

# A clinical review of the pathophysiology, diagnosis, and treatment of pyothorax in dogs and cats

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## Abstract

**Objective** – To review the current literature in reference to the pathophysiology, diagnosis, and treatment of pyothorax in dogs and cats.

**Etiology** – Pyothorax, also known as thoracic empyema, is characterized by the accumulation of septic purulent fluid within the pleural space. While the actual route of pleural infection often remains unknown, the oral cavity and upper respiratory tract appear to be the most common source of microorganisms causing pyothorax in dogs and cats. In human medicine, pyothorax is a common clinical entity associated with bacterial pneumonia and progressive parapneumonic effusion.

**Diagnosis** – Thoracic imaging can be used to support a diagnosis of pleural effusion, but cytologic examination or bacterial culture of pleural fluid are necessary for a definitive diagnosis of pyothorax.

**Therapy** – The approach to treatment for pyothorax varies greatly in both human and veterinary medicine and remains controversial. Treatment of pyothorax has classically been divided into medical or surgical therapy and may include administration of antimicrobials, intermittent or continuous thoracic drainage, thoracic lavage, intrapleural fibrinolytic therapy, video-assisted thoracic surgery, and traditional thoracostomy. Despite all of the available options, the optimal treatment to ensure successful short- and long-term outcome, including the avoidance of recurrence, remains unknown.

**Prognosis** – The prognosis for canine and feline pyothorax is variable but can be good with appropriate treatment. A review of the current veterinary literature revealed an overall reported survival rate of 83% in dogs and 62% in cats. As the clinical presentation of pyothorax in small animals is often delayed and nonspecific, rapid diagnosis and treatment are required to ensure successful outcome.

(*J Vet Emerg Crit Care* 2015; 25(1): 113–129) doi: 10.1111/vec.12274

**Keywords:** canine, feline, infection, thoracic empyema, thoracostomy tubes

## Abbreviations

DNase	deoxyribonuclease
NT-proBNP	N-terminal pro-B-type natriuretic peptide
RPE	reexpansion pulmonary edema
SIRS	systemic inflammatory response syndrome
VATS	video-assisted thoracic surgery

## Introduction

Pyothorax, also known as thoracic empyema, is characterized by the accumulation of septic purulent fluid within the pleural space. Although numerous retrospective studies, case reports, and nonpeer reviewed articles have been published on the subject, no data exist on the actual incidence of pyothorax in dogs and cats. Furthermore, the actual route of pleural infection often remains unknown with identification of an underlying cause reported in only 2–22%<sup>1–3</sup> of dogs and 35–67%<sup>4–7</sup> of cats. Current evidence suggests parapneumonic spread may be the most common route of infection in cats,<sup>4,5,7–9</sup> while the most common cause of pyothorax in dogs may be more regionally dependent, with grass awns migration common in endemic areas.<sup>3,10</sup> As the clinical presentation of pyothorax in small animals is often delayed and nonspecific, rapid diagnosis and treatment are required to ensure successful outcome. Definitive diagnosis is made

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The authors declare no conflict of interests.

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Submitted April 24, 2014; Accepted September 15, 2014.

based on cytologic examination of pleural effusion or subsequent aerobic and anaerobic bacterial culture results. The approach to treatment for pyothorax varies greatly in both human and veterinary medicine and remains controversial.

While studies have provided useful information on possible etiologies, risk factors, treatment strategies, and patient outcome, prospective studies evaluating the efficiency of different therapeutic options are lacking. Despite a lack of evidence-based guidelines, there appears to be general consensus that antimicrobial therapy in combination with thoracic drainage should be the mainstay of therapy.<sup>11–18</sup> Treatment of pyothorax has classically been divided into medical or surgical therapy and may include administration of antimicrobials, intermittent or continuous thoracic drainage, thoracic lavage, intrapleural fibrinolytic therapy, video-assisted thoracic surgery (VATS), and traditional thoracostomy. Despite all of the available options, the optimal treatments to ensure successful short- and long-term outcome, including the avoidance of recurrence, remain unknown.

In human medicine, pyothorax is a common clinical entity associated with bacterial pneumonia and progressive parapneumonic effusion.<sup>11–13,19–36</sup> The incidence of pyothorax secondary to bacterial pneumonia in adults is reportedly between 5% and 15%<sup>13,14,37–39</sup> with mortality rates of 10–20%.<sup>11,40,41</sup> Higher mortality rates may be more reflective of patient age and comorbidities as death rates related to pneumonia are generally higher in elderly persons.<sup>14,42</sup> Parapneumonic effusion and empyema are relatively rare in pediatric patients with reported mortality rates of <3%.<sup>21,29,43</sup> In order to facilitate establishment of treatment guidelines, the American Thoracic Society divides pleural infections into three stages based on chronicity: an exudative stage, fibropurulent stage, and organizational stage characterized by formation of a pleural peel (scar tissue).<sup>11,14,15,22</sup> Pleural infection occurs most commonly in pediatric and elderly human patients and risk factors mirror those for pneumonia, including immunosuppression, gastro-esophageal reflux, aspiration, poor oral hygiene, diabetes mellitus, alcohol, and intravenous (IV) drug abuse.<sup>11,14,42</sup>

### Pathophysiology

The pleural cavity is a potential space between the lungs and the rest of the thoracic cavity, lined by the visceral and parietal pleura. The mediastinum separates the pleural cavity into left and right sides and, in people, no anatomical communication normally exists between the two pleural spaces.<sup>44</sup> In cats and dogs, controversy exists as to whether a complete membrane prevents movement of fluid and air from one side to the other or if

$$J_v = K_f[(P_c - P_{pl}) - \sigma(\pi_c - \pi_{pl})]$$

$J_v$  = net fluid movement between compartments

$K_f$  = filtration coefficient

$P_c$  = capillary hydrostatic pressure

$P_{pl}$  = pleural hydrostatic pressure

$\sigma$  = reflection coefficient

$\pi_c$  = capillary osmotic pressure

$\pi_{pl}$  = pleural osmotic pressure

**Figure 1:** Starling forces determining pleural fluid turnover.

communication via fenestrations occurs.<sup>45–47</sup> While most cases of pyothorax in small animals involve bilateral effusion, unilateral effusion is not uncommon.<sup>1,3,4,48–50</sup> Regardless of whether the mediastinum is complete or fenestrated, these membranes may be easily disrupted by inflammatory effusion or fenestrations may become occluded secondary to inflammatory debris. Thus, unilateral disease may remain unilateral or progress to a bilateral distribution.

A small amount of fluid is present in the pleural cavity of healthy animals, which serves to lubricate the lungs and to minimize friction during respiration.<sup>16,17,45,51</sup> The production and absorption of pleural fluid is a continuous and dynamic process controlled by Starling's forces and pleural lymphatic drainage (Figure 1).<sup>16,17,45,51,52</sup> Increases in capillary hydrostatic pressure or decreases in colloid osmotic pressure generally result in the formation of a transudate or modified transudate within the pleural cavity.<sup>16,53</sup> The amount of fluid within the pleural cavity remains constant in healthy animals because of a balance between fluid filtration, fluid absorption, and lymphatic drainage.

Pleural membranes consist of a single layer of mesothelial cells and a deeper layer of elastic fibers and sparse smooth muscle cells. Arteries, veins, capillaries, and lymphatics course through this deep connective tissue layer.<sup>45,51,52</sup> The amount of fluid within the pleural space is dependent on a net gradient of pressures, surface area of the pleural membranes, and drainage mechanisms.<sup>53,54</sup> The high hydrostatic pressure within the parietal pleural capillaries and the low oncotic pressure within the pleural space create a net filtration pressure of approximately 9 cm H<sub>2</sub>O, favoring the movement of fluid into the pleural space.<sup>51,54</sup> Approximately 75% of normal pleural fluid is drained via the lymphatics, with smooth muscle contractions and respiratory movement enhancing lymphatic flow.<sup>45,51,52,54</sup> Any fluid remaining in the pleural space then moves into the visceral pleural venous capillaries due to their lower hydrostatic pressure. The great vascularity of the visceral pleura further reduces the resistance to flow and increases net fluid absorption.

