Idiopathic Chylothorax: Pathophysiology, Diagnosis, and Thoracic Duct Imaging

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Abstract: Idiopathic chylothorax is a debilitating disease that can lead to respiratory and metabolic compromise and fibrosing pleuritis. Previous investigation has provided theories for the etiology of this poorly understood disease. This article provides an overview of the pathophysiology and diagnosis of chylothorax. Thoracic duct imaging, including minimally invasive techniques, is also discussed, as it is frequently performed in the perioperative period. A companion article reviews nonsurgical and surgical techniques for treating and managing idiopathic chylothorax in dogs and cats.

Chylothorax is a debilitating disease that occurs when disruption of the thoracic duct (TD) results in chyle leakage into the pleural space (FIGURE 1). Trauma to the TD during cardiothoracic surgery is the most common cause of chylothorax in humans. While traumatic causes of chylothorax have been reported in veterinary patients, most cases in dogs and cats are considered idiopathic because a predisposing cause cannot be identified.

The Lymphatic System
The human anatomist Gaspar Aselli is credited with the indirect discovery of the lymphatic system in a dog in 1622. In his experiments, he noted that “a great number of cords […] were spread over the whole mesentery and intestine.” Aselli first believed these white cords were nerves, but he realized this was not the case when incising the largest cord yielded a “white milk- or creamlike liquid.” This fluid was not seen after incision of a white cord in a subsequent experimental dissection of a dog that had been fasted, and Aselli linked digestion to the formation of the milky fluid.

The lymphatic system has three primary roles: (1) maintain fluid balance, (2) generate an immune response, and (3) perform uptake and transport of dietary fats. Approximately 10% of fluid extravasated into the interstitial space enters blind-ended lymphatic capillaries and becomes lymph. These capillaries connect to larger lymphatic vessels that arborize into the TD. The TD, which is the largest lymphatic vessel in the body and located in the tissues dorsal to the aorta and ventral to the thoracic vertebrae, returns lymph to the vascular system by emptying into the venous system (lymphaticovenous anastomosis) at the level of the jugulocaval angle (FIGURE 2). This maintains fluid balance and prevents tissue edema by returning interstitial fluid to the vascular system, thereby acting as an adjunct to the cardiovascular system.

Figure 1. Intraoperative image of a dog after right fifth intercostal thoracotomy. The patient’s head is to the right, and the abdomen is to the left. Finochietto rib retractors have been applied to improve visualization. Chyle is seen bathing the heart and lungs within the pleural space.
The lymphatic system plays a key role in many immune functions in the body, including creating immune cells and defending the body against infection and the spread of cancer. The TD provides a conduit for immune cells as well as an entry point to the systemic circulation.4

Dietary fats are absorbed from small intestinal enterocytes in the form of chylomicrons, which are large lipoprotein molecules (75 to 1200 nm).3 Chylomicrons predominantly consist of triglycerides but also contain phospholipids, cholesterol, and other proteins. After they are expelled from enterocytes, they are collected by villous lacteals via exocytosis and eventually empty into the cisterna chyli (CC). The CC is the abdominal lymphatic reservoir located in the craniodorsal abdomen, and its cranial extension is the TD3 (FIGURE 2). The “milky” appearance of intestinal lymph, or chyle, is proportional to the concentration of chylomicrons1 (FIGURE 3).

**Pathophysiology of Chylothorax**

Numerous causes of chylothorax have been reported in the veterinary literature, all resulting in obstruction or impedance of TD outflow at the lymphaticovenous anastomosis. They include fungal granuloma, trauma, cranial vena caval thrombosis, congenital abnormalities of the TD, diaphragmatic hernia, lung lobe torsion, and mediastinal and pulmonary neoplasia.1 Cardiac diseases, including constrictive pericarditis, dirofilariasis, right ventricular failure, double-chambered right ventricle, and tricuspid dysplasia, have also been reported as causes of chylothorax.5 However, in veterinary patients, a predisposing cause is rarely identified and chylothorax is most often deemed idiopathic.1 Idiopathic chylothorax is poorly understood.

