Review Article

Medication-induced esophageal injury in cats and dogs: A comprehensive review

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Abstract

Medication-induced esophageal injury (MIEI) is a significant concern in veterinary medicine, affecting the health and well-being of animals undergoing various pharmaceutical treatments. If not addressed promptly, MIEI can lead to severe complications such as esophagitis, esophageal stricture, perforation, and even mortality. This review aims to provide a comprehensive examination of MIEI in veterinary medicine, covering essential aspects such as the basic structure of the esophagus, the epidemiology and etiology of MIEI, and the factors influencing susceptibility. The mechanisms of injury are discussed in detail, focusing on direct mechanical injuries, chemical injuries from medication components, and systemic effects. The review also explores the clinical manifestations of MIEI, highlighting common signs and symptoms, as well as diagnostic approaches. Treatment strategies are extensively covered, emphasizing immediate interventions, pharmacological treatments for symptom relief, and supportive care. The article underscores the importance of prevention strategies and pet owner education in mitigating the risk of MIEI, including proper medication administration techniques. A thorough understanding of MIEI is vital for veterinary practitioners to minimize the risk of adverse events associated with medication use. This knowledge promotes medication safety, enhances diagnostic accuracy, refines treatment methods, and improves patient well-being. Additionally, it aids in educating clients within the veterinary field, ensuring a collaborative approach to animal health care. This comprehensive review serves as a valuable resource for veterinary professionals, offering insights and practical guidance for effectively managing and preventing MIEI in clinical practice.

Keywords: Capsules, cats, dogs, esophagitis, Medication-induced esophageal injury, pills, tablets, veterinary medicine

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Introduction

Medication-induced esophageal injury (MIEI), also referred to as pill-induced esophagitis, presents a significant challenge in veterinary patients. MIEI encompasses a spectrum of adverse effects resulting from the ingestion of pharmaceutical agents, typically in the form of pills or capsules. These medications can cause irritation, inflammation, or damage to the esophageal lining, primarily due to direct contact between the medication and the esophageal mucosa during swallowing, leading to varying degrees of tissue damage. While medications are essential for managing various medical conditions in animals, their potential to cause esophageal damage requires careful consideration (Saleem & Sharma, 2023). MIEI can manifest as esophagitis, erosions, ulcers, perforations, or strictures of the esophageal wall, influenced by factors such as the type of medication, its properties, and individual patient characteristics. These injuries can result in discomfort, pain, dysphagia, and potentially life-threatening complications in affected animals (Pemmada *et al*., 2023). This article aims to provide a comprehensive overview of MIEI in animals, particularly focusing on cats and dogs. It addresses the epidemiology, etiology, risk factors, mechanisms, clinical presentation, diagnostic approaches, therapeutic strategies, and preventive measures related to this condition.

Basic Structure and Function of the Esophagus

The esophagus plays a crucial role in transporting ingested material from the pharynx to the stomach and in preventing the backward flow of gastrointestinal contents (Jaspersen, 2000). Peristaltic contractions facilitate this transport, while the closure of the two esophageal sphincters between swallows prevents regurgitation (Kahrilas & Hirano, 2022). In dogs and cats, the esophagus is composed of the upper esophageal sphincter, the body of the esophagus, and the lower esophageal sphincter (König & Liebich, 2020). It is positioned dorsally to the trachea in the neck, traverses through the thoracic cavity via the mediastinum, lies dorsal to the heart base, and passes between the lungs. Upon entering the abdominal cavity through the esophageal hiatus of the diaphragm, it continues its path (Aspinall & Cappello, 2020). Both the upper and lower esophageal sphincters relax to allow the passage of ingested material into the esophagus and stomach, respectively. Normally, they remain in a tonic state to prevent laryngopharyngeal and gastroesophageal reflux, thereby reducing the risk of aspiration (Ullal *et al*., 2022).

The esophagus is a neuromuscular tubular structure consisting of circular and longitudinal muscle fibers that generate peristaltic waves to propel food along its length. The transit time for food typically ranges from 15 to 30 seconds, though this can vary depending on the type of food, with liquids generally passing through more quickly than solids (Aspinall & Cappello, 2020). In dogs, the entire esophagus is made up of striated muscle fibers. In contrast, the caudal portion of the esophagus in cats, situated behind the heart base, consists of smooth muscle. This structural variation causes an oblique folding of the mucosa in cats, resulting in a distinctive herringbone pattern visible during contrast imaging studies (Stieger-Vanegas, 2020). The esophageal mucosa is composed of stratified squamous epithelial cells, which are interconnected by tight junctions, desmosomes, claudins, occludins, and other proteins, forming a protective barrier (Blevins *et al*., 2018). Beneath the mucosa, mucous glands secrete mucus, which lubricates the esophagus and facilitates the passage of ingested materials. The submucosa houses blood vessels, nerves, and collagenous connective tissue (Jennings & Premanandan, 2017).