Exudative effusions, such as pyothorax, occur when inflammatory conditions within the pleural space lead

to the release of cytokines and vasoactive mediators and subsequent changes in capillary wall permeability or lymphatic outflow impairment.<sup>11,16,44,51,53–56</sup> During inflammation, the release of mediators, such as kinins and histamines, as well as increases in body temperature may lead to endothelial damage and subsequent increases in capillary permeability.<sup>51,54</sup> Protein-rich fluid, cells, and macromolecules leak into and accumulate within the pleural space as a consequence of increased capillary permeability. With inflammation, capillary hydrostatic pressure may increase secondary to increased blood flow, leading to additional fluid accumulation within the pleural space. Thickening of the parietal pleura secondary to inflammation, edema, and fibrin deposition may impede lymphatic outflow and further contribute to pleural fluid accumulation.<sup>54</sup> Impaired protein resorption, secondary to lymphatic obstruction, also leads to increases in pleural space colloid osmotic pressure, also favoring fluid movement into the pleural cavity.<sup>16,54</sup> Bacteria may enter the pleural space via damage to the thoracic wall, trachea, bronchi, lung parenchyma, or esophagus.<sup>17,54</sup>

### **Etiology in Dogs**

Reported causes of pyothorax in dogs include migrating foreign bodies, penetrating or blunt thoracic trauma, hematogenous or lymphatic spread, esophageal perforation, parasitic migration, progression of discospondylitis or vertebral osteomyelitis, parapneumonic spread, previous thoracocentesis, thoracic surgery or internal cardiac massage, neoplasia, and ruptured lung abscesses.<sup>1–3,10,16,17,50,51,57–64</sup> Despite the numerous routes by which the pleural space may become infected, the cause of pyothorax is commonly not found. A review of the veterinary literature identified a reported cause for pyothorax in only 2–22% of cases with the most commonly documented cause of pyothorax being a migrating grass awn or plant material.<sup>1–3</sup> The incidence of inhaled foreign bodies seems to vary depending on geographical location, climate, and vegetation, and occurrence in sporting, hunting, or working-type breeds of dog is common.<sup>16,17,51,59,61</sup> However, despite being frequently cited as a potential initiating event for pyothorax, there are only a handful of documented cases of pyothorax proven to be secondary to the inhalation of foreign plant material in the literature. In a retrospective study of 50 cases of pyothorax in United Kingdom and Ireland, only 3 cases were related to grass inhalation<sup>2</sup> and a large retrospective study of 182 dogs and cats with documented grass awn migration confirmed thoracic migration in only 3 cases.<sup>10</sup> Even with surgery or postmortem examination, foreign plant material is often not identified in the pleural cavity.<sup>3,61,65</sup> Possible explanations for this include failure to visualize foreign

plant material due to its size, location, body-liquid imbibition, inflammatory reaction, migration into another location, or degradation of the plant.<sup>3,51,57,59</sup>

Pyothorax may occur secondary to iatrogenic causes. In a retrospective study of 232 dogs undergoing thoracic surgery, pyothorax occurred as a postoperative complication in 6.5% of cases (15/232).<sup>64</sup> Thoracic surgery for treatment of idiopathic chylothorax, intrathoracic biopsy, and preoperative thoracocentesis was demonstrated to be independent risk factors for postoperative pyothorax, but these findings require further study.

### **Etiology in Cats**

Multiple mechanisms have been implicated in the pathogenesis of pyothorax in cats. While controversy exists as to the predominant cause for feline pyothorax, penetrating thoracic wounds, parapneumonic spread, and foreign-body migration have all been reported.<sup>2,4,5,7,9,16,17,49,66–70</sup> Similar to dogs, identification of an inciting cause remains undetermined in most cases.

One of the most common mechanisms believed to be responsible for pyothorax in cats is direct inoculation of the pleural space by bite wounds from other cats.<sup>16,17,49,71</sup> This belief stems from the fact that bacterial isolates are often similar between pleural infection and cat-bite abscesses.<sup>16,17,49,72</sup> Cats with pyothorax are 3.8 times more likely to live in a multiple-cat household and the assumption made is that cats in multiple-cat households are at increased risk for bite wounds from intercat aggression.<sup>49</sup> Cats with pyothorax are also more likely to present during later summer and fall months, which has been suggested to be related to an increase in outdoor activities, such as fighting and mating behavior.<sup>16,49</sup> However, no association between sex or outdoor access and increased risk for pyothorax has been found.<sup>49,66</sup> A review of the veterinary literature revealed evidence of bite wounds in only 20 cases (15.6%) of the 128 cases of feline pyothorax described.<sup>2,4,49,71</sup>

Several recent studies have provided evidence to suggest pleural infection secondary to parapneumonic spread may be more common than penetrating bite wounds.<sup>4,5,7–9</sup> Pyothorax can occur secondary to extension of infection from the lungs following aspiration of oropharyngeal flora. In fact, cats in multiple-cat households may simply be at greater risk for developing upper respiratory tract infections, predisposing them to development of pyothorax.<sup>66</sup> Necropsy and lung histopathology findings in cats with pyothorax also support pneumonia and pulmonary abscessation as common underlying etiologies for pleural infection.<sup>5,7,49</sup>

Pyothorax secondary to parasitic migration of *Aelurostrongylus abstrusus* and *Toxocara cati* has been reported in cats.<sup>73</sup> Pyothorax associated with aberrant

migration of *Cuterebra* has also been described.<sup>49</sup> Migrating parasites within the pulmonary parenchyma can damage the lung tissue, predisposing to secondary bacterial infection. Hematogenous or lymphatic spread as a cause of pyothorax seems to occur infrequently in cats, but may occur in young animals affected by septicemic diseases.<sup>2,4,5</sup> No association has been demonstrated between pyothorax and feline leukemia virus or feline immunodeficiency virus status.<sup>2,4,5,49,70</sup>

### Microbiology

The oral cavity and upper respiratory tract appear to be the most common source of microorganisms causing pyothorax in dogs and cats.<sup>4,9,16,49,51,66,68,72,74</sup> There is a high prevalence of polymicrobial infection and obligate anaerobes or a mixture of obligate anaerobes with facultative aerobic bacteria are commonly cultured. The most common aerobic organisms isolated in canine and feline pyothorax include *Escherichia coli*, *Pasteurella* spp., *Actinomyces* spp., *Nocardia* spp., *Streptococcus* spp., *Staphylococcus* spp., and *Corynebacterium* spp. Common anaerobic isolates include *Fusobacterium* spp., *Peptostreptococcus anaerobius*, *Bacteroides* spp., *Prevotella* spp., and *Porphyromonas* spp.<sup>1,4,16,48,49,72,74</sup> The population of organisms isolated is likely influenced by geographical location as *Actinomyces* and *Nocardia* spp. are often associated with inhalation of grass-awns, and incidence is regionally dependent.<sup>3,10,48,50,75</sup>

Common isolates in feline pyothorax include *Pasteurella* spp., *Clostridium* spp., *Fusobacterium* spp., *Bacteroides* spp., *Actinomyces* spp., *Peptostreptococcus* spp., and *Prevotella* spp.<sup>49,72,74</sup> Additional uncommon pathogens isolated in less than 20% of cases include *Staphylococcus* spp., *Rhodococcus equi*, *Nocardia* spp., *E. coli*, *Salmonella* spp., *Klebsiella* spp., and *Proteus* spp.<sup>4,66</sup> In kittens and immunosuppressed adults *Mycoplasma* species may be a potential cause of pneumonia and pyothorax.<sup>4,66,68,76,77</sup>

Fungal organisms are uncommonly cultured from feline and canine pleural effusions and isolates include *Cryptococcus* spp., *Candida albicans*, and *Blastomyces dermatitidis*.<sup>4,66,78</sup> Fungal empyema is also rare in people and accounts for less than 1% of adult pleural infections.<sup>11,32</sup> Fungal organisms are most commonly isolated in immunosuppressed and critically ill patients and, although rare, mortality rates up to 73% have been reported.<sup>79</sup> *Candida* spp. are frequently isolated and risk factors that may predispose to infection include use of broad-spectrum antimicrobials intravascular devices and hyperalimentation, previous abdominal surgery, and gastrointestinal dehiscence.<sup>79,80</sup>