An experimental model of chylothorax developed by ligating the cranial vena cava has been used to help determine the pathophysiology of idiopathic chylothorax.6 In dogs with experimentally induced chylothorax, and in dogs and cats with naturally occurring idiopathic chylothorax, injection of contrast medium into a mesenteric lymphatic vessel (mesenteric lymphangiography) reveals large, tortuous, dilated lymphatic vessels in the cranial mediastinum6 (FIGURE 4). These abnormal vessels in the cranial mediastinum are characteristic of lymphangiectasia. It has been theorized that lymphangiectasia of the TD, its tributaries, and/or the cranial mediastinal lymphatic vessels leads to transmural leakage of chyle into the pleural space, causing chylothorax.6 Why the spontaneous occurrence of a flow disturbance in the TD results in thoracic lymphangiectasia has not been determined and is the focus of ongoing research.

**Role of Venous Hypertension in Chylothorax**

Several diseases that could elevate right-sided venous pressures, such as restrictive pericarditis, cranial vena caval thrombosis, and right ventricular failure, have been reported to cause chylothorax. However, it has not been determined why all patients with elevated right-sided venous pressures do not develop chylothorax (e.g., all cases of right ventricular failure do not lead to chylothorax). In two independent studies, ligation of the TD at its entry into the venous system at the level of the jugulocaval angle did not lead to chylothorax.6,7 This was thought to be a result of redirected lymphatic flow through collateral channels that enter the cranial vena cava caudal.
Figure 5. Fluoroscopic image of the cranial thorax after contrast lymphangiography in a normal dog. Multiple collateral TD branches (arrowheads) are seen entering into circular structures (presumably lymph nodes) or the venous system caudal to the entry point of the main TD (arrow) at the lymphaticovenous anastomosis.

Figure 6. Lateral thoracic radiograph of a canine thorax demonstrating soft-tissue opacity in the pleural space. Note the retraction and scalloping of lung lobes (arrowheads). Also, the cardiac silhouette is obscured.

to the lymphaticovenous anastomosis (FIGURE 5). These findings provide evidence for the presence of, or the ability to recruit, collateral lymphatic channels within the thoracic cavity and could explain why chylothorax secondary to elevated central venous pressure is rare.6–8

Diagnosis

Physical Examination

A complete physical examination often leads the clinician to diagnose pleural effusion. The color of the patient’s mucous membranes can vary from normal to pale blue, according to the level of respiratory compromise. Thoracic auscultation may reveal reduced heart and lung sounds in the ventral thorax from the gravity-dependent accumulation of pleural fluid. Increased bronchovesicular sounds have been found in 45% and 50% of dogs9 and cats10 with chylothorax, respectively. Some patients exhibit respiratory compromise when placed in lateral recumbency (orthopnea). Thoracic percussion in a patient with pleural effusion produces a dull, low, hyporesonant sound. Most patients with chylothorax are normothermic.9,10

Chyle comprises proteins, dietary fats, electrolytes, fat-soluble vitamins, and cells of the immune system. Chronic loss of chyle into the pleural space can lead to metabolic compromise characterized by hypoproteinememia, electrolyte abnormalities (hyponatremia and hyperkalemia), fat depletion, and immunocompromise from lymphocyte loss.1,9–11 Patients with chylothorax may also present with a history of anorexia, lethargy, and weight loss.1,10 Additional diagnostic evaluation should only be performed once the patient is in stable condition.

Thoracic Radiography

Small volumes of pleural effusion may form radiopaque pleural fissure lines from the peripheral margin of the lungs toward the hilar region. Large amounts of pleural effusion lead to retraction and “scalloping” of lung lobes (FIGURE 6). Pleural effusion can obscure the cardiac silhouette, and repeat thoracic radiography after pleural evacuation may be required to evaluate cardiac size. Chyle is a bacteriostatic fluid that irritates the pleural and pericardial surfaces, and chronic chylous effusion can lead to life-threatening fibrosing pleuritis and pericarditis.12 Fibrosing pleuritis should be suspected when the lungs are rounded in the presence of minimal pleural fluid or when pneumothorax develops after thoracocentesis (FIGURE 7).

