of the various causes of chylothorax in infants and children. Current methods of diagnosis and management, and some associated complications, will be reviewed.

ANATOMY AND PHYSIOLOGY OF THE LYMPHATIC SYSTEM

The human lymphatic system has 3 main functions: (1) transport lipids and lipid-soluble vitamins to the systemic circulation; (2) collect and return excess fluid and extravasated proteins from the interstitial spaces to the circulation; and (3) return lymphocytes to the circulation. From the lacteals, the chyle is transported to the cisterna chyli, which overlies the anterior surface of the second lumbar vertebra. The duct passes through the esophageal hiatus of the diaphragm into the thoracic cavity, ascends extrapleurally in the posterior mediastinum to the right of the vertebral column, and lies between the azygous vein and the descending aorta, in close proximity to the esophagus and the pericardium. At the fourth to sixth thoracic vertebrae, the duct crosses to the left of the vertebral column and continues cephalic to enter the superior mediastinum between the aortic arch and the subclavian artery and the left side of the esophagus. Once past the thoracic inlet, it arches 3 to 5 cm above the clavicle and passes anterior to the subclavian artery, vertebral artery, and thyrocervical trunk to terminate near the left jugular and subclavian veins. Many anatomic variations can exist in all portions of the thoracic duct.

Chyle is a noninflammatory, alkaline, and bacteriostatic fluid composed mainly of fat, cholesterol, electrolytes, proteins, glucose, and abundant lymphocytes (Table 1). The protein content of chyle is usually >3 g/L, and the electrolyte composition is similar to that of serum. The lymphocyte count ranges from 400 to 6800/mm³, with most being T lymphocytes. Chyle appears as a milky, opalescent fluid that separates into 3 layers upon standing: a creamy uppermost layer containing chylomicros, a milky intermediate layer, and a dependent layer containing cellular elements, most of which are small lymphocytes. Chyle may be slightly turbid if an individual has not eaten recently because its lipid content will be reduced. The thoracic duct transports between 1.5 and 2.5 L of chyle daily (maximum 4 L/day in a healthy adult). Flow varies depending on the diet, medications, intestinal function, and physical activity, and it can increase by two- to 10-fold for 2 to 3 hours after ingestion of fat, and by 20% after drinking water.

CAUSES OF CHYLOTHORAX

There are several causes of chylothorax in infants and children (Table 2), which vary according to the age of the child or mechanism of injury to the thoracic duct. The most common form of pleural effusion in neonates is congenital chylothorax. This is caused by several congenital malformations of the thoracic duct, including the most common cause, lymphatic malformations. There are several causes of chylothorax in children (Table 2), which vary according to the age of the child or mechanism of injury to the thoracic duct. The most common form of pleural effusion in neonates is congenital chylothorax. This is caused by several congenital malformations of the thoracic duct, including the most common cause, lymphatic malformations.

TABLE 1 Components of Chyle

<table>
<thead>
<tr>
<th>Component</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>7.4–7.8</td>
</tr>
<tr>
<td>Absolute cell count</td>
<td>&gt;1000 cells/L</td>
</tr>
<tr>
<td>Lymphocytes</td>
<td>400–4800/mm³</td>
</tr>
<tr>
<td>Erythrocytes</td>
<td>50–600/mm³</td>
</tr>
<tr>
<td>Calories</td>
<td>200 kcal/L</td>
</tr>
<tr>
<td>Total fat</td>
<td>0.4–0.8 g/dL</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>65–220 mg/dL</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>&gt;110 mg/dL</td>
</tr>
<tr>
<td>Chylomicrons</td>
<td>(&gt;1.1 mmol/L)</td>
</tr>
<tr>
<td>Total protein</td>
<td>2–6 g/dL</td>
</tr>
<tr>
<td>Albumin</td>
<td>1.2–4.1 g/dL</td>
</tr>
<tr>
<td>Globulin</td>
<td>1.1–3.1 g/dL</td>
</tr>
<tr>
<td>Glucose</td>
<td>2.7–11 mmol/L</td>
</tr>
<tr>
<td>Sodium</td>
<td>104–108 mmol/L</td>
</tr>
<tr>
<td>Potassium</td>
<td>3.8–5.0 mmol/L</td>
</tr>
<tr>
<td>Chloide</td>
<td>85–130 mmol/L</td>
</tr>
<tr>
<td>Calcium</td>
<td>3.4–6.0 mmol/L</td>
</tr>
<tr>
<td>Phosphate</td>
<td>0.8–4.2 mmol/L</td>
</tr>
</tbody>
</table>