Importance of Recognizing Medication-Induced Esophageal Injury in Veterinary Medicine

The significance of MIEI lies in the various complications that medications can induce within the esophagus (Saleem & Sharma, 2023). In veterinary practice, awareness of MIEI is crucial for several reasons:

Patient Welfare: Early identification and management of MIEI are essential for safeguarding the well-being of veterinary patients. Animals with esophageal injuries often experience discomfort, pain, and difficulty swallowing, which can severely diminish their quality of life if not appropriately treated (Pemmada *et al*., 2023).

Medication Safety: Awareness of the risks associated with MIEI encourages veterinarians to exercise caution when prescribing or administering medications. This vigilance can help prevent accidental injuries and promote safer medication practices within veterinary settings (Jaspersen, 2000).

Diagnostic Accuracy: Knowledge of MIEI allows veterinarians to consider this condition as a differential diagnosis when evaluating patients presenting with relevant clinical signs. Accurate diagnosis ensures that appropriate treatment strategies are selected, ultimately improving patient outcomes (Kahrilas & Hirano, 2022).

Treatment Optimization: A deep understanding of MIEI mechanisms and management strategies enables veterinarians to provide effective and timely treatment. This may involve discontinuing the offending medication, providing symptomatic relief, adjusting the diet, and offering tailored supportive care to meet each patient's specific needs (Defarges, 2022).

Client Education: Educating pet owners about the risks of MIEI is vital for improving medication administration practices at home. Owners can learn proper pill administration techniques, recognize potential signs of esophageal injuries, and seek veterinary assistance promptly if needed (Zoran, 2005).

In conclusion, a thorough understanding of MIEI is crucial for enhancing patient welfare, promoting safe medication practices, improving diagnostic accuracy, optimizing treatment approaches, and supporting

client education in veterinary medicine. Neglecting to address MIEI can result in severe complications, such as esophagitis, pleural inflammation, aspiration pneumonia, and even mortality (Defarges, 2022; Zoran, 2005).

Epidemiology and Etiology of MIEI

The first reported case of esophageal ulcers caused by medication ingestion dates back to 1970, when Pemberton described a patient who developed ulcers following the intake of potassium chloride tablets (Pemberton, 1970). Since then, numerous medications have been identified as potential causes of esophageal damage. By 1999, approximately 1,000 cases of MIEI in humans had been recorded in the literature (Noffsinger, 2009; Roro *et al*., 2021). The estimated annual incidence of MIEI is 3.9 cases per 100,000 individuals (Kikendall *et al*., 1983), although this figure likely underestimates the true scope of the problem due to underreporting and undetection, which may have significant implications for patient care and public health.

In veterinary medicine, many cases of MIEI in animals also remain undetected or unpublished. Severe cases are more likely to prompt owners to seek veterinary assistance, which makes determining the accurate incidence or prevalence of this condition challenging. Among companion animals, cats seem particularly vulnerable to MIEI when given oral medications (Kook, 2021; Beatty *et al*., 2006). The exact reasons for this susceptibility are not fully understood, but it could be linked to the anatomy of the feline esophagus. Unlike other domestic animals, the feline esophagus has several sharp angles that increase the likelihood of medication entrapment (Abd Elkader *et al*., 2020).

Additionally, the size of medications may play a role; many pills are too large for cats, which require smaller pill sizes due to their smaller body size. However, commercially available medications are often not formulated in sizes suitable for cats, creating challenges in administration and raising the risk of esophageal injuries. While reports of MIEI specifically in dogs are less common in the veterinary literature, dogs more frequently experience esophageal foreign bodies than cats. In dogs, bone fragments and rawhide chews are the most common culprits. In contrast, cats are more prone to issues with linear foreign objects, such as strings, which often become attached at the base of the tongue (Ruaux, 2020).