### Signalment

Pyothorax appears to predominantly affect younger animals, although animals of any age can be affected. In dogs and cats, the mean age at time of diagnosis is generally between 3 and 6 years.<sup>4,5,16,17,48–51,70</sup> Individual case reports have described the treatment of pyothorax in a neonatal Boxer<sup>62</sup> and in a 4- and 12-week-old kitten.<sup>68,77</sup> No overt sex or breed predisposition has been identified. While male animals have been overrepresented in several studies, this finding has not proven to be statistically significant.<sup>3,4,48,49</sup> Domestic short- and longhaired cats constitute the majority of reported cases of feline pyothorax, but pyothorax in purebred cats has also been described.<sup>5,48</sup> In dogs, medium-to-large breeds are typically affected with hunting/working breed dogs overrepresented. Common breeds reported include Labrador Retrievers, Springer Spaniels, Border Collies, German Shepherd Dogs, Brittany Spaniels, Golden Retrievers, Pointers, and Airedale Terriers.<sup>3,17,48,50,59</sup>

### Clinical Findings

Pyothorax is often insidious in nature and associated with nonspecific clinical signs. Dogs and cats may present acutely or after several days to months of illness and it is not uncommon for a patient to present late in the course of the disease.<sup>16,66,81</sup> Time from onset of clinical signs to presentation varies and has been reported between days and months.<sup>4,5,48,59</sup> Disease presentation in neonatal and pediatric patients is also highly variable and, in animals that die without clinical signs of illness, diagnosis must be made postmortem.<sup>68,82</sup>

Common clinical signs in dogs and cats with pyothorax include tachypnea, dyspnea, cough, lethargy, weight loss, and anorexia.<sup>5,16,17,66,81</sup> Signs found on physical examination include dyspnea, fever, and poor body condition. However, absence of a fever does not rule out pyothorax, as up to 50% of cats present are with normal or low body temperature.<sup>4,48,49</sup> When pleural effusion is significant enough to restrict lung expansion, a restrictive breathing pattern, characterized by rapid, shallow respirations, may be observed. Auscultation of the chest generally reveals loss of normal breath sounds and “muffled” heart sounds. In severe cases, signs consistent with systemic inflammatory response syndrome (SIRS) or sepsis can occur, including pale mucous membrane, hypothermia, tachycardia or bradycardia, and dehydration.<sup>8,49</sup> Sepsis appears to be a common sequel to pyothorax in cats with 40% of cats in one retrospective study meeting the criteria for SIRS or sepsis.<sup>49</sup> In the same study, nonsurvivors had lower heart rates than survivors, but not all nonsurvivors were bradycardic, limiting the clinical application of this observation.

Bradycardia was significantly more common in cats that were also hypothermic. Additionally, pyothorax was found to be the most common underlying etiology in a retrospective study of severe sepsis in cats.<sup>8</sup> To the authors' knowledge, the prevalence of sepsis and SIRS in dogs with pyothorax has not been reported.

### Diagnosis

Diagnosis of pyothorax in small animals is generally straightforward and should be considered in any patient presenting with a supporting clinical history and consistent physical exam findings. Thoracic imaging can be used to support a diagnosis of pleural effusion, but cytologic examination or culture of pleural fluid are necessary for a definitive diagnosis of pyothorax.

### Clinicopathologic findings

Although results are generally nonspecific and nondiagnostic for pyothorax, a minimum database, consisting of hematology, biochemistry, and urinalysis can be performed, as results may guide patient management. The most common hematologic finding is a neutrophilic leukocytosis with or without a left shift, which occurs in 56–93% of dogs<sup>48,50,59,60,83</sup> and 36–73% of cats.<sup>4,48</sup> However, its absence does not rule out a diagnosis of pyothorax as sepsis and neutrophil sequestration can manifest as a neutropenia with a degenerative left shift. One study in cats demonstrated a higher total white blood cell count in animals that survived, although the finding was nonsignificant when neutrophil counts were compared.<sup>49</sup> Similar associations have not been demonstrated in dogs.<sup>3</sup> Mild-to-moderate normocytic normochromic anemia is also common in patients with chronic disease.<sup>4,16,17,48,60,71,81,84,85</sup>

Biochemical results may include hypoproteinemia, hypoglycemia or hyperglycemia, electrolyte abnormalities, and increases in liver-enzyme activity and total bilirubin concentration.<sup>3,16,48,49</sup> There have been no prospective studies evaluating biochemical abnormalities as prognostic markers in dogs or cats. Lower cholesterol concentrations were found to be prognostic for survival in one retrospective study in cats with pyothorax, although all cats in the study had cholesterol concentrations within reference limits, making the clinical significance of this finding questionable.<sup>49</sup>

### Diagnostic Imaging

#### Ultrasonography

The increasing availability of portable bedside thoracic ultrasonography has allowed clinicians a means to rapidly diagnosis pleural effusion in critical patients with respiratory distress. Ultrasound can be used to

estimate the size of an effusion, to differentiate free from loculated fluid, and to determine the echogenicity of the fluid.<sup>16,66,86,87</sup> Exudative effusions are generally echogenic in appearance and fibrinous adhesions may be visualized extending between the pleura. Pulmonary abscesses, intrathoracic masses, and foreign bodies can also sometimes be visualized ultrasonographically.<sup>5,16,66,88,89</sup> In human medicine, ultrasonography remains the most sensitive method to visualize loculations and septations in an effusion, but it is not commonly performed as a purely diagnostic tool.<sup>13,87,90</sup> An added benefit of ultrasound is that it can also be used to guide thoracocentesis, chest drain insertion, and aspiration or biopsy of parenchymal or pleural mass lesions.<sup>11,12,24,59,87,90</sup>

#### Radiography

Thoracic radiographs are often the initial imaging modality of choice for diagnosis of pleural effusion in human and veterinary patients. However, if a patient's respiratory distress is severe, therapeutic thoracocentesis should be performed prior to obtaining radiographs. A single dorsoventral view can be used, with minimal patient stress, to confirm the presence of large volume effusion when ultrasonography is not available. Horizontal beam radiography can also be used in a standing patient to detect pleural effusion. If imaging is performed before thoracocentesis, radiographs will demonstrate the classic signs of pleural effusion, including retraction of lung lobes from the thoracic wall, pulmonary atelectasis, interlobar fissure lines, and loss of the cardiac silhouette.<sup>91</sup> Although unilateral effusions are not uncommon, bilateral effusion occurs frequently and has been reported in 70–90% of cats<sup>4,48,49</sup> and 50–93% of dogs<sup>1,48,50</sup> with pyothorax. In contrast, effusions are typically unilateral in human empyema patients<sup>12,39</sup> and bilateral effusions are associated with increased mortality in patients with community-acquired pneumonia.<sup>39</sup> Radiographs should be repeated following pleural effusion drainage to look for evidence of underlying etiology, such as a mass, foreign body, or pulmonary pathology.<sup>16,17</sup>

#### Computed tomography

Contrast-enhanced computed tomography (CT) is commonly used in human medicine, and is being used with increasing frequency in veterinary medicine for the assessment of pyothorax. When compared to thoracic radiography, CT scanning has a greater sensitivity for detection of small pleural effusion and it can provide additional information about the extent and nature of thoracic disease.<sup>92,93</sup> With CT scanning, one is able to view the chest cavity in its entirety, including the mediastinum, lung parenchyma, and chest wall. Also, conditions that thicken the pleura, such as exudative pleural

effusions, render them visible on CT scan. In human patients, contrast enhancement of the parietal and visceral pleura and their separation by pleural fluid on CT scan is referred to as the "split pleura sign."<sup>11,13,94</sup> While non-specific, when seen in patients with supporting clinical signs, such as fever and pneumonia, it is suggestive of empyema. Contrast-enhanced CT is also used to differentiate empyema from lung abscess with nearly 100% accuracy.<sup>14,95</sup> In veterinary patients, CT may also be used to screen for pulmonary abscess or foreign bodies, as identification of these lesions may indicate a need for surgical therapy.<sup>96</sup> In cats and dogs with intrathoracic migration of grass awns, CT was able to trace the path of the foreign body and to identify more sites of abnormality when compared to radiographic and ultrasonographic findings.<sup>89</sup> However, a thorough exploration of the thoracic cavity should be performed in all surgical cases as lesion location may not be reliably predicted based on pleural fluid distribution on CT.<sup>96</sup> British Thoracic Society guidelines for children with empyema do not recommend routine use of CT as the radiation from scans can be high and radiography and ultrasonography are sufficient for diagnosis in the majority of cases.<sup>12</sup> Cost, accessibility, the need for anesthesia, and radiation exposure from CT may also be of considerations in small animals.