TABLE 2 Causes of Chylothorax in Children

<table>
<thead>
<tr>
<th>Cause</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. Congenital chylothorax</td>
</tr>
<tr>
<td>A. Congenital lymphatic malformations</td>
</tr>
<tr>
<td>1. Lymphangiomatosis</td>
</tr>
<tr>
<td>2. Lymphangiectasia</td>
</tr>
<tr>
<td>3. Atresia of thoracic duct.</td>
</tr>
<tr>
<td>B. Associated with syndromes</td>
</tr>
<tr>
<td>1. Down syndrome</td>
</tr>
<tr>
<td>2. Noonan syndrome</td>
</tr>
<tr>
<td>3. Turner syndrome</td>
</tr>
<tr>
<td>4. Gorham-Stout syndrome</td>
</tr>
<tr>
<td>5. X-linked myotubular myopathy</td>
</tr>
<tr>
<td>6. Missense mutation in integrin αvβ3</td>
</tr>
<tr>
<td>7. Hydrops fetalis</td>
</tr>
<tr>
<td>8. Yellow nail syndrome</td>
</tr>
<tr>
<td>II. Traumatic</td>
</tr>
<tr>
<td>A. Associated with surgeries for</td>
</tr>
<tr>
<td>1. Excision of lymph nodes</td>
</tr>
<tr>
<td>2. Congenital heart disease</td>
</tr>
<tr>
<td>3. Scoliosis</td>
</tr>
<tr>
<td>4. Vascular ring</td>
</tr>
<tr>
<td>5. Diaphragmatic hernia</td>
</tr>
<tr>
<td>B. Invasive diagnostic and therapeutic procedures</td>
</tr>
<tr>
<td>1. Subclavian vein catheterization</td>
</tr>
<tr>
<td>C. Other trauma</td>
</tr>
<tr>
<td>1. Blunt force or penetrating trauma to the chest</td>
</tr>
<tr>
<td>2. Hyperexpansion or stretching of chest wall or thoracic spine</td>
</tr>
<tr>
<td>3. Coughing</td>
</tr>
<tr>
<td>4. Vomiting</td>
</tr>
<tr>
<td>5. Child birth</td>
</tr>
<tr>
<td>6. Child abuse</td>
</tr>
<tr>
<td>III. High central venous pressure</td>
</tr>
<tr>
<td>A. Thrombosis of superior vena cava</td>
</tr>
<tr>
<td>B. Post-Fontan surgery</td>
</tr>
<tr>
<td>IV. Associated with tumors</td>
</tr>
<tr>
<td>A. Neurogenic</td>
</tr>
<tr>
<td>B. Lymphoma</td>
</tr>
<tr>
<td>C. Teratoma</td>
</tr>
<tr>
<td>D. Wilms</td>
</tr>
<tr>
<td>E. D ovarian</td>
</tr>
<tr>
<td>F. Kaposi sarcoma</td>
</tr>
<tr>
<td>V. Miscellaneous</td>
</tr>
<tr>
<td>A. Granulomatous infections</td>
</tr>
<tr>
<td>1. Tuberculosis</td>
</tr>
<tr>
<td>2. Histoplasmosis</td>
</tr>
<tr>
<td>3. Sarcoïdosis</td>
</tr>
<tr>
<td>B. Other</td>
</tr>
<tr>
<td>1. Staphylococcal discitis</td>
</tr>
<tr>
<td>2. Henoch-Schönlein purpura</td>
</tr>
</tbody>
</table>
duct. It may result from congenital abnormalities of the lymphatics, which do not always present in the neonatal period.2

Pulmonary lymphangiomas and lymphangiectasia are the 2 major lymphatic abnormalities associated with chylothorax,2 but absence or atresia of the thoracic duct can also lead to this problem.10 Pulmonary lymphangiomatosis is a focal proliferation of well differentiated lymphatic tissues often associated with lymphatic abnormalities in other organs, whereas pulmonary lymphangiectasia is diffuse dilatation of the interlobular and subpleural lymphatics.3 Lymphangiomas usually present by 2 years of age, but they may not be recognized until adulthood. If they occur in the head, neck, or axial skeleton, they can extend into the mediastinum. About 1% of lymphangiomas are confined to the chest.2 Lymphangiectasia can be a primary condition that is often fatal in newborns, or it can be secondary to other conditions, such as congenital heart disease or pulmonary venous obstruction, where there is abnormal drainage or an increase in lymph production.2 Diagnosis of pulmonary lymphangiomatosis and lymphangiectasia can be made by lymphoscintigraphy,11 computerized tomography,12 or MRI.13 Lung biopsy is often necessary for confirmation.14-15 Lymphangiomas are treated with surgical excision or sclerotherapy.14 There are reports of the successful use of radiotherapy for cases in which chylothorax was refractory to surgical management.16-17

