

CHYLOTHORAX IN THE DOG AND CAT: A REVIEW

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ABSTRACT

Chylothorax is a rare but complex disorder in domestic animals. Etiologies include neoplasia, fungal infections, heartworm infestation, cardiac disease, thrombosis of the cranial vena cava, and congenital anomaly of the thoracic duct. Most cases of chylothorax in dogs and cats are idiopathic. Positive contrast lymphangiography on dogs and cats with chylothorax consistently reveals extensive lymphangiectasia of mediastinal and pleural lymphatics. Reported treatment modalities for chylothorax in animals include removal of the etiologic agent, such as a mediastinal tumor, thoracic duct ligation, and implantation of active or passive drainage devices such as a pleuro-peritoneal shunt. Thoracic duct ligation has been most successful in our experience, but continued study is needed since treatment failures are common.

Chylothorax, the accumulation of chylous fluid in the pleural space, is rare in animals but has been reported in dogs (1-7), cats (8-21), and rats (22). Chylothorax in animals is a complicated disease that can be due to a variety of etiologies and can be difficult to manage. Clinical and experimental research has been conducted in recent years that have increased our understanding of the disorder and improved success of treatment. However, many cases of chylothorax remain a diagnostic enigma, and treatment failures are common.

The purpose of this paper is to review the recent veterinary literature on experimental

and spontaneous chylothorax in dogs and cats, and especially on substantive studies done in the last 10 years that have shaped our current concepts regarding its diagnosis and treatment.

ETIOLOGY

Chylothorax has been associated with a number of diseases. Historically, veterinary clinicians have attempted to relate chylous effusions with rupture of the thoracic duct (TD) due to blunt trauma such as being hit by a car (7,19,21). However, we and others have performed lymphangiograms on clinical cases of chylothorax for several years and have yet to document leakage from a TD rupture (3,4,13,14). Even dogs and cats with a history of trauma that preceded the onset of clinical signs of pleural effusion have not been shown to have a rupture of the TD. In a recent study, Hodges et al sought to create chylothorax by surgically incising or transecting the TD (23). Chronic effusion did not develop in any of the experimental animals. Lymphangiography performed 7 days after the TD had been experimentally lacerated revealed that the TD had spontaneously reestablished patency.

Obstruction of the TD or cranial vena cava has been clearly shown to cause chylothorax. This obstruction may be due to neoplasia (2,5,11,17), fungal granuloma (1), or thrombus secondary to chronic intravenous jugular catheters (24). Reported neoplasms that have been associated with chylothorax include thymoma, lymphosarcoma, lymphangiosarcoma, and aortic body tumors.