### Thoracentesis and pleural fluid evaluation

Pleural fluid should initially be sampled via a diagnostic or therapeutic thoracentesis to aid in fluid classification. Ultrasonographic guidance may be helpful if difficulty is encountered in obtaining pleural fluid or if the effusion is small. Pleural fluid samples should ideally be collected before beginning antimicrobial therapy and fluid should be sent for aerobic and anaerobic bacterial culture and gram stain to identify underlying pathogens and to ultimately tailor antimicrobial therapy based on antimicrobial sensitivities. Fluid samples should be collected into an ethylenediaminetetraacetic tube for cytology and into a serum (red top) tube or culturette for microbiological culture.<sup>16,53,81</sup> The prompt collection of specimens, with minimal exposure to air, is particularly important for isolation of anaerobic organisms. Sample collection into an anaerobic bacterial transport medium (BBL, Port-A-Cul) is recommended as culturing from a serum tube or culturette may result in false-negative results. Anaerobic cultures should not be refrigerated and should ideally be processed within 24 hours of sample collection.<sup>53</sup> Culturing pleural effusion in blood culture bottles, in addition to standard laboratory culture, may increase microbial yield, independent of the inoculum volume.<sup>97</sup> Pending microbiological culture results, finding intracellular bacteria on effusion

cytology is the gold standard for initial diagnosis of a septic effusion.<sup>4,48,53,71,74,98</sup>

The gross appearance of the pleural fluid should be noted as septic effusions are often turbid or opaque and may be malodorous.<sup>5,16,17,71,98</sup> If the fluid collected is not obviously purulent, additional laboratory fluid analysis may be useful. The traditional method of fluid classification and analysis categorizes effusions based on protein count and cellularity as either transudates, modified transudates, or exudates.<sup>53,99</sup> However, overlap can occur within the three traditional categories and additional classification schemes, which focus on categorizing effusions based on underlying etiology, have been proposed.<sup>100,101</sup> Human pleural effusions have classically been divided into transudate or exudate based on the Light criteria that consists of measurement of the protein and lactate dehydrogenase (LDH) concentration in the pleural fluid and serum.<sup>102</sup> Generally, an effusion glucose of <3.3 mmol/L (60 mg/dL), LDH of >1,000 U/L (1000 units/dL), and a pH of <7.2 is suggestive of an empyema.<sup>11,13,14,22,23,38,44</sup> A meta-analysis of pleural fluid analysis in patients with parapneumonic effusions identified a pleural fluid pH of <7.2 as the strongest indicator of complicated parapneumonic effusion requiring chest tube drainage.<sup>103</sup> An algorithm, based on results of pleural fluid biochemical analysis in people, exists to determine the risk of poor outcome and to determine which patients would benefit from more aggressive treatment options, such as pleural fluid drainage.<sup>11,13,19</sup> Currently, no such algorithm exists in veterinary medicine and there is no evidence to support that these findings are applicable to the investigation of canine and feline pyothorax. Light's criteria have been evaluated in the classification of feline pleural effusion.<sup>66,104</sup> In a recent prospective study, pleural fluid LDH and pleural fluid/serum total protein ratio were found to be the most sensitive and specific markers when classifying pleural fluid as a transudate or exudate, although pleural fluid pH was not measured.<sup>105</sup> Biochemical markers of sepsis have also been evaluated in dogs and cats with peritoneal effusion. Differences in blood and fluid glucose and lactate concentrations were found in dogs with nonseptic versus septic effusions, but fluid cytology and total nucleated cell counts were more reliable in differentiating septic from nonseptic effusions in cats with peritoneal effusion.<sup>106</sup> While these results may apply to patients with septic pleural effusions, additional studies are needed to evaluate glucose and lactate concentrations in both sterile inflammatory as well as septic effusions.

In cats with pleural effusion, the utility of blood and pleural N-terminal pro-B-type natriuretic peptide (NT-proBNP) concentrations in differentiating cardiac from noncardiac causes of pleural effusion has been evaluated.<sup>107,108</sup> In general, plasma and pleura

NT-proBNP concentrations appear to be higher in cats with pleural effusion secondary to cardiac disease. However, high plasma concentrations of NT-proBNP have been found in cats with pyothorax and no echocardiographic evidence of cardiac dysfunction.<sup>107</sup> Serum and pleural NT-proBNP concentrations have also been evaluated in people with pleural effusion and concentrations appear to be higher in patients with pleural effusion secondary to cardiac disease.<sup>109</sup> However, patient comorbidities, such as sepsis, renal disease, and diabetes mellitus, can also lead to increased NT-proBNP concentrations, making the utility of this biomarker limited without further studies.<sup>110,111</sup>

Additional biochemical markers, such as tumor necrosis factor (TNF)- $\alpha$ , C-reactive protein, and procalcitonin, have been evaluated in human empyema patients and, while these markers may help differentiate septic from other exudative effusions, further studies are needed to elicit their exact role.<sup>112–114</sup> To the authors' knowledge, there are no studies to date evaluating biomarkers in dogs with pleural effusion.

### Treatment

Treatment of pyothorax has classically been divided into medical or surgical therapy. Although evidence-based guidelines are lacking in both veterinary and human medicine, antimicrobial therapy in combination with thoracic drainage is generally accepted as the mainstay of therapy.<sup>1,3,4,11–13,16–18,24,48,49,59,81,83</sup> In patients who present with signs of SIRS or sepsis, cardiovascular stabilization with IV fluids to correct shock, dehydration, electrolyte, and acid-base abnormalities is an important step in patient management. Supplemental oxygen should also be administered to patients with hypoxemia or cardiovascular instability.

### Medical Management

#### Antimicrobial therapy

Given the wide variety of pathogens associated with canine and feline pyothorax, initial antimicrobial therapy should be broad-spectrum and based on local antimicrobial policies and resistance patterns. For treatment of empyema, combination antimicrobial therapy with both anaerobic and aerobic coverage is recommended.<sup>11–13,16,17,81</sup> Once culture and susceptibility results are known, antimicrobial treatment can be altered to a narrower spectrum. Negative culture can occur from antimicrobial use prior to pleural fluid evaluation or errors in sample handling.<sup>11,12</sup> Approximately 40–83% of pleural fluid cultures are negative in adults and children with pleural infection, as most patients with pleural infection will have already received

antimicrobials.<sup>11,12,40,115</sup> British Thoracic Society guidelines recommend aerobic and anaerobic blood cultures be performed in all patients with suspect pleural infection as positive blood culture results, which occur in roughly 10–22% of patients with empyema, are often the only source of positive microbiology.<sup>11,12,116,117</sup>

Empiric antimicrobial therapy for canine pyothorax may include use of a potentiated penicillin, such as ampicillin with sulbactam in combination with a fluoroquinolone for improved gram-negative coverage. Aminoglycosides should be avoided as they have poor penetration into the pleural space and are potentially nephrotoxic and ototoxic.<sup>11–13,18</sup> Antimicrobial therapy for feline pyothorax should include coverage for *Pasteurella* spp., which are susceptible to penicillin and its derivatives.<sup>18,72</sup> As enterobacteriaceae are infrequently isolated in feline pleural infection, monotherapy with a potentiated penicillin may provide adequate coverage.<sup>4,18,48,71,72,74</sup>

The ideal route of antibiotic administration in patients with pyothorax is unknown. British Thoracic Society guidelines for children with empyema recommend all cases initially be treated with IV antimicrobials.<sup>12</sup> Guidelines in adults with complicated parapneumonic effusions are similar with the recommendation to change from IV to oral therapy with clinical evidence of improvement in sepsis.<sup>11</sup> Generally, IV antimicrobials are continued until the patient is afebrile and thoracostomy tubes have been removed and then the patient is switched to oral antimicrobials for an additional 1–4 weeks. While there are no evidence-based guidelines in veterinary medicine, antimicrobials are generally administered IV until the patient is stable and eating. Although their use has not been critically evaluated in veterinary patients with pyothorax, infusion of intrapleural antimicrobials is not recommended in human medicine.<sup>11</sup> In a recent veterinary study, duration of thoracostomy tube placement was shorter in patients who received intrapleural antimicrobials versus those who did not (4.8 versus 6.3 d).<sup>48</sup> However, only 6 patients received intrapleural antimicrobials and the statistical significance of this finding was not investigated.