Chylothorax can be a manifestation of Down,18-21 Turner,18-20 and Noonan syndromes.18-20,22-24 Congenital and pulmonary lymphangiectasia occur in these syndromes.2 Other syndromes associated with chylothorax are X-linked myotubular myopathy,25 missense mutation in integrin αβ1,26,27 and Gorham-Stout syndrome.28-34 Members of the integrin family of adhesion receptors mediate both cell-cell and cell-matrix interactions and have been shown to play vital roles in embryonic development, wound healing, and other biologic processes. Gorham-Stout disease, characterized by proliferation of vascular structures within bones, leads to osteolytic lesions evident on radiography. It has no known inheritance pattern. Chylothorax is associated with the disease, possibly related to dysplasia of lymphatic vessels at the pleura. Children are more commonly affected than adults, and presenting symptoms may include cough, dyspnea, and pain. The presence of chylothorax is associated with worsened prognosis.35 Anecdotal reports suggest that interferon α2b may be trialed in the treatment of this disease.31,35 Chylothorax can occur in the presence of hydrops fetalis.36,37 It has been seen in a newborn infant with nonimmune hydrops fetalis and yellow nail syndrome.38 Trauma can cause chylothorax by rupture or laceration of the thoracic duct.2 It occurs as a postoperative complication after various surgeries involving structures in the neck and thorax.39-44 Other surgeries that can be complicated by chylothorax in children include those for treatment of scoliosis,45-48 vascular rings,49,50 and diaphragmatic hernia.51 In children, the reported incidence of chylothorax after cardiothoracic surgery is between 0.85% and 6.6%.39,52-54 Another traumatic cause of chylothorax is laceration of the thoracic duct during catheterization of the subclavian vein.55,56

Noniatrogenic trauma can lead to the development of chylothorax. These include blunt force or penetrating trauma to the chest,57-61 sudden hyperextension, or stretching of the chest wall or thoracic spine with fracture of a vertebra,2 severe coughing or vomiting,62 and the force of child birth.2,63 Child abuse, such as heavy blows to the back or stomach, can cause rupture of the thoracic duct, leading to the development of chylothorax.64-66 Chylothorax due to closed trauma is usually on the right side, with the site of rupture most commonly in the region of the ninth or 10th thoracic vertebra.67 Venous thrombus or obstruction in the superior vena cava or subclavian vein may lead to rupture of the thoracic duct.55,56,68 Chylothorax can complicate innominate vein69 or left subclavian vein thrombosis70 and the Fontan procedure.71-73

Chylothorax can be associated with various tumors and malignancies (neurogenic,74,75 lymphoma,76 teratoma,76 Wilms,76 ovarian,77 and Kaposi sarcoma78). Lymphoma is the most common tumor associated with chylothorax (60% to 70% of cases),2 and it may be the presenting symptom.7,79,80 The presence of a nontraumatic chylothorax is an indication for a diligent search for a lymphoma.1

Granulomatous infections such as tuberculosis,81-83 histoplasmosis,84 and sarcoidosis85 can be associated with the development of chylothorax attributable to lymphadenopathy obstructing the thoracic duct. Other etiologies include staphylococcal discitis86 and Henoch-Schönlein purpura.87

**CLINICAL MANIFESTATIONS OF CHYLOTHORAX**

The initial symptoms of chylothorax are usually related to accumulation of fluid in the pleural space.1,2 Patients can be asymptomatic; however, dyspnea, cough, and chest discomfort develop with time.2 Pleuritic chest pain and fever are rare.1 With traumatic chylothorax, a latent period of 2 to 10 days usually occurs between the trauma and the onset of the pleural effusion.67 Lymph collects extrapleurally in the mediastinum after the thoracic duct
disruption, forms a chyloma, and produces a posterior mediastinal mass. The mediastinal pleura ruptures, chyle gains access to the pleural space, and dyspnea is produced by the chyle compressing the lung. Rapid accumulation of a large volume of fluid can lead to adverse hemodynamic complications with significant cardiorespiratory difficulties, such as hypotension, cyanosis, and significant respiratory distress. In patients with non-traumatic chylothorax, symptom onset is gradual. Congenital chylothorax presenting antenatally can act as a space-occupying lesion and restrict normal development of the lungs. At birth, the infant develops respiratory distress; 50% of patients have symptoms within the first 24 hours, whereas 75% have symptoms by the end of the first week. On physical examination, there is bilateral or unilateral dullness to percussion, and poor air entry. Among patients with chronic chylothorax, muscle wasting, weight loss, and other signs of malnutrition can be present. The patients may be compromised immunologically because of lymphocyte depletion and hypogammaglobulinemia.