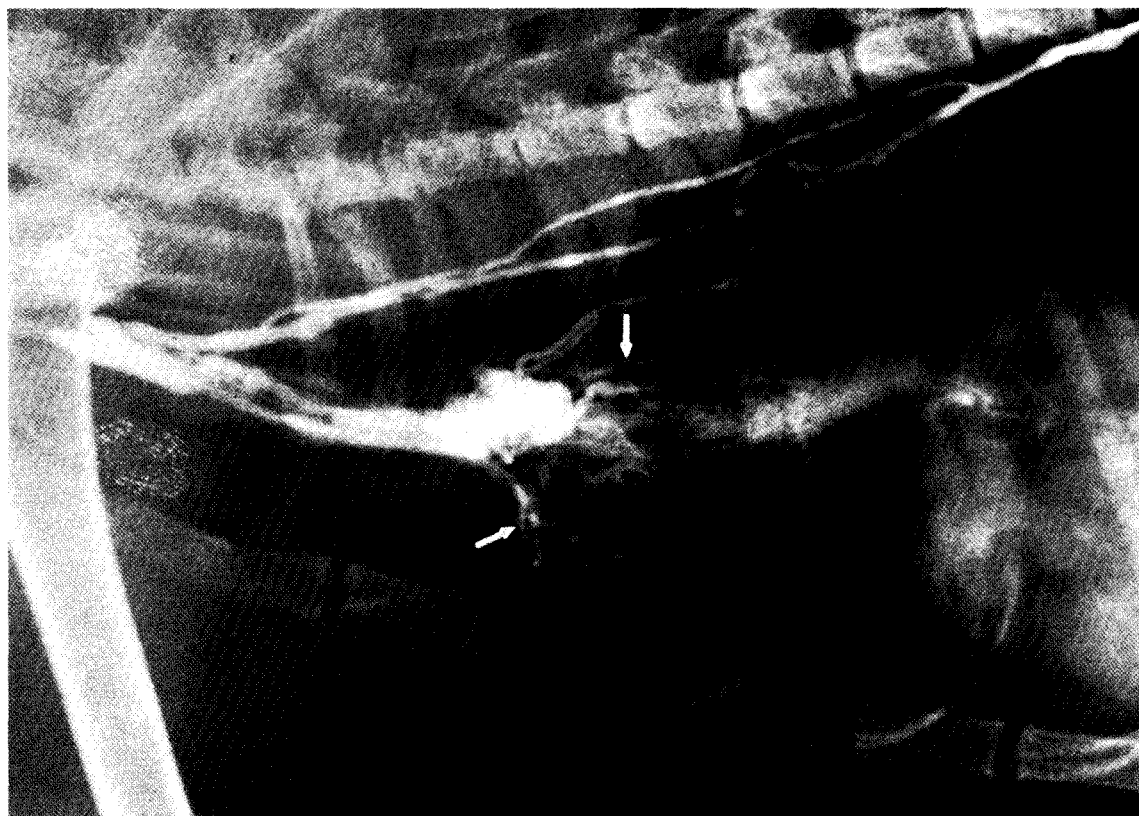


Fig. 1. Positive contrast lymphangiogram of the thoracic duct in a cat with heartworm disease and chylothorax. Note evidence of cranial vena cava obstruction and filling of mediastinal lymphatics (arrows). (Reprinted with permission from reference #16.) Compare with Fig. 3.

Naturally occurring and experimental heartworm disease (*Dirofilaria immitis*) in cats has also been associated with chylothorax (16,25). In one case, the heartworms appeared to cause at least a partial obstruction of the cranial vena cava on positive-contrast lymphangiography (16) (*Fig. 1*). The contrast appeared to fill multiple, dilated mediastinal lymphatics rather than filling the cranial vena cava as in normal animals.

Experimental obstruction of the cranial vena cava has also been shown to result in chylothorax in dogs and cats (26-29). Days to weeks after ligating the cranial vena cava just superior to the azygos vein, 70 to 100% of experimental animals will develop pleural effusion (26,29). Although the effusion may begin as a serous hydrothorax, it subsequently

may change to a chylous appearance. Lymphangiograms of the TD have been studied in dogs with experimentally induced chylothorax after cranial vena caval ligation (26). The lymphangiographic pattern is one of marked dilation and proliferation of mediastinal lymphatics, and is similar to that found in dogs with idiopathic chylothorax.

Chylothorax has been shown to occur secondary to heart disease in dogs and cats (10,15). Multiple reports have described chylothorax secondary to dilated cardiomyopathy in cats (10,15), and we have seen several cases of chylothorax in dogs related to cardiac failure or pericardial disease. Prior to recent studies, the milky fluid that developed in cats with cardiac disease was called a "pseudo-chylous" effusion (30). It was thought unlikely

for this fluid to be chylous because no rupture or lesion involving the TD could be documented. Further study has shown that chylous effusion can occur with cardiac disease.

Chylothorax secondary to a congenital abnormality of the TD has been reported in an Afghan hound (6). Positive contrast lymphangiography and postmortem examination revealed an abnormal termination of the TD at the brachiocephalic vein. Poor lymph flow to the venous system may have resulted in lymphatic dilation and effusion in this animal. Afghans are one of the breeds identified as being predisposed to chylothorax (5), leading some clinicians to speculate that a familial tendency for TD abnormalities may exist. There have been no studies to substantiate this theory. Positive contrast lymphangiograms have been performed on several normal Afghans and no abnormalities were found (31). The lymphangiographic pattern seen in Afghans with chylothorax is similar to that seen in other breeds.