The ideal duration of antimicrobial treatment for pleural infection is unknown and remains a topic of controversy. There is also a lack of data on whether different organisms require different durations of therapy. Prescribed antimicrobial therapy in human and veterinary patients is often prolonged, although there is a lack of clinical evidence to support this recommendation. Guidelines are also lacking as to the duration of antimicrobial therapy in patients treated medically versus those treated surgically. British Thoracic Society guidelines for adults with empyema recommend a minimum of 3 weeks of oral antimicrobial treatment.<sup>11</sup> Ultimate

duration of therapy is based on each patient's clinical and radiographical improvement. One standard approach in veterinary medicine is the continuation of oral antimicrobials for 2 weeks past resolution of pleural effusion on thoracic radiographs.

### Thoracic drainage

Antimicrobial therapy alone is generally an ineffective treatment for pyothorax and successful medical management includes drainage of purulent material from the pleural cavity.<sup>11,12,22,48</sup> The goal of thoracic drainage is to remove as much infected fluid as possible to improve the patient's symptoms, to minimize the potential for subsequent procedures, and to optimize postdrainage chest imaging. Needle thoracocentesis should be performed immediately in patients who present in respiratory distress. However, following initial emergency stabilization, there is considerable debate as to the optimal strategy for continued thoracic drainage. Options for drainage include single or repeated needle thoracocentesis and chest tube thoracostomy. To the authors' knowledge, there have been no prospective randomized studies in veterinary or human medicine comparing needle thoracocentesis to chest tube thoracostomy in the management of pyothorax. Even when the decision is made to place an indwelling chest tube, there is controversy regarding optimal size, number, and dwell time. Further studies are also needed to determine the benefit of pleural lavage, thoracostomy tube flushing and suction, and the use of adjunct treatments, such as intrapleural fibrinolytics.

### Thoracocentesis

Therapeutic drainage of pleural effusion via single or repeated needle thoracocentesis has been reported in veterinary medicine.<sup>1,4,6,17,49,71</sup> Successful outcome likely depends on patient selection and the presence of underlying pathology, such as loculations, pulmonary abscess, or migrating foreign material.<sup>3,16</sup> Use of single or repeat needle thoracocentesis in the successful management of feline pyothorax has been reported.<sup>4,49,71,82</sup> However, treatment with needle thoracocentesis alone in cats has also been associated with a low cure rate and mortality rates between 50% and 80% in several studies.<sup>6,18</sup> British Thoracic Society guidelines recommend repeated chest taps not be performed in children with significant pleural infection.<sup>12</sup> Repeat needle thoracocentesis is also generally not recommended in dogs and cats because of the morbidity and risk associated with this technique.<sup>16-18,49,81</sup> When performing repeat needle thoracocentesis, patient comfort, risk of infection, and the need for sedation or general anesthesia should be considered.

Numerous techniques for performing needle thoracocentesis have been described and reported complications include pneumothorax, hemothorax, pulmonary hemorrhage, organ laceration, infection, and reexpansion pulmonary edema (RPE).<sup>24,118,119</sup> The incidence of pneumothorax following thoracocentesis in dogs and cats is unknown. Pneumothorax secondary to laceration of lung tissue is the most common complication of thoracocentesis in adult patients, with a reported incidence of 6%.<sup>120</sup> Of those patients who develop pneumothorax, 34% go on to require chest drain insertion.<sup>120</sup> Hemorrhage can occur secondary to laceration of intercostal and pulmonary arteries.<sup>24</sup> Imaging guidance of thoracocentesis has been associated with a reduced risk of pneumothorax, hemorrhage, and organ laceration in human patients and it is recommended whenever possible.<sup>11,121</sup>

RPE is not well documented in small animals, although it has been reported following treatment of chronic chylous effusion and with diaphragmatic hernia repair.<sup>122,123</sup> RPE has been reported as a potentially life-threatening complication of thoracocentesis in people, with a reported incidence of 0.2–14% and a mortality rate of 20%.<sup>24,124,125</sup> Noncardiogenic edema can occur secondary to rapid reexpansion of chronically collapsed lung lobes. Clinical presentation varies and onset of symptoms may occur within several hours up to 24 hours following pleural drainage. Symptoms include tachypnea, dyspnea, cough, and cardiovascular instability.<sup>125</sup> Radiographic evidence of RPE has also been demonstrated in asymptomatic patients.<sup>121</sup> Controversy exists as to whether or not RPE is related to the total amount of pleural fluid initially removed from the chest cavity. Recommendations exist for limiting initial volume of pleural fluid removed to <1 L at a time in adults and 10 mL/kg body weight in children, but these guidelines are based only on expert opinion.<sup>12,23,125</sup>

The actual incidence of infection secondary to thoracocentesis is low in people with one study finding no evidence of infection following 2,489 ultrasound-guided thoracocentesis in 2,489 patients.<sup>126</sup> The incidence of infection secondary to single or repeat thoracocentesis in dogs and cats is unknown. Preoperative thoracocentesis was identified as an independent risk factor for development of postoperative pyothorax in dogs undergoing thoracic surgery. Dogs with evidence of preoperative pyothorax were excluded from the study.<sup>64</sup>

### Tube thoracostomy

While small parapneumonic effusions may respond to antimicrobials plus simple drainage, this protocol has been associated with a prolonged duration of illness and hospital stay in children.<sup>12</sup> British Thoracic Society guidelines recommend chest tube drainage if pleural fluid is obviously purulent on aspiration, results of



The patient should be placed in lateral or sternal recumbency and the lateral side of the affected hemithorax should be clipped from the caudal margin of the scapula to the last rib and from the spine to the sternum. Based on patient temperament and clinical stability, sedation or anesthesia should be provided. The skin should be aseptically prepared prior to drain placement.

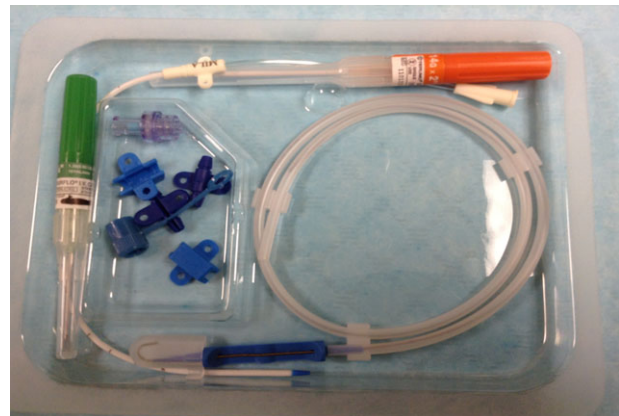
1. Using a scalpel blade, make a small skin incision at the 7th or 8th intercostal space, in the middle third of the chest, to facilitate drain placement.
2. Enter the pleural cavity with the introducer catheter at the cranial edge of the rib and advance the catheter directly into the thorax over the stylet.
3. Remove the stylet and thread the guidewire through the catheter and advance in a cranioventral direction until resistance is encountered.
4. Once the guidewire has been advanced to the desired length, the catheter is removed over the guidewire, leaving the latter in place.
5. Slide the distal end of the chest drain onto the guidewire and advance until the guidewire comes through the hub.
6. Grasp wire above the chest drain and advance the drain into the chest cavity by grasping the drain near the insertion site and gently pushing in a cranioventral direction.
7. Remove the guidewire and attach the closed valve and cap to the drain hub. Using a syringe, immediately aspirate the drain for air and fluid.
8. The chest drain should be secured to the skin by suturing each wing through the suture holes and across the suture groove.
9. The drain insertion site should be covered with an adhesive dressing to minimize movement of the drain.