**DIAGNOSIS OF CHYLOTHORAX**

A chest radiograph can reveal pleural fluid and assess the size and location of the effusion. Use of lateral decubitus radiographs or ultrasound can determine whether there is free fluid in the pleural space or whether it is organized. Chyle obtained on thoracentesis is white, odorless, and milky in appearance. When this type of fluid is obtained, the differentiation is between empyema and pseudochylothorax with a chyliform pleural effusion. A pseudochylothorax is a long-standing (mean 5 years) pleural effusion that is turbid or milky, containing large amounts of cholesterol or lecithin-globulin complexes (chyliform).

It does not result from disruption of the thoracic duct. The visceral pleura in a pseudochylothorax is thickened and may be calcified, whereas with chylothorax there is acute onset and the pleural surfaces are normal. The milkeness of the fluid from an empyema is caused by suspended white blood cells. If the fluid is centrifuged, the supernatant will be clear. Chylous and chyliform pleural fluids remain opaque after centrifugation. If cholesterol crystals are responsible for the turbidity, they may be easily demonstrated by examination of the pleural fluid sediment. If the turbidity is because of high levels of cholesterol, it will clear with the addition of 1 to 2 mL ethyl ether. If it is due to chylomicrons or lecithin complexes, the fluid will not clear.

The best way to diagnose chylothorax is by measuring the triglyceride and cholesterol levels in the pleural fluid. If the triglyceride level is above 110 mg/dL and the ratio of the pleural fluid to serum cholesterol is <1.0, the diagnosis is established. In a pseudochylothorax, the ratio will exceed 1.0. If there is still doubt about whether the pleural effusion is a chylothorax or a pseudochylothorax, the fluid should be analyzed for chylomicrons by lipoprotein analysis. Demonstration of chylomicrons confirms the diagnosis of chylothorax. With congenital chylothorax, the pleural fluid is serous and becomes chylous when milk feedings are started. Pleural fluid triglyceride and lipoprotein analysis should be performed in all newborns with pleural effusion.

**OTHER INVESTIGATIONS**

Once chylothorax has been diagnosed, other radiologic studies will likely be needed to further investigate the lymphatic system. Studies to outline the lymphatic vessels, identify the site of chyle leakage, and determine the cause of the chylothorax should be performed. Imaging studies such as computerized tomography scans, lymphangiography, and lymphoscintigraphy can be helpful. Occasionally, MRI is used, particularly if the mediastinum needs to be imaged.

Lymphangiography and lymphoscintigraphy both require the administration of a contrast agent. This can be done by interstitial (intradermal or subcutaneous) administration, administration into a cannulated lymphatic vessel, intravenous injection, or injection into a lymph node. Lymphangiography implies the administration of an iodinated contrast agent into a cannulated lymph vessel. A simultaneous chest radiograph or computerized tomography scan will delineate the lymphatic anatomy. The sensitivity of lymphangiography can be low because it is difficult to visualize the entire length of the thoracic duct because of poor mixing of oily contrast medium and chyle.

Successful identification rates of up to 81% have been reported in adults. Limitations include the technical skills needed to cannulate lymph vessels, pain, infection, respiratory distress, and damage to the lymphatics. Thus, many medical centers no longer perform lymphangiograms. An alternative is lymphoscintigraphy, a faster and less traumatic nuclear imaging technique that utilizes filtered Tc injected intradermally or subcutaneously as a contrast agent.

Computerized tomography can be useful to image the mediastinum, especially if nontraumatic chylothorax is suspected, and can detect small amounts of contrast material in the pleural space. It has been used in at least 1 case to aid in the diagnosis of lymphangiomatosis in a child.