Other disorders that have reportedly been associated with chylothorax are diaphragmatic hernia (19) and lung lobe torsion (32). With both of these conditions, it remains unclear how the primary disease is related to the chylothorax. An important cause of chylothorax in humans is direct injury to the TD during thoracic surgery or other procedures. Chylothorax secondary to iatrogenic trauma to the TD is very rare in domestic animals. Even after extensive diagnostic evaluation of dogs and cats with spontaneous chylothorax, many remain without an obvious primary etiology and thus are classified as "idiopathic." Lymphangiographic studies on dogs and cats with idiopathic chylothorax have revealed extensive lymphangiectasia, especially of the cranial mediastinum (4,14). (Fig. 2) Current theories explaining the mechanism of effusion in these dogs are examined in the next section.

PATHOPHYSIOLOGY

As in other species, the TD in the dog and

cat drains lymph from most of the body except the right forelimb and right side of the head and neck (33). Chyle drains from the intestinal lymphatics to mesenteric lymph nodes and then to large ducts that coalesce to form the cisterna chyli. The TD travels from the cisterna chyli cranially as one or more vessels that ultimately empty into the brachiocephalic vein (3,34) (Fig. 3). In the dog, the cisterna chyli and caudal portion of the TD are located on the right side of the mediastinum, close to the aorta. In the mid-mediastinum, the duct crosses from right to left to empty in the left brachiocephalic vein. In the cat, the duct is usually located entirely on the left side from caudal to cranial (20).

In the dog, chyle is produced and drained by the TD at a rate of approximately 2-4 ml/kg/hr. Chylous effusion can occur when obstruction of TD drainage supervenes. Obstruction of either the TD or cranial vena cava causes stasis of flow in thoracic lymphatics with resultant dilation. Increased pressure probably occurs in the lymphatics, although this has yet to be substantiated. Based on results of experimental and clinical studies, it is likely that chyle leaks out of these dilated lymphatics similarly to lymphedema in a limb or other body part secondary to insufficient lymph drainage.

In dogs and cats with cardiac disease, chylous effusion can develop due to impaired lymph drainage to the venous circulatory system. A recent clinical report documented several cats that developed chylous effusion secondary to right heart failure (10). All cats had evidence of jugular distention on physical examination. Additionally, it has been shown in experimental studies of heart failure that significant increases in hepatic lymph production occur (35). Hepatic congestion can increase TD flow and create a relative or functional obstruction of the lymphaticovenous anastomosis at the brachiocephalic vein.

The pathophysiology of idiopathic chylothorax remains unclear. Obvious obstructive lesions of either the TD or cranial vena cava have not been identified, yet

Fig. 2. Positive contrast lymphangiogram of the cranial portion of the thoracic duct in a dog with idiopathic chylothorax. Note filling of mediastinal lymphatics (arrows). (Reprinted with permission from reference #3.) Compare with Fig. 3.