Pleural Fluid Evaluation

Thoracocentesis and retrieval of pleural fluid is recommended for diagnostic purposes and to relieve the patient's respiratory compromise. Chyle has a characteristic “milky” appearance; however, this appearance alone cannot be used to make a definitive diagnosis of chylothorax because other effusions, including pyothorax, may have a similar appearance.2 In anorectic patients, chyle may have an uncharacteristically clear appearance that can be

Key Points

- Although numerous causes of chylothorax have been reported in the veterinary literature, an underlying cause is rarely identified.
- Although chyle has a characteristic “milky” appearance, a definitive diagnosis of chylothorax can be made only if triglyceride levels in the pleural fluid are greater than those in serum.
- Chronic chylous effusion can lead to life-threatening fibrosing pleuritis and pericarditis. Fibrosing pleuritis should be suspected when the lungs are rounded in the presence of minimal pleural fluid.
- TD imaging is recommended before and after TD ligation. Preoperatively, it provides the surgeon with a view of TD anatomy, and postoperatively, it confirms occlusion of all TD branches.
- Minimally invasive TD imaging techniques are associated with less morbidity and shorter procedure times compared with traditional imaging techniques.
If chylous effusion is suspected, further diagnostic tests should be performed to confirm the diagnosis. These tests include cytologic, physical, and biochemical evaluation of the sampled effusion. Cytologically, chylous effusion contains large numbers of small, mature lymphocytes and lower numbers of macrophages that contain lipid droplets (FIGURE 8). Chylomicrons should be evident on a wet mount preparation of a chylous effusion. In patients with chronic chylothorax that have undergone multiple thoracocenteses, the effusion can be laden with nondegenerate neutrophils. This finding could also be a result of the inflammatory effect of chyle on the pleura and pericardium. Biochemical evaluation includes measuring triglyceride, cholesterol, and total protein levels; performing a total cell count; measuring specific gravity; and assessing for the presence of chylomicrons. A definitive diagnosis of chylothorax is made by comparing triglyceride levels in paired pleural fluid and serum samples. In cases of chylous effusion, the level of triglycerides in the pleural fluid is greater than that in the serum. It is common for the ratio of triglycerides in pleural fluid to triglycerides in serum to be 10:1 to 20:1 or higher. The specific gravity and total protein concentration of feline chylous effusion have been reported to be 1.030 to 1.032 and 5.0 to 5.32 g/dL, respectively. Historically, several other diagnostic tests have been performed to determine whether an effusion is chylous. These include the ether clearance test and Sudan II stain, which provide crude estimates of lipid content in the fluid; however, these tests are seldom used at our institution. Pleural and serum cholesterol levels can also be compared, with cholesterol levels being lower in a chylous effusion than in serum.

Although chyle is a bacteriostatic substance, multiple thoracocenteses for pleural evacuation can increase the risk of developing pyothorax. Bacterial culture and sensitivity testing of pleural fluid samples is recommended if chylothorax is suspected.

**Further Diagnostic Evaluation**

Once a diagnosis of chylothorax has been made, the clinician should attempt to determine whether there is an underlying cause. In addition to a complete blood cell count, serum biochemistry panel, heartworm antigen testing, and coagulation evaluation, the diagnostic evaluation should include thoracic ultrasonography (ideally before thoracocentesis, to provide an acoustic window) and three-view thoracic radiography (after pleural evacuation has been performed) to determine if there is underlying pathology. Thoracic computed tomography (CT) provides three-dimensional detail of thoracic structures and can be combined with preoperative TD imaging. As cardiac diseases are reported causes of chylothorax, a complete cardiac evaluation, including echocardiography, is warranted in all cases. In cats, FeLV and FIV testing should also be performed.

**Thoracic Duct Imaging**

Kagan and Breznock first described the use of aqueous contrast medium injected directly into a mesenteric lymphatic vessel (mesenteric lymphangiography) for imaging the TD in normal dogs...
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(FIGURE 9). Since that landmark study, several published reports have described the use of mesenteric lymphangiography to highlight the TD in dogs and cats undergoing surgical treatment for idiopathic chylothorax.1,6,18,19 The most common surgical treatment for idiopathic chylothorax in dogs and cats is TD ligation.20