Magnetic resonance lymphography involves interstitial or intravenous injection of gadolinium-based contrast agents. This technique has been used in adults with good delineation of
lymphatic vessels. MRI has been used in at least 1 case of disseminated lymphangiomatosis in a child to help assess the extent of the disease. If direct visualization of a chyle leak point is needed, thoracoscopy can be useful. It also allows for biopsies of any suspect areas.

MEDICAL MANAGEMENT OF CHYLOTHORAX

The goals of management of chylothorax are relief of respiratory symptoms by drainage of the pleural fluid, prevention of recurrence by treatment of the underlying cause, and prevention/treatment of malnutrition and immunodeficiency (Fig 1).

The initial step is aspiration of the pleural fluid for diagnostic purposes. If the effusion is large and compromising respiration, or if the effusion is likely to reoccur, then a chest tube should be inserted for continuous drainage of the pleural space. Quantification of drainage is useful to guide treatment of fluid imbalances. Some centers use daily drainage as a guide for clinical improvement or failure (<10 mL/kg per day of pleural drainage is considered to be an improvement; >10 mL/kg per day of pleural drainage is considered to be a failure after 4 weeks of nonsurgical management). In severely ill patients, assisted ventilation may be necessary. The use of positive end-expiratory pressure ventilation may tamponade the injured duct, helping to decrease chyle flow. There is 1 report of the successful use of high-frequency oscillatory ventilation in severely ill neonates with congenital chylothoraces.

There are several nonsurgical methods (dietary modifications and/or adjunctive medications) that have been used to try to prevent or treat chylothorax reoccurrence if the leak does not spontaneously resolve. Most series performed in children recommend up to a 2- to 4-week trial of nonsurgical therapies before surgery is considered. Nonoperative management of chylothorax in children is successful in >80% of reported cases, including those patients with chylothorax after cardiothoracic surgery.

To reduce the flow of chyle through the thoracic duct while waiting for spontaneous healing to occur, a fat-free diet with the addition of medium-chain triglycerides is instituted. Medium-chain triglycerides with saturated fatty acids of 8 to 12 carbon chain lengths are absorbed directly into the portal venous system, bypassing lymphatic drainage. Several enteral formulas are available commercially that contain a high percentage of medium-chain triglycerides but also contain some long-chain fatty acids as well: Optimental (Abbott Nutrition, Columbus, OH), Peptamen (Nestle Health Science, Vevey, Switzerland), Peptamen AF (Nestle Health Science), Peptamen 1.5 (Nestle Health Science), Perative (Abbott Nutrition), Portagen (Mead Johnson Nutrition).

FIGURE 1
Algorithm for evaluation and treatment of chylothorax in children.

Pleur effusion
Thoracentesis

Chylothorax diagnosed
Triglyceride level in pleural fluid ≥ 110 mg/dL, pleural fluid cholesterol/serum cholesterol < 1.0, presence of chylomicrons

Determine mechanism of injury/etiology (Table 2)

Determine site of rupture
Lymphangiography, lymphoscintigraphy, thoracoscopy, computed tomography, magnetic resonance lymphography

Management:
Goals: Relieve respiratory symptoms, prevent recurrence, prevent/treat malnutrition and immunodeficiency

Medical management

Dietary management
Enteral diet containing medium chain triglycerides
Consider trial of octreotide or somatostatin
High chyle output, enteral diet not working, patient can’t take enteral diet
Parenteral nutrition containing IV lipid emulsion

Chylothorax persists after 2-4 weeks of medical management

No
Yes

Chyle volume > 100 mL/year of age, well-identified site of chyle leakage, high risk of malnutrition/immunosuppression
Thoracic duct ligation
Surgery
Unsuccessful or unable to be performed
Consider pleurodesis
Consider pleuropertitoneal shunt placement