**Figure 2:** Placement of a 14-gauge small-bore wire-guided chest drain (MILA International, Inc, Erlanger, KY, USA) using a modified Seldinger technique.

pleural fluid culture are positive, pleural fluid pH < 7.2, loculations are present on thoracic radiographs or ultrasound, or if there is poor clinical progress with antimicrobial therapy alone.<sup>11,13</sup> There is currently no consensus on optimal thoracostomy tube size for drainage and there have been no randomized clinical trials evaluating clinical outcome in patients with pleural infection treated with differing sized chest drains.

Placement of indwelling thoracostomy tubes is generally well tolerated and may provide superior drainage to needle thoracocentesis.<sup>1,17,18,49</sup> Thoracostomy tube insertion can be done using either blunt dissection, the trocar, or modified Seldinger technique (Figure 2). As there are currently no guidelines in veterinary medicine, the decision to place unilateral versus bilateral thoracostomy tubes should be made based on the volume and distribution of pleural fluid.<sup>16–18,48,70</sup> Traditionally, large-bore trocar tubes have been recommended due to the belief that smaller tubes would become obstructed by thick exudate and fibrin and fail to completely drain effusion.<sup>15,16,22,24,127</sup> The reported complication rate of large-bore chest tube insertion in people varies between 5% and 35%.<sup>127</sup> Complications associated with large-bore thoracostomy tube insertion include pneumothorax, hemorrhage, lung laceration, arrhythmias, pain, anesthetic complications, subcutaneous fluid leakage, and infection.<sup>4,12,17,127</sup>

Because there is no evidence that large-bore chest drains are more efficacious in the treatment of pleural infection, small-bore (8–16 Fr) chest tubes are being used with increasing frequency in human



**Figure 3:** MILA small-bore wire-guided chest drain kit.

medicine.<sup>12,24,40,115,128</sup> Use of small-bore (14 Fr) wire-guided chest tubes has been reported in the treatment of dogs and cats with pyothorax (Figure 3).<sup>127</sup> Proponents of small-bore chest tubes advocate their use because they are easier and less traumatic to insert, they can often be placed under sedation, are better tolerated once in place, and they may be associated with fewer placement-related complications.<sup>15,16,18,24,127</sup> Regular flushing of small-bore chest tubes has been recommended to avoid catheter blockage, but there is no evidence to support this practice. In contrast to data published in the human literature, drain obstruction was not reported in a study evaluating the use of small-bore chest drains in dogs and cats with pleural effusion<sup>127</sup> and further studies are necessary to determine if routine flushing is necessary.

Regardless of size, correct positioning of the chest tube is likely more important for effective pleural drainage. Routine use of imaging guidance (ultrasound or CT) is recommended for thoracostomy tube insertion in pediatric and adult empyema patients.<sup>11,12</sup> Postplacement thoracic radiographs are routinely used in veterinary medicine to verify tube positioning.<sup>16–18,70,81</sup> Inability to aspirate effusion through a thoracostomy tube does not equate with failure of medical management and should prompt the clinician to investigate with diagnostic imaging. If, based on thoracic radiography, the tube is not properly positioned within the thoracic cavity, then the tube should be removed. If the thoracostomy tube is properly positioned but pleural effusion is present, flushing the drain with sterile saline can be attempted to relieve obstruction. If the tube is obstructed and cannot be flushed or if fluid is not aspirated following flushing, it should be pulled and another drain can be placed at the discretion of the attending clinician.

As there is no information on optimal thoracostomy tube dwell time in veterinary medicine, timing of thoracostomy tube removal is essentially a clinician decision. While insertion of a temporary unilateral chest drain for initial drainage of effusion has been reported,<sup>59</sup> most drains are left in place for an extended period of time. The reported median duration of indwelling thoracostomy tubes in cats and dogs is between 4 and 8 days.<sup>1,4,48,49,71</sup> Proposed criteria for thoracostomy tube removal include clinical patient improvement, a decrease in pleural fluid volume to less than 2 mL/kg/day, resolution of infection on cytologic evaluation of aspirated fluid, and radiological evidence of successful pleural fluid drainage.<sup>12,13,16,18,24,70,81,129,130</sup> Cytologic findings consistent with resolution of infection include absence of microorganisms and decreased numbers of neutrophils with a less degenerative appearance.<sup>70,81</sup> Neutrophil numbers alone may not be reliable indicators of persistent infection as cell numbers may be artifactually increased when fluid production is minimal.<sup>41</sup> When cytology is inconclusive, serial aerobic and anaerobic culture of pleural fluid may be useful in documenting resolution of infection. There is no evidence supporting routine chest radiographs immediately following thoracostomy tube removal.

#### **Intermittent versus continuous suction**

There are few evidence-based data in veterinary and human medicine to guide optimal thoracostomy drain management. Although believed to improve drainage of exudative fluid and to decrease the incidence of drain obstruction, indications for flushing and suction of chest drains are unclear. Thoracostomy tube suction can be done intermittently or continuously using a unidirectional flow drainage system. To date, there have been no

large prospective veterinary studies comparing intermittent to continuous suction drainage in the treatment of pyothorax and, although studies have reported success using suction in the management of pyothorax,<sup>50,57,61,83</sup> this has not been compared to cases managed without suction. Application of continuous suction (5–20 cm H<sub>2</sub>O) using a 3-chamber system is often employed in the treatment of adult and pediatric empyema, although there is little evidence to guide this recommendation.<sup>11–13</sup>

Tube thoracostomy with continuous suction has the proposed benefit of maximal effusion drainage although it may not necessarily decrease the time needed to manage pyothorax.<sup>16,18,81,83,130</sup> Continuous chest drainage units are labor and equipment intensive as tube obstruction, dislodgement, or leakage can be rapidly fatal.<sup>18,81,83,130</sup> Closed-tube thoracostomy with intermittent suction requires minimal expense and less monitoring, which may make it more ideal in most practice settings. There are no standards for frequency of intermittent suction, although it is often performed more frequently during the initial 24–48 hours and then less often as pleural fluid volumes decrease.<sup>17,18,81,130</sup> Ideally, all patients with indwelling chest tubes should be referred to a 24-hour facility for continued overnight monitoring.

#### **Thoracic Lavage**

Many veterinary studies have recommended regular pleural lavage in the treatment of pyothorax.<sup>1,4,48,71,81,104</sup> However, there are currently no evidence-based guidelines regarding the ideal lavage solution, optimal dwell time, frequency, or duration of pleural lavage therapy in veterinary patients. Volume and gross characteristics of the aspirated fluid are often used to guide the frequency of lavage and suction.<sup>18,81</sup> Lavage is generally performed using warm physiologic saline via a thoracostomy tube, although use of buffered balanced crystalloid solutions has been described.<sup>1,18,48,81,104</sup> Proposed benefits of pleural lavage include reduction of pleural fluid viscosity, facilitation of fluid drainage, prevention of thoracostomy tube obstruction, dilution and reduction of bacteria and inflammatory mediators, and debridement of the pleural cavity with breakdown of adhesions.<sup>1,16,18,131</sup> Standard therapy protocols for the treatment of human empyema do not include routine pleural lavage.<sup>11,12,131</sup> There have been no randomized clinical trials comparing treatment with intermittent pleural lavage via thoracostomy tube to standard treatment without lavage. There are also no prospective studies evaluating whether thoracic lavage is associated with shorter indwelling thoracostomy tube times or length of hospitalization. In a study evaluating outcome in dogs treated for pyothorax, pleural lavage was associated with higher short- and long-term survival rates when compared to dogs treated with

thoracocentesis or thoracostomy tube without lavage.<sup>1</sup> Demetriou et al reported shorter duration of thoracostomy tube placement and faster recovery in dogs and cats treated with pleural lavage.<sup>48</sup> However, only 8 of 50 (16%) patients did not have pleural lavage performed, making it difficult to draw conclusions from these results.