Over 100 distinct medications have been identified as potential causes of MIEI in humans (Kahrilas, 2024). Table 1 provides a compilation of frequently reported medications associated with MIEI (Kahrilas, 2024; Abdi *et al*., 2022; Zimmer and Emrich, 2021; Winstead and Bulat, 2004; Kikendall, 1999; Saleem and Sharma, 2023; Katzka, 2021). This table includes a variety of commonly prescribed drugs known to cause direct damage to the esophageal mucosa. However, it is important to note that this compilation is not exhaustive. Additional medications, including those within the mentioned drug categories, combination drugs containing these compounds, and others, may also pose a risk of esophageal injury. Among the offending agents, antibiotics such as doxycycline, tetracycline, and clindamycin account for more than 50% of reported cases (Kahrilas, 2024). Other commonly implicated drugs include acetaminophen, alprenolol, ascorbic acid, aspirin, bisphosphonates, ferrous sulfate, potassium chloride, quinidine, warfarin, and various steroidal and non-steroidal anti-inflammatory drugs (NSAIDs) (Levine, 1999; Funes and Ruaux, 2020). Additionally, anticancer chemotherapy agents such as bleomycin, cytarabine, dactinomycin, daunorubicin, 5-fluorouracil, methotrexate, and vincristine can induce esophagitis, possibly due to associated oropharyngeal mucositis (Saleem and Sharma, 2023). MIEI has also been documented with minerals like iron and calcium (Nasir *et al*., 2020; Patel *et al*., 2010; Zijlstra *et al*., 2022; Wardlaw *et al*., 2007). The wide range of implicated medications highlights the necessity of careful medication administration and monitoring for signs of esophageal injury.

As mentioned, antibiotics are among the most common causes of MIEI. Within this category, doxycycline and tetracycline are particularly well-documented as leading to MIEI in humans (Geagea and Cellier, 2008). Other antibiotics known to cause esophagitis include amoxicillin, clindamycin, ciprofloxacin, metronidazole, and rifaximin. Antibiotic-associated esophageal injuries have also been observed in cats treated with doxycycline, clindamycin, and oxytetracycline (Funes and Ruaux, 2020). The tendency of certain antibiotics to cause MIEI may be linked to their specific properties or methods of administration, indicating a need for further research in this area.

Factors Influencing Susceptibility to MIEI

Risk factors that increase the likelihood of MIEI in veterinary patients can be categorized into two main groups: (1) medication-related factors, which include the dosage forms and chemical properties of the drugs, and (2) patient-related factors, such as species, anatomical features, age, health status, and pre-existing esophageal conditions (Geagea and Cellier, 2008).

Medication-Related Factors: Medication-related factors play a crucial role in the development of MIEI. Key properties of medications that significantly contribute to esophageal injuries include their formulations, chemical characteristics, and pharmacological properties (Pemmada *et al*., 2023; Dağ *et al*., 2014).

Table 1 A compilation of frequently cited medications implicated in MIEI.

Category	Subcategory	Examples
Antimicrobial drugs	Lincosamides	Clindamycin, lincomycin
	Macrolides	Azithromycin, clarithromycin, erythromycin, spiramycin
	Penicillins	Amoxicillin, amoxicillin-clavulanic acid, ampicillin, cloxacillin, penicillin, pivmethicillin
	Sulfonamides	Sulfamethoxypyridazine, trimethoprim-sulfamethoxazole
	Tetracyclines	Doxycycline, minocycline, oxytetracycline, tetracycline
	Fluoroquinolones	Ciprofloxacin
	Others	Cephalexin, emepronium, metronidazole, nelfinavir, rifampin (rifampicin), tinidazole, zalcitabine, zidovudine
Antiinflammatory drugs	Glucocorticoids	Prednisone, prednisolone
	NSAIDs	Aspirin, diclofenac, ibuprofen, indomethacin, naproxen, piroxicam
Cardiovascular drugs	Antiarrhythmics	Mexiletine, quinidine
	Antihypertensives	Captopril, nifedipine
	Vasodilators	Naftidrofuryl (nafronyl)
Anticancer drugs	Chemotherapeutic drugs	Bleomycin, cytarabine, crizotinib, dactinomycin, daunorubicin, 5-fluorouracil, methotrexate, vincristine
Osteoporosis inhibitors	Bisphosphonates	Alendronate, etidronate, ibandronate, pamidronate
Others	Vitamins and minerals	Ascorbic acid, calcium dobesilate, iron preparations (e.g., ferrous sulfate), l-arginine, multivitamins, potassium chloride, sustained-release potassium preparations
	Miscellaneous	Acetaminophen, aminophylline, caffeine, clomethiazole, estramustine, glyburide (glibenclamide), lansoprazole, oral contraceptives, phenytoin, pinaverium, quinidine, retinoic acid derivatives (e.g., isotretinoin), theophylline, warfarin