TD imaging has been recommended before and after TD ligation.18–20 Preoperative imaging of TD anatomy can allow the surgeon to ligate the TD at a location with minimal branching in the caudal thorax, which may optimize surgical success (FIGURE 10). Postoperative lymphangiography can confirm successful occlusion of all TD branches with no flow of contrast cranial to the ligation site so that if postoperative effusion persists, the surgeon can be more certain that it is not from a failure to occlude all TD branches at the time of surgery. If postoperative lymphangiography reveals persistent TD flow, ligation for the missed TD branch(es) should be reattempted or chylothorax will persist.18,19

Some authors21 have reported concern with the accuracy of post-TD ligation lymphangiography in confirming occlusion of all TD branches. In an experimental study in eight cats, six cats had TD ligation performed and two cats had the TD dissected but not ligated as a sham procedure.21 Immediate postoperative lymphangiography showed no contrast flowing cranial to the site of dissection in all cats, including the two that did not undergo TD ligation.21 Repeat lymphangiography in the two nonligated cats 4 weeks postoperatively revealed a patent TD. The authors concluded that simply dissecting around the TD was sufficient to cause short-term occlusion of the TD.21 Additional studies are required in dogs to determine if dissection of the TD alone is sufficient to obstruct the flow of contrast at the time of lymphangiography. Lymphangiography is challenging to perform in cats and is associated with several limitations, including difficulty in locating and injecting mesenteric lymphatic vessels.

Although radiographic visualization of TD anatomy using aqueous contrast material is advantageous before and after TD ligation, it does not provide the surgeon with intraoperative information about the TD and its branches. Injection of mesenteric lymph nodes or lymphatic vessels with methylene blue is reported to facilitate intraoperative visualization of the TD and its branches during TD ligation.20,22 However, intravenous injection of methylene blue can lead to toxicosis; reported complications include renal failure, Heinz body anemia, and increased serum alkaline phosphatase levels.23,24 Preoperative administration of a fatty meal (oil or 35% cream) to increase the chylomicron content of chyle has also been reported to facilitate intraoperative identification of lymphatic vessels and the TD.20

The standard imaging modality for mesenteric lymphangiography has been orthogonal view radiography.17,18 Some authors question the accuracy of radiographs because superimposition of TD branches and overlying spinal and soft tissue structures can make interpretation challenging. In one study25 that compared CT with radiography after direct mesenteric lymphangiography in dogs, CT was found to identify a significantly greater number of TD branches. The ability to observe TD branches in a three-dimensional plane and the limited need for patient repositioning for image acquisition were other advantages of CT identified in this study.25 CT also has greater contrast resolution, and small, poorly opacified branches can still be identified (FIGURE 11). The study authors speculated that by improving the ability for surgical planning, CT mesenteric lymphangiography would improve success rates of resolving chylothorax with TD ligation.25

Minimally Invasive Techniques for Thoracic Duct Imaging

Traditional TD imaging techniques require an exploratory laparotomy and injection of contrast medium into a mesenteric lymphatic vessel or lymph node, followed by either radiography or CT.17,18,25 The exploratory laparotomy required for mesenteric lymphangiography prolongs anesthesia time and can increase morbidity in
an already metabolically compromised chylothorax patient. The goal of developing minimally invasive TD imaging techniques is to reduce morbidity and anesthesia times and to eliminate the need for intraoperative patient transfer to the radiology suite while providing optimal imaging studies to maximize success for the veterinary surgeon.

**Percutaneous Mesenteric Lymphadenography**
Ultrasound-guided percutaneous injection of a mesenteric lymph node with contrast medium followed through thoracic CT has been reported to produce diagnostic lymphangiograms in dogs. The success of this technique lies in the operator’s experience with ultrasound-guided mesenteric lymph node injection.

**Laparoscopic Mesenteric Lymphadenography**
Laparoscopic surgery has several advantages over laparotomy, including decreased morbidity, faster recovery, improved visualization, and improved cosmesis. Laparoscopic mesenteric lymphadenography followed by radiography has been described for mesenteric lymph node injection for TD imaging in dogs. This technique was less successful than direct mesenteric lymphadenography (performed via a paracostal laparotomy) at producing diagnostic lymphadenograms, which was attributed to the lack of manual stabilization of the injected lymph node, allowing the node to fall away from the needle during injection.