The authors of one study did not recommend routine pleural lavage in cats because of the perceived risk of introducing nosocomial infection and the potential for not being able to aspirate the large volume of fluid placed into the thoracic cavity.<sup>49</sup> Volume overload is a potential complication of pleural lavage as absorption of lavage fluid can occur via inflamed pleural tissues. Close monitoring of “ins and outs” is recommended and the volume of fluid instilled and aspirated should be recorded. Recovery of 75% or more of the volume infused is expected and lower aspirate volumes should prompt the clinician to investigate for thoracostomy tube complications or loculations.<sup>18,81</sup> Hypokalemia secondary to pleural infusion of a large volume (50 mL/kg) of physiologic saline has been reported in a cat.<sup>4</sup>

#### **Intrapleural fibrinolytics**

Inflammation within the pleural cavity leads to fibrin deposition, adhesions, and loculation of pleural fluid, making it difficult to effectively drain pleural effusion. The role of fibrinolytics in the management of pleural effusions is controversial. The largest trial to date in human medicine, the Multicenter Intrapleural Sepsis Trial (MIST1), failed to demonstrate improvement in mortality, the rate of surgery, or the length of hospitalization with intrapleural administration of streptokinase.<sup>40</sup> This conclusion was subsequently supported by a meta-analysis<sup>132</sup> and current British Thoracic Society guidelines do not recommend the routine use of intrapleural fibrinolytics in adult empyema patients.<sup>11</sup> In contrast, British Thoracic Society guidelines for the management of empyema in children recommend the use of intrapleural fibrinolytics in the treatment of complicated parapneumonic effusion or empyema.<sup>12</sup> This recommendation is based solely on findings from one small multicenter randomized placebo-controlled trial evaluating urokinase use in children with empyema and several other case series reporting on the use of intrapleural fibrinolytics.<sup>115,133,134</sup> Side effects associated with intrapleural fibrinolytic use include immediate hypersensitivity reaction, fever, bleeding, and discomfort during intrapleural injection.<sup>11,12</sup>

Use of other intrapleural agents, in combination with fibrinolytics, has been reported in experimental and clinical animal and human trials.<sup>41,135,136</sup> The intrapleural administration of tissue plasminogen activator and deoxyribonuclease (DNase) has been shown to improve

fluid drainage and to reduce the need for surgery and length of hospitalization in adults with pleural infection.<sup>41</sup> Interestingly, treatment with either tissue plasminogen activator or DNase alone was ineffective. The authors propose that the addition of DNase, a mucolytic that cleaves bacterial DNA and decreases fluid viscosity and biofilm formation, is necessary for fibrinolytics to clear pleural fluid. While the use of fibrinolytics has been described in the treatment of canine and feline pyothorax,<sup>18</sup> the efficacy of these agents has not been evaluated and there is currently insufficient data to support their routine use in veterinary patients.

Administration of intrapleural anticoagulants, such as heparin, is advocated by some veterinary clinicians.<sup>1,81,130</sup> A recent retrospective study found the addition of heparin (10 U/mL) to lavage fluid improved short-term, but not long-term, survival in dogs treated for pyothorax.<sup>1</sup> Additional prospective studies are needed before routine intrapleural administration of heparin can be recommended.

#### **Indications for surgery**

To date, there have been no large clinical trials, in people or veterinary patients, comparing surgical with medical therapy. No objective evidence-based criteria exist to define the point at which surgical intervention is required in patients with pyothorax and the decision to operate remains subjective. Controversy exists as to whether surgery should be the initial treatment of choice or if it should be reserved only for cases that fail medical management.

There is conflicting evidence in the veterinary literature that surgery improves long-term outcome in dogs and cats with pyothorax. In Rooney and Monnet, surgical treatment was associated with a better long-term outcome than medical therapy, with 78% and 25% of dogs disease free after 1 year, respectively.<sup>3</sup> In the same study, treatment was 5.4 times more likely to fail in dogs treated medically. In a more recent study, surgical intervention was associated with better short-term but not long-term outcome in dogs treated for pyothorax.<sup>1</sup> In a study of feline pyothorax, the short-term survival rate for cats treated surgically was significantly higher than the survival rate for cats treated with medical therapy alone (100% versus 62.9%).<sup>49</sup> All 5 cats that underwent thoracotomy failed to respond to initial medical therapy and surgery was curative. Length of hospitalization was also significantly longer in the surgical group when compared to other surviving cats and information on long-term outcome was not available. A recent retrospective study evaluating treatment approach and outcome in cats with pyothorax found cats who underwent delayed

thoracotomy had the highest cure rate, although long-term follow-up was only available for one cat.<sup>6</sup>

British Thoracic Society guidelines in adults and children with empyema recommend patients receive surgery if they are persistently septic after 5–7 days of medical therapy with antibiotics and chest tube drainage.<sup>11,12</sup> Subjective criteria for failure of medical therapy in small animals include persistence of pleural effusion or infection despite appropriate antimicrobial therapy and chest tube drainage or absence of clinical improvement after 3–7 days.<sup>1,16,18,48,49,70,81</sup> Early observational studies in adults with empyema indicated patients with loculations or purulent fluid were more likely to require surgical drainage. However, many of these patients recovered without surgery and these findings have not been supported by recent data. Recommendation for early surgical intervention in dogs and cats has been made based on evidence of pulmonary or mediastinal lesions or foreign material on diagnostic imaging and isolation of *Actinomyces* spp.<sup>3,4,9,16,17,48,49,59,61,65,67,70,81</sup> While this recommendation may be valid in areas where grass awns are prevalent, *Actinomyces* spp. exist as part of the normal oropharyngeal flora in dogs and cats and, when isolated in pleural effusion, infections have been shown to resolve without surgery.<sup>4,6,83,137</sup>

Surgical options include VATS and thoracotomy. The type of procedure performed depends on patient age and comorbidities, surgeon's preference and availability of equipment. Goals of surgery include identification and removal of any inciting cause for effusion (eg, grass awn foreign body, pulmonary abscess), removal of grossly abnormal or necrotic tissue, breakdown of fibrous adhesions, lavage of the pleural cavity to remove infected fluid and to decrease bacterial load, and placement of bilateral thoracostomy tubes.<sup>9,16–18,49,67,81</sup>

### Thoracotomy

When surgical intervention is elected in the treatment of pyothorax, the preferred approach to the thorax is a median sternotomy, as it allows for exploration of the entire thoracic cavity.<sup>3,9,17,48,81,130</sup> If pathology is isolated to one hemithorax, an intercostal lateral thoracostomy may be performed. In a study evaluating short-term outcome following thoracic surgery in dogs, median sternotomy was chosen in 85% of dogs treated surgically for pyothorax.<sup>138</sup> Interestingly, wound complications were also more common following median sternotomy versus intercostal lateral thoracotomy, with a wound complication rate of 71% and 23%, respectively.<sup>138</sup> Surgical procedures are dictated by the location and extent of lesions and may include subtotal pericardectomy, mediastinectomy, lung lobectomy, pneumonectomy, or decortication.<sup>1–3,9,17,18,59,81,138</sup> Decortication involves surgical removal of the thick fibrinous peel that forms

on the pleural surfaces secondary to inflammation in an effort to help improve lung expansion.<sup>18,38,81</sup> Severe hemorrhage, edema, pneumothorax, and pulmonary fistula formation are possible complications from decortication and, as the procedure is difficult to perform, it is generally not recommended in small animals.<sup>18,81</sup> Pneumonectomy has been reported in cats with chronic pneumothorax and appears to be well tolerated.<sup>9</sup>

Excised tissue should be submitted for histopathologic examination and samples collected for bacterial culture and sensitivity analysis. The thoracic cavity and excised tissues should also be thoroughly inspected for foreign material that is often only identified with histopathology.<sup>81</sup> Unilateral or bilateral thoracostomy tubes should be placed during surgery and postoperative management includes continued systemic antibiotic therapy, thoracic drainage, and analgesia.<sup>1,3,9,17,48,49</sup>