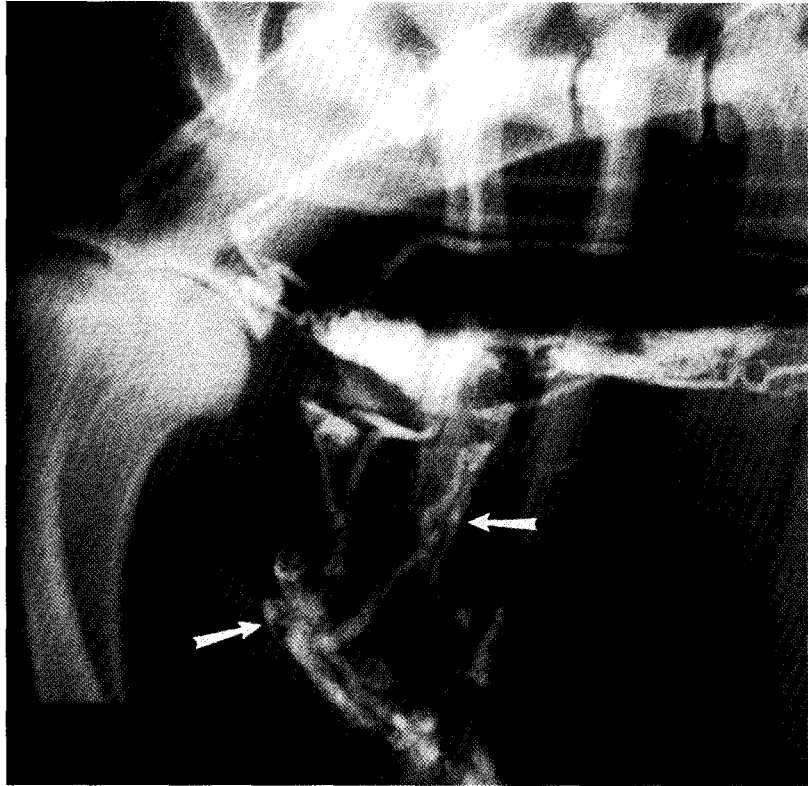
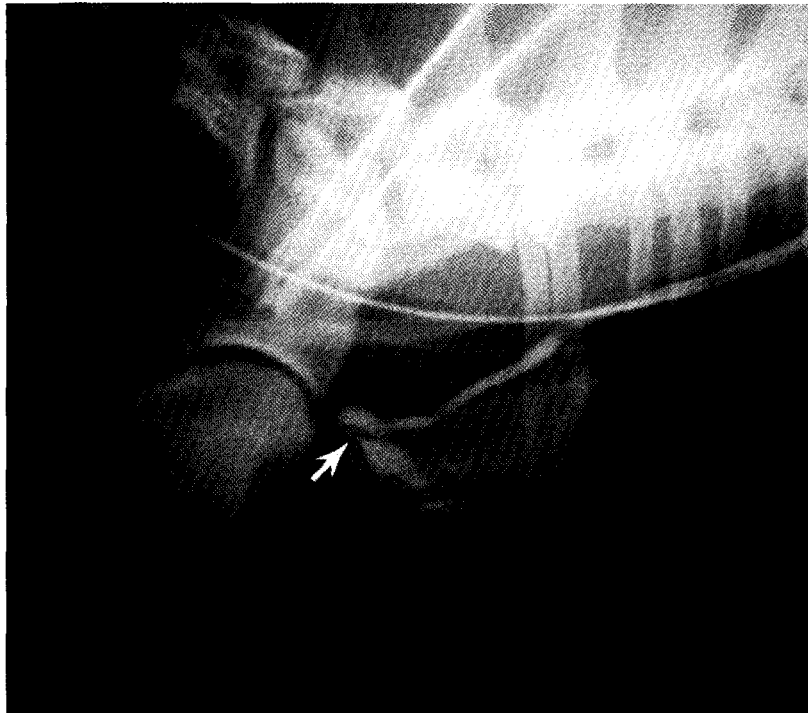


Fig. 3. Positive contrast lymphangiogram of the cranial portion of the thoracic duct in a normal dog. Arrow indicates the point where the thoracic duct enters the brachiocephalic vein. (Reprinted with permission from reference #3.)



extensive lymphangiectasia and poor filling of the cranial vena cava is evident on positive-contrast lymphangiograms. (4,14).

Thoracotomy and necropsy have also failed to reveal a structural cause of the lymphatic dilation. Some have proposed that the chylothorax is due to primary lymphatic abnormalities or congenital anomaly of the lymphaticovenous junction of the TD (4,6). Further studies are, however, needed to better define the etiology and pathophysiology of idiopathic chylothorax in dogs and cats.

After TD ligation in animals with chylothorax, persistence of a non-chylous effusion sometimes occurs (4). The origin of this fluid is unknown, but one study suggests that lung lymphatics may play a role in this phenomenon (29). Using the experimental model of chylothorax previously mentioned (ligation of the cranial vena cava), lymphangiograms of pulmonary efferent lymphatics revealed severe dilation. Therefore, in chylothorax due to cranial vena caval obstruction, lung lymphatic drainage may also be impaired and thus lung lymph may contribute to the pleural effusion. This derangement may also explain the persistence of pleural effusion after TD ligation.

Intense fibrosing pleuritis is a sequela of chronic chylothorax in dogs and especially cats (9,18,36). The inflammatory changes may result in marked restriction of the lungs with impairment of ventilatory capacity. Few studies have been done to specifically characterize the inflammation and determine the pathophysiology of its development. The prognosis for animals with this complication is usually poor.

Other sequelae of chronic chylothorax are dehydration, hypoproteinemia, and weight loss. Although drainage of pleural fluid is an important palliative measure in animals with chylothorax, loss of protein, electrolytes, and fats can result in a weak and emaciated host.