Chest tube placement

FIGURE 1
Algorithm for evaluation and treatment of chylothorax in children.
Glenview, IL), Monagen (Nutricia, Gaithersburg, MD), Enfaport (Mead Johnson Nutrition), Pregestimil (Mead Johnson Nutrition), Vital HN (Abbott Nutrition), Vital HN 1.5 (Abbott Nutrition), and Vivonex TEN (Nestle Health Science). Medium-chain triglyceride formulas do not contain essential fatty acids, so those will need to be supplemented if these formulas are used for >3 weeks. There is a report of the successful use of an enteral formula containing long-chain triglycerides, and a report of the combined use of low-fat breast milk and octreotide, to treat postoperative chylothorax. A more aggressive option is complete enteric rest by using total parenteral nutrition. There are several intravenous lipid emulsions that are designed to be delivered directly into the blood stream: Intralipid and Liposyn. They do not travel through the lymph system and do not contribute to chyle flow. They also provide essential fatty acids. In adults, enteral nutrition may be effective if chyle output is <1000 mL/day. A low fat semielemental formula may be effective if chyle output is <500 mL/day. Parenteral nutrition will be required if chyle output is >1000 mL/day in adults, or if patients are not responding to a modified oral or enteral regimen, or if they are having increased chyle output on enteral nutrition. Whether enteral or parenteral nutrition is chosen, the calories, electrolytes, and volume must at least match those lost in the chyle output. In a group of 51 children with chylothorax, the use of conservative enteral or parenteral therapy for 1 to 3 weeks resulted in resolution of the chylothorax in 41 (80%) of the children. Somatostatin is an endogenous hormone with actions that include effects on the gastrointestinal tract. Octreotide is a synthetic, long-acting somatostatin analog. These agents, whose mechanism(s) of action is(are) not clear, have been used in the management of chylothorax with varying results. It may be that they cause a reduction in intestinal blood flow by vasoconstriction of the splanchnic circulation, with reduction of lymphatic fluid production. Alternately, the lymphatic vessels may have somatostatin receptors, and their stimulation could result in decreased lymphatic flow. These agents also decrease gastrointestinal motility, and decrease the volume of gastric, pancreatic, and biliary secretions, which in turn decreases lymphatic flow. In comparison with somatostatin, octreotide has a longer half-life, greater potency, and the option of subcutaneous administration. Either drug can be given as a continuous intravenous infusion or as an intravenous bolus twice daily. The starting dose of somatostatin is 3.5 μg/kg per hour, which can be increased to 10 μg/kg per hour. The dose for octreotide in children has ranged from 0.3 to 1.0 μg/kg per hour. The optimal timing of introduction and duration of treatment is unknown. Side effects of somatostatin and octreotide include hyperglycemia, hypothyroidism, cramps, nausea, diarrhea, renal impairment, necrotizing enterocolitis, and liver dysfunction. A case of anaphylaxis has been reported in a child after the use of octreotide. Shah and Sinn reported the use of octreotide in 6 patients with congenital chylothorax by using a dose range of 0.5 to 10 μg/kg per hour. Octreotide was started at a median age of 13.5 days (range, 8 to 22 days) and was given for a median of 20 days (range, 12 to 27 days). Five of the 6 patients had resolution of their chylothoraces with this therapy. Roehr et al performed a systematic literature review of the use of somatostatin and octreotide in 35 children with primary or secondary chylothorax. Most studies reported a significant decrease in chylous drainage within 5 to 6 days of starting octreotide or somatostatin. A 2010 Cochrane report described the use of octreotide in 20 neonates with chylothorax. Fourteen of the case reports described successful resolution of chylothorax, 4 reported no resolution, and 1 reported equivocal results. No practice recommendation was made based on this evidence. Horvers et al reported on the use of octreotide in 7 patients with congenital chylothorax. Pleural effusions eventually decreased in all patients after administration of 5 to 6 μg octreotide/kg per minute, but the authors felt that the decrease might reflect the natural history of congenital chylothorax and, hence, no clear, consistent effect of octreotide was identified. They noted that pulmonary hypertension was a common problem in the patient group. A randomized, controlled, multicenter trial is needed to assess the safety and efficacy of octreotide and somatostatin use in the treatment of chylothorax in children. Other agents used in the treatment of chylothorax include nitric oxide and etilefrine. A case report described the use of nitric oxide in a neonate who developed a chylothorax after surgery for congenital heart disease. At an inhaled nitric oxide dose of 20 ppm, the chest tube drainage markedly decreased and finally ceased 8 days later. Nitric oxide was discontinued 19 days after initiation with no recurrence of the chylothorax. The authors proposed that functional venous obstruction due to the patient’s moderate pulmonary hypertension was a contributor to the persistence of the chylous leak. The nitric oxide caused a decrease in pulmonary artery pressure and decreased systemic venous pressures by augmenting forward flow through the right side of the heart. Etilerine is a sympathomimetic drug that has been used
in a small number of adults for the management of postoperative chylothorax with no side effects. It causes systemic smooth muscle contraction and is thought to decrease chyle flow by constriction of the thoracic duct.\textsuperscript{126,127}