### Video-assisted thoracoscopic surgery

VATS is an alternative to traditional thoracotomy surgery that allows evaluation of the thoracic cavity with minimal invasion. VATS is increasingly used as a first-line therapy in the management of human empyema, although there is little evidence to support its use over open thoracotomy.<sup>11–13,139,140</sup> There have also been no randomized trials to show that VATS is more effective or safe when compared to traditional surgical techniques. Diagnostic and therapeutic VATS have been reported in the veterinary literature, although the utility of VATS for the management of pyothorax in small animals has yet to be determined.<sup>17,141,142</sup> Indications for VATS include treatment and investigation of pericardial, pulmonary, mediastinal, and pleural disease.<sup>141,143</sup> Thoracoscopic procedures allow excellent visualization and exploration of the pleural cavity with subsequent localization of intrathoracic abnormalities and removal of potential foreign bodies. Resection of adhesions and necrotic tissue, biopsy, lung lobectomy, and decortication can be performed. Breakdown of loculated effusion can also be accomplished, allowing complete drainage of the pleural cavity. With thoracoscopy, optimal placement of thoracotomy tubes can be achieved. In small animals, thoracoscopy has been proven safe and effective for performing pericardectomy, vascular-ring anomalies division, lung lobectomy, thoracic duct ligation, mediastinal mass resection, biopsy, and foreign body removal.<sup>142–148</sup> Thoracoscopy can also be used to determine the underlying cause for pleural effusion in dogs and cats.<sup>149</sup>

A review of the current literature revealed a single case report describing the use of VATS for the management of pyothorax in a dog.<sup>142</sup> This case report described the successful treatment of pyothorax with thoracoscopic foreign body removal and right middle lung lobectomy in a 3-year-old dog. Additional studies are necessary to

investigate the use of VATS in the management of our small animal pyothorax patients.

Proposed advantages of VATS compared to traditional thoracotomy include shorter operation times, decreased tissue trauma, decreased postoperative pain, fewer wound complications, and reduced hospital stay.<sup>12,141,142,150,151</sup> In children with empyema, hospital length of stay was shorter for children treated with VATS or thoracotomy than for children treated with chest tube alone or in combination with fibrinolytic therapy. However, hospital length of stay was not significantly different for patients treated with VATS compared to patients treated by thoracotomy.<sup>140</sup> Disadvantages of thoracoscopy include the need for specific and expensive instrumentation and video equipment and the potential for longer surgical times with surgeon inexperience.<sup>11,12,142,150</sup>

In human medicine, the need for conversion to open thoracotomy varies considerably, from 5.6% to 61%, in patients initially treated with VATS.<sup>13,15,152–155</sup> Negative predictive factors for conversion to thoracotomy include delayed referral and surgical intervention, pleural thickening, infection with gram-negative organisms, and fever on presentation.<sup>152,153</sup> In small animals, complications of thoracoscopy, including hemorrhage, pneumothorax, pleural adhesions, anesthetic complications, or an inability to complete the intended procedure, may necessitate conversion to open thoracotomy.<sup>143,150</sup>

### **Analgia, Nutrition, and Monitoring**

Use of intrapleural analgesia in the treatment of pyothorax is controversial. Administration of intrapleural bupivacaine buffered with sodium bicarbonate is advocated in patients with indwelling thoracostomy tubes.<sup>12,18,156,157</sup> However, absorption of intrapleural analgesia may be unreliable in patients with pleural infection and effusion and there is a risk for diaphragmatic paralysis.<sup>158,159</sup> Use of systemic opioids is generally safe and efficacious in patients with respiratory compromise.

Continuous patient monitoring is recommended while thoracostomy tubes are in place. Sterile gloves should be worn any time a chest drain is handled. The chest drain insertion sites should be checked at least twice daily for signs of inflammation or infection and the skin around the drain should be kept clean and dry. The drain insertion sites should be covered by a light chest bandage to keep the area clean and to prevent any self-trauma. It is essential the bandage not be placed too tight as this can lead to compromised ventilation. The chest bandage should be checked routinely and changed once every 24 hours. If at any time the bandage becomes soiled or strike-through occurs, the bandage should be changed immediately. An Elizabethan collar may also

be required if there is any indication that the patient may cause trauma to the chest drains. The volume of thoracostomy fluid lavaged and aspirated should be recorded. Daily evaluation of electrolytes, acid-base status, serum albumin, blood glucose, hematocrit, and total plasma protein should be performed and body weight should be monitored.

While the relationship between poor nutrition and clinical outcome in veterinary patients with pyothorax is unknown, malnutrition in people with pleural infection has been associated with poor outcome.<sup>20</sup> Nutritional support should be tailored to meet each patient's specific needs and should be provided as soon as feasible. Early enteral nutrition should be provided via a feeding tube in malnourished or critically ill patients. Proposed benefits of early enteral nutrition include preservation of intestinal mucosal integrity, reduction of systemic inflammation, preservation of immune function, reduction of antigenic leak from the gut, and reduced incidence of hyperglycemia.<sup>160,161</sup> Nasoesophageal, nasogastric, esophagostomy, and gastrostomy feeding tubes are commonly used in small animal patients. The type of feeding tube placed will depend on the anticipated duration of nutritional support, clinician experience, and the patient's ability to tolerate anesthesia. Nasoesophageal and nasogastric tubes are generally tolerated in critical animals as they are easy to place and require minimal to no sedation. In patients where recovery is expected to be prolonged, esophagostomy tube or percutaneous endoscopic gastrostomy tube placement may be considered once the patient is cardiovascularly stable and can withstand anesthesia.

### **Prognosis**

The prognosis for canine and feline pyothorax is variable but can be good with appropriate treatment.<sup>3,4,9,48,57,59,61</sup> The lack of standard therapy, multiple etiologies, and multiple patient populations confound survival data. Animals who present with respiratory decompensation, SIRS, or sepsis generally have a worse outcome than their clinically stable counterparts.<sup>8,16,49</sup> A review of the literature since 2000 revealed an overall survival rate of 83% in dogs (range 29–100%) and 62% in cats (range 8–100%).<sup>16</sup> Cats who survive beyond the first 24 hours of hospitalization have a fair to good prognosis as most nonsurvivors die or are euthanized within the first 48 hours after presentation.<sup>8,18,48,49,71</sup> Owners may elect for humane euthanasia because of a perceived poor prognosis, financial constraints, and risk of or incidence of recurrence. Reported recurrence rates in dogs and cats with pyothorax range from 0% to 14%.<sup>3,4,17,42,48,49,59,61,65</sup> In dogs, recurrence has been shown to be associated with a high mortality rate. In Boothe et al, recurrence occurred

in 7 dogs and 5 of them (71%) died or were euthanized.<sup>1</sup> Infection with *Nocardia* spp. or *Actinomyces* spp. and inhalation and migration of plant material are thought to be risk factors for recurrent pyothorax.<sup>3,17,61</sup>

To date, there are no reliable clinical, radiological, or pleural fluid characteristics that accurately predict patient outcome or long-term survival at initial presentation. Early diagnosis and intervention remain essential to improving the chance of successful outcome in veterinary patients with pleural infection. Even though the prognosis can be favorable, management of pyothorax can be expensive and prolonged and owners should be informed of the potential for lengthy hospitalization, frequent and regular recheck visits, and long-term antimicrobial therapy.

### Conclusion

Pyothorax is a life-threatening condition characterized by the accumulation of septic purulent exudate within the pleural space. Many potential causes have been described in both cats and dogs; however, the underlying etiology is not always identified. Rapid diagnosis is required and is made based on history and clinical signs, laboratory findings, pleural fluid analysis, and diagnostic imaging. Antimicrobial therapy in combination with thoracic drainage is generally accepted as the mainstay of therapy. However, prospective multicenter studies with standardized treatment protocols are needed to determine how specific therapies affect outcome in our veterinary patients. There is great opportunity for potential research into the diagnosis and treatment of pyothorax in dogs and cats. This includes investigation into biochemical markers, patient risk factors, and epidemiology as predictors of patient outcome and need for surgery. Optimal medical management for pyothorax is unknown and questions remain in regards to indications for thoracostomy tube placement, optimal chest tube size, number, dwell time, and management. The ideal duration of antimicrobial treatment is also unknown. It remains to be determined if pleural lavage, suction, and use of intrapleural fibrinolytic therapy should be part of routine treatment and if they ultimately affect patient outcome. The role of thoracic surgery in the management of pyothorax is unclear and randomized studies comparing surgery to medical therapy and VATS to open thoracotomy are needed.

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