DIAGNOSIS

Animals with chylothorax tend to have

clinical signs typical of diseases causing pleural space impingement, namely dyspnea, tachypnea, decreased exercise tolerance, and coughing. Weight loss also occurs depending on chronicity of the effusion.

Plain film radiography of the chest typically reveals hydrothorax. Thoracic ultrasound may be used before or after fluid aspiration to rule out a mediastinal or intrathoracic mass.

Full cardiac evaluation is routinely performed including auscultation, checking for jugular distention and pulse waves, radiographic appearance, electro- and echocardiography. The areas around the heart are also carefully examined for tumor, and the pericardium and pericardial space is evaluated for masses, thickening, or fluid accumulation.

Laboratory Evaluation

Standard laboratory tests are recommended. A complete blood count may reveal lymphopenia in longstanding chylothorax. Hypoproteinemia, predominantly due to low albumin, is common. The ELISA test for occult dirofilariasis (heartworms) should also be performed.

Analysis of pleural fluid consists of cytology, ether clearance, and assay of cholesterol and triglyceride concentrations. Chylous fluid is suspected based upon its white color and failure to clear after centrifugation. Cytology reveals large numbers of lymphocytes. Chylomicrons are seen on wet mount. Chronic effusions complicated by inflammation or fluid from animals undergoing repeated thoracentesis appear more inflammatory and contain numerous neutrophils (5). Cytology may also help if neoplastic cells are detected.

If the pleural fluid cholesterol/triglyceride ratio is less than 1, the fluid is probably chylous (37).

Lymphangiography

Many techniques for TD lymphangi-

ography have been reported, but positive contrast lymphangiography using water soluble contrast agents injected into mesenteric lymphatics has proved very useful in dogs and cats with chylothorax (3,4,14). Although laparotomy is required, the studies can be performed rapidly and yield excellent details of the lymphatics. For the past 12 years, we have used mesenteric contrast lymphangiography both before and after TD ligation (4,14). The pre-ligation study helps define the anatomy of the TD system and displays lymphatic abnormalities. The post-ligation study verifies that the TD system has been interrupted without "missed branches." The use of lymphangiography seems to have improved outcomes of treatment, although no controlled clinical comparison have been performed. Some authors have expressed concern as the immediate post-ligation lymphangiogram does not necessarily accurately assess complete occlusion of the TD. Thus, in one study in cats, simply dissecting the TD without ligature seemed to show (pseudo) obstruction on immediate post-ligation lymphangiography (38).

Lymphangiography may also be helpful in long-term follow-up of animals with recurrent pleural effusion. In rare instances after thoracic duct ligation, lymphatic collaterals have developed that bypass the ligatures and are associated with recurrence of chylous pleural effusion (39). These animals have been treated with either re-ligation of the thoracic duct collaterals or implantation of an active drainage device.

Lymphoscintigraphy may also be used to diagnose TD abnormalities. In one experimental study, lymphoscintigraphy was performed in dogs with thoracic duct laceration or transection, dogs with cranial vena caval ligation, and normals (40). No difference was seen between normal dogs and those with TD laceration or transection. However, dogs with chylothorax secondary to cranial vena caval ligation showed diffuse radioactivity in the thorax, compatible with thoracic lymphangiectasis. Clinical studies

using this modality have yet to be performed.

TREATMENT

Non-operative

Many forms of medical treatment of chylothorax have been attempted. Most agree that palliative chest drainage is important to alleviate respiratory signs and make the animal more comfortable. Low fat diets have been suggested to decrease TD flow and thereby reduce the volume of effusion (41). Medium chain triglyceride (MCT) oil has also been used to supplement the low-fat diet. Medium chain triglycerides reportedly are absorbed directly into the portal system (42,43). However, Jensen et al described a woman with chylothorax who was treated with MCT and found a significant quantity of MCT in the chyle (42). They found significantly more decanoic acid (C10:0) than octanoic acid (C8:0) in the chyle even though more octanoic acid was present in the original diet. Recently, we have studied the effect of diet and MCT oil on TD flow and composition of lymph in dogs (44,45). TD lymph was continuously collected in experimental dogs for several days while they were fed diets with differing fat content. Although the diet had a significant effect on the triglyceride content of the chyle, there was no difference in lymph flow among groups. Also, dogs fed MCT oil were found to have significant amounts of the MCT in TD lymph. This preliminary study suggests that, contrary to previous reports, low-fat diet and MCT oil may have little beneficial effect on dogs with chylothorax. More studies are needed to evaluate the absorption of MCTs and what role they should play in the management of chylothorax.