**SURGICAL MANAGEMENT OF CHYLOTHORAX**

Surgery should be considered when medical management of chylothorax has failed to reduce chyle flow and allow healing of the duct. There is no consensus on the timing of surgery.\textsuperscript{2} Some recommend surgery if the effusion persists for more than 2 weeks. Others regard a particular volume, such as >100 mL per year of age in children, as an indication for surgery.\textsuperscript{128–130} Most recommend an extended period (3 to 4 weeks) of conservative management before proceeding to surgical treatment.\textsuperscript{131} If there is a well-identified site of chyle leak and high flow that precludes spontaneous healing, a case for earlier surgery can be made.\textsuperscript{131}

Successful surgery can shorten hospitalization and reduce the risks of malnutrition and immunosuppression.\textsuperscript{2}

There are several procedures that can be used for the treatment of chylothorax. If the site of rupture of the thoracic duct can be identified by lymphangiography, direct surgical ligation of the duct represents a definitive treatment of chylothorax.\textsuperscript{9,52,132} Thoracoscopy has a low rate of complications and is cost-effective.\textsuperscript{133,134} Pego-Fernandez et al\textsuperscript{134} performed duct ligation in 20 pediatric patients with chylothorax after cardiothoracic surgery. They were successful in 16 patients (80%), but noted that patients with thrombus of upper body venous vessels or prolonged chest tube drainage were more likely to fail and/or die. They recommended that duct ligation be done within 2 weeks of recognizing the chylothorax. If needed to visualize the thoracic duct and the site of leakage during surgery, the patient can be given a 200-mL mixture of milk and cream a few hours before surgery, or an intraoperative injection of 1% Evans blue dye.\textsuperscript{131,135,136} If the site of leakage cannot be identified, a mass ligation of the thoracic duct and its surrounding tissue is done around the aorta, azygos vein, and esophagus, adjacent to the vertebral body,\textsuperscript{137} or by ligation of the cistern chyli.\textsuperscript{138}

Another procedure used to manage chylothorax is obliteration of the pleural space, either chemically or surgically. Various agents, such as tetracycline, talc, bleomycin, fibrin glue, and povidone-iodine, have been used.\textsuperscript{139–143} Povidone-iodine 10% dermique diluted with saline or povidone-iodine 4% scrub was instilled directly through a chest tube into the pleural space in a group of 4 neonates with chylothoraces. Systemic analgesia was achieved with a morphinomimetic (fentanyl or sufentanil), and sedation was provided with intravenous midazolam. Thyroid function was reported to be normal before and after instillation of povidone-iodine in 3 of the infants; it was not checked in the fourth infant.\textsuperscript{139} The intrapleural administration of talc can lead to the development of the acute respiratory distress syndrome.\textsuperscript{1} OK-432, an inactive preparation of *Streptococcus pyogenes*, has also been used as an effective sclerosing agent in neonates.\textsuperscript{144,145} OK-432-induced pleurodesis has been used as an antenatal treatment of severe chylothorax associated with nonimmunologic hydrops fetalis.\textsuperscript{145} Pleurodesis is performed with thoracoscopy, although the sclerosing agent can be instilled through a chest tube. Pleurodesis has effectively been used in cases where medical therapies for chylothorax failed and direct surgical duct ligation was not performed.\textsuperscript{146}

A third surgical method to manage chylothorax is the placement of a pleuropertitoneal shunt. This provides a way of draining chyle from the pleural space without losing the fluid. The shunts are a 1-way subcutaneous connection between the pleura and the peritoneum that can be inserted with local anesthesia.\textsuperscript{1,2} They have been used in children whose chylothoraces have been refractory to treatment with dietary management, thoracentesis, or tube thoracostomy, and are reported to be 75% to 90% effective.\textsuperscript{129,149–151} After a shunt is implanted, the lymphatic defect closes spontaneously in most cases and the shunt can be removed 30 to 90 days after insertion.\textsuperscript{149} Murphy et al\textsuperscript{129} recommended placing the shunt if drainage from the chylothorax persisted beyond 5 days. Shunts have also been used to treat chylothoraces in preterm infants and in fetuses.\textsuperscript{37,151} There are case reports of 2 other separate methods that have been used to manage chylothorax. Fluoroscopically guided percutaneous embolization of the thoracic duct has been used to manage chylothorax.\textsuperscript{152,153} There are also reports of autoinfusion of chylothorax fluid in patients who were undergoing hemodialysis.\textsuperscript{154,155}