**Percutaneous Popliteal Lymphangiography**
Percutaneous popliteal lymph node contrast injection has been evaluated in dogs (FIGURE 12). Initial studies determined that the TD could be seen radiographically after experimental injection with 1 mL/kg of contrast medium injected at 2 mL/min in dogs. Major complications were not reported with percutaneous popliteal lymph node injection. In a recent study, CT was used to identify TD anatomy after percutaneous popliteal lymphangiography in normal dogs. CT delineated a significantly greater number of TD branches compared with both lateral and ventrodorsal radiographs.

One concern with percutaneous or ultrasound-guided popliteal lymphangiography is whether enough pressure is generated during the injection to open all TD branches. This concern is based on the fact that high injection pressures cannot be used during this technique and the fact that the popliteal lymph node is much farther away from the CC and TD compared with mesenteric lymphatic branches. Millward et al did not find a significant difference in TD branches after direct mesenteric and popliteal lymphangiography in normal dogs when CT was used to image the lymphatic system. Studies support the use of percutaneous popliteal lymphangiography in the perioperative period as a minimally invasive alternative to mesenteric lymphangiography or lymphadenography.

**Conclusion**
The pathogenesis of idiopathic chylothorax remains poorly understood in veterinary patients. Advances in the diagnostic evaluation of chylothorax patients will facilitate the generation of high-quality images for presurgical planning with minimal patient morbidity.

**References**
1. What is the most common cause of chylothorax in dogs and cats?
   a. trauma
   b. cranial vena caval thrombosis
   c. idiopathic
   d. cardiac disease

2. Which of the following is/are not a function(s) of the lymphatic system?
   a. maintain fluid balance and act as an adjunct to the cardiovascular system
   b. generate an immune response against invading pathogens
   c. transport dietary fats
   d. regulate circadian rhythm

3. Which statement(s) is/are correct regarding chyle?
   a. It comprises lymphocytes, fat-soluble vitamins, proteins, and electrolytes.
   b. Chronic loss of chyle into the pleural space can lead to metabolic and immune compromise.
   c. Chyle is an irritant, and chronic exposure of the pleural and pericardial lining to chyle can lead to fibrosing pleuritis.
   d. all of the above

4. Which statement is correct regarding the TD?
   a. It is located in the tissues dorsal to the aorta and ventral to the thoracic vertebrae.
   b. It transports chyle from the CC and empties it into the venous system at the jugulocaval angle.
   c. It can have variable anatomy at the lymphaticovenous anastomosis and along its course through the thoracic cavity
   d. all of the above

5. Which statement is correct regarding fibrosing pleuritis?
   a. It is a benign condition.
   b. It can be suspected on radiographs if the lung margins are rounded in the presence of minimal pleural effusion.
   c. It does not affect long-term prognosis.
   d. It occurs only in cats.

6. Cytologic evaluation of chyloous pleural effusion reveals
   a. small, mature lymphocytes and lower numbers of macrophages.
   b. degenerate neutrophils.
   c. large, immature lymphocytes and lower numbers of macrophages.
   d. large, immature lymphocytes and higher numbers of macrophages.

7. A definitive diagnosis of chylothorax can be made when
   a. the ratio of triglycerides in pleural fluid to serum is 10:1 to 20:1.
   b. the ratio of cholesterol in pleural fluid to serum is 10:1 to 20:1.
   c. the ratio of triglycerides in serum to pleural fluid is 10:1 to 20:1.
   d. sampled pleural fluid has a characteristic “milky” appearance.

8. Repeated thoracocentesis of chylothorax can lead to
   a. restrictive pleuritis.
   b. loculated fluid.
   c. pyothorax.
   d. hemothorax.

9. Which statement is true concerning TD imaging?
   a. It is recommended before and after TD ligation.
   b. Traditional techniques do not risk increased morbidity.
   c. Radiographic and CT lymphangiography are equivalent in delineating TD branching.
   d. It does not prolong anesthesia time in the operative period.

10. Which statement(s) is/are true concerning percutaneous popliteal lymphangiography?
    a. It represents a minimally invasive technique for TD imaging.
    b. Followed by CT, it delineates a greater number of TD branches than radiography.
    c. It does not delineate as many TD branches as direct mesenteric lymphangiography.
    d. a and b