Pleurodesis has been suggested as a useful treatment modality for chylothorax (46-48). Anecdotal reports in the veterinary literature have described some success with this method (46,48). However, when evaluated in a controlled setting, we found limited effectiveness of tetracycline, a pleural irritant,

in creating pleural adhesions in dogs with experimental effusion (49). Also, our clinical experience with tetracycline pleurodesis for chylothorax has been unrewarding.

Surgical

Operative treatment of chylothorax has mainly involved either TD ligation (3,4,14) or implantation of active or passive drainage devices (8,50,51). TD ligation has been used since the 1950's as a means of diverting lymph flow from the TD to alternate lymphatic pathways (7,21). It has been shown that ligation of the duct in the caudal mediastinum in normal dogs results in diverting lymph drainage to alternate lymphaticovenous anastomoses such as to the caudal vena cava or azygos vein (3). As treatment for chylothorax, TD ligation was only occasionally successful until development of pre- and post-ligation lymphangiography techniques. A study of 15 dogs with idiopathic chylothorax found a 55% success rate (complete resolution of effusion) with TD ligation in conjunction with lymphangiography (4). One study in cats found TD ligation to be less successful with only 20% having good results (12). More recently, 19 cats with chylothorax were studied and showed a 53% success rate after ligation (14). The effusion that persists after TD ligation may either be chylous or non-chylous. Persistent or recurrent chylous effusion after ligation may result from missed TD branches or development of collateral branches around the ligature. As mentioned earlier, the etiology of post-ligation non-chylous effusion is unclear but may be due to changes within lymphatics not directly associated with the TD, such as pulmonary lymphatics.

TD embolization has also been investigated as a means of treating chylothorax (52). In one study, isobutyl 2-cyanoacrylate was injected through a mesenteric lymphatic catheter in several experimental animals. The embolization compound was mixed with a positive contrast agent to allow fluoroscopic

monitoring of the material in the TD. Complete obstruction of the TD was achieved and complications were minimal. Clinical application of this technique has yet to be evaluated.

Passive or active drainage systems have been advocated by many authors (8,50,51). This mode of therapy has been used either as an initial treatment of chylothorax, or as a secondary treatment in animals that have persistent effusion after TD ligation. Active drains, such as the Denver® pleuroperitoneal shunt, have been used to shunt pleural fluid to the peritoneal cavity or to the venous system. Both methods have been successful in some cases, but complications are common. The drains can become obstructed, especially if the fluid remains chylous. Also, the peritoneal cavity may gradually fail to absorb all of the shunted fluid causing chylous ascites. In our experience, the best results with the Denver shunt has been in dogs with non-chylous pleural fluid (51).

Passive drains have also been used to shunt fluid from the pleural to the peritoneal cavity (8). Penrose drains or fenestrated silastic disks have been placed in the diaphragm to allow passive movement of fluid and subsequent absorption by the peritoneal surfaces. Only a few case reports have described success with this method. A recent study evaluated fenestrated silastic disks implanted in experimental cats (53). Scintigraphic studies were performed to determine whether the disks facilitated long-term drainage. Complete occlusion of the disks was observed by the liver, omentum, and fibrin by days 83-112 in 5 of the 6 cats. These results are consistent with our clinical experience. Poor results were seen due to obstruction of the drains or disks by the abdominal viscera.

CONCLUSIONS

Chylothorax remains a difficult disease to treat, probably because the etiology and pathophysiology are still not fully understood.

Although certain diseases have been shown to be primary causes of chylous effusion in dogs and cats, most cases do not have an identifiable cause. Advancements in lymphangiographic studies have improved our understanding of idiopathic chylothorax, but additional research is needed to help pinpoint specific etiologies.

Although controversial, we favor TD ligation as the best treatment option for idiopathic chylothorax. Results of TD ligation have improved over the past 20 years, but failures are still common. Isolated reports of treatment successes using alternatives to TD ligation are abundant, but few large case series are available to help veterinarians formulate rational treatment plans. Further experimental and clinical research is needed and should continue to focus on the disease mechanism as well as alternative treatment methods.

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