**COMPLICATIONS OF CHYLOTHORAX**

Several complications can occur in association with the development of chylothorax. These include malnutrition, hyponatremia, fluid imbalance, respiratory distress, increased risk of thrombosis,\textsuperscript{156} and secondary immunodeficiency.\textsuperscript{2} In 1 reported case of selenium deficiency because of loss of selenium in chylous fluid, myopathy associated with severe cardiomyopathy developed.\textsuperscript{157}
Chylothorax leads to hypogammaglobulinemia and lymphopenia. In 16 children who developed chylothoraces after cardiac surgery, there were decreases in the absolute numbers of B lymphocytes (CD19+), T lymphocytes (CD3+), helper T-cells (CD4+), and suppressor/cytotoxic T-cells (CD8+), but a normal CD4+:CD8+ ratio. The absolute number of natural killer cells (CD16+) and metabolic activity of polymorphonuclear leukocytes was normal. In another study of 5 children with chylothorax, 2 had reduced absolute numbers and percentage of CD3+ T-lymphocytes, and all the children had decreased numbers and percentage of CD4+ T-lymphocytes. The percentage of CD8+ lymphocytes was normal in all patients and the CD4+:CD8+ ratio was reversed. Because of this secondary immunodeficiency, children with chylothorax are at risk for development of infections. Of 7 infants with congenital chylothorax due to nonimmune nosocomial infections. In 2 children who developed chylothorax after surgery for congenital heart disease, intravenous immunoglobulin G was given prophylactically, after the development of chylothorax or early in the course of septicemia. In a later study of 8 children with hypogammaglobulinemia and lymphopenia attributable to chylothorax, intravenous immunoglobulin G administration did not lead to discernible protection from infectious complications.161

CONCLUSIONS

Chylothorax is a rare cause of pleural effusion in children except during the neonatal period, when it is the most common cause. Diagnosis is made by measurement of the triglyceride level, determination of the pleural fluid to serum cholesterol ratio, and demonstration of chylomicrons in the pleural fluid. There are multiple etiologies of chylothorax in children. Knowledge of the anatomy and physiology of the lymphatic system, particularly the thoracic duct, is vital for assessment and management. Initial treatment involves drainage of the effusion, dietary modifications, and other medical therapies to diminish chyle flow so that the thoracic duct can heal. Somatostatin and octreotide are of variable usefulness. Failure of medical management, particularly if the child develops complications from the chylothorax, should result in early surgical intervention. There are several surgical procedures that have been effective in the treatment of chylothorax. The prognosis of children who develop chylothorax depends on the etiology of the effusion, its response to medical/surgical therapies, and the complications that result from the chylothorax.

ACKNOWLEDGMENT

The author thanks Andrea B. Patters for her editorial assistance with the preparation of this article.

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BIRTHPLACE OF BUDDHA: I enjoy ecclesiastical architecture and the architectural history of religions. While I have visited many innumerable temples, churches, pilgrimage sites, shrines, and Buddhist temples, I have not known for sure which one marked the birthplace of Buddha. The most commonly accepted date for Buddha’s lifespan is 563-483 BC, but the exact date of his birth and whereabouts of his birthplace are not known; much of what we know of his early life comes from oral histories. As reported on CNN (World: November 25, 2013), scientists have uncovered archaeological evidence to suggest that Buddha was most likely born in the sixth century BC in current Nepal. Scientists excavating in Nepal (at a site believed by many to be Buddha’s birthplace) have uncovered an ancient Buddhist shrine dating back to that time. The Lumbini site in Nepal, in an area bordering India and the Siwalik Range of the Himalayas, has long been associated with Buddha, and pilgrims routinely visited the site through the 16th century. Currently, there is a temple at the site built over earlier Buddhist temples. A sandstone pillar found here in the late 19th century has an inscription stating that Emperor Ashoka visited this early temple in the third century BC because it was the birthplace of Buddha. Scientists have now found evidence that the third century temple was built over an even earlier temple. Carbon dating of post-hole fragments date the earliest structure to the sixth century BC. Interestingly, the structure most likely was open in the middle and had a central tree – consistent with the tradition that Buddha’s mother gave birth to him while holding onto a tree branch. It would appear that belief, customs, and science actually may all agree. I for one am excited about these recent archaeological discoveries and hope to be able to visit the site soon.

Noted by WVR, MD
Chylothorax in Infants and Children
James D. Tutor
Pediatrics 2014;133;722
DOI: 10.1542/peds.2013-2072 originally published online March 31, 2014;

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DOI: 10.1542/peds.2013-2072 originally published online March 31, 2014;

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