Medication Formulations: Medication formulations, or dosage forms, refer to the specific physical form in which a medication is administered, such as capsules, tablets, sustained-release formulations, irregularly shaped pills, solutions, suspensions, creams, and ointments (Brunton and Knollmann, 2022). Medications are commonly administered orally to dogs and cats in the form of capsules or tablets. MIEI occurs when these capsules or tablets become lodged in the esophagus, leading to tissue damage. Although detailed information about the movement of capsules and tablets through the esophagus in animals is limited, studies indicate that capsules generally pose a higher risk of inducing esophageal injuries or esophagitis compared to tablets (Johnson-Arbor, 2023). This increased risk is mainly due to the larger size and smoother surface of capsules, which can increase the likelihood of them becoming lodged in the esophagus and causing mechanical irritation. Additionally, capsules may contain medications with properties or formulations more likely to irritate the esophageal lining chemically (Dağ *et al*., 2014; Kim *et al*., 2014). Sustained-release formulations are particularly prone to causing pill esophagitis compared to immediate-release forms, as the gradual release of their contents can lead to prolonged exposure and continued damage to the esophageal tissue (Johnson-Arbor, 2023).

Chemical Characteristics of Medications: Certain chemical properties of medications, such as acidity, alkalinity, or the presence of irritant compounds, can directly impact the esophageal mucosa upon contact during swallowing, contributing to the development of MIEI (Pemmada *et al*., 2023). These chemical traits also influence how a drug is released and absorbed. When a medication becomes lodged in the esophagus, its intended delivery mechanism can be disrupted, potentially increasing the risk of toxicity (Grissinger, 2013). The formulation of a drug also plays a role in esophageal injury. For instance, tablets containing cellulose fibers and guar gum can swell upon absorbing water in the esophagus, leading to potential obstruction (Antunes and Sharma, 2023).

Patient-Related Factors: The risk of MIEI is also affected by anatomical characteristics, such as the orientation of the esophagus. Companion animals like dogs and cats may be more susceptible to pill or capsule retention in the esophagus due to its horizontal alignment, which differs from the vertical orientation in humans that allows gravity to assist in swallowing (Graham *et al*., 2000). Additionally, the patient's posture can influence the passage of pills through the esophagus. In humans, factors such as lying down during or shortly after drug ingestion, especially at bedtime, have been identified as risk factors for drug-induced esophagitis (de Groen *et al*., 1996; Jaspersen, 2000). Similarly, administering medication to immobilized animals that remain recumbent for extended periods can present challenges. Elevating the head and neck during medication administration may be beneficial for bedridden animals.

Moreover, concurrent conditions such as dryness, motility disorders, and esophageal reflux can affect the transit of pills through the esophagus, predisposing patients to MIEI (Jaspersen, 2000). Conditions like xerostomia, which leads to dryness, can arise due to aging, sicca syndrome, or the use of anticholinergic drugs. MIEI is often associated with underlying medical conditions that prolong contact between the

medication and the esophagus, such as achalasia, strictures, ineffective esophageal motility, age-related changes, and other motility disorders (Geagea and Cellier, 2008). Additional anatomical variations, such as aortic aneurysms or left atrial enlargement, may also contribute to the development of MIEI. However, MIEI can also occur in animals with normal esophageal function (Boyce, 1998; German *et al*., 2005).

In summary, these examples demonstrate that numerous factors can contribute to the development of MIEI in cats and dogs, emphasizing the need to carefully consider potential risks when prescribing or administering medications orally. Veterinarians must be well-informed about a patient's status, comorbidities, all medications the patient is currently taking, and the composition of these drugs. This information is crucial for evaluating the risk of esophageal injury and implementing preventive measures to minimize adverse effects. For a concise overview of the discussed risk factors, please refer to Table 2.

Table 2 Risk factors that predispose to pill-induced esophageal injury.

Risk factors	Pill-induced esophageal injuries
Medication-related factors	Medication formulations: Capsules, large tablets, irregularly shaped pills, sustained-release formulations
Patient-related factors	Chemical characteristics of medications: Acidity, alkalinity, presence of irritant compounds Anatomical factors: Horizontal alignment of the esophagus Patient's posture: Reclining, lying down Co-occurring health problems: 1 Xerostomia: Aging, sicca symptoms, anticholinergic medications 2 Disordered esophageal motility: Achalasia, strictures, ineffective esophageal motility, age-related changes, and other esophageal motility disorders 3 Disorders of local anatomy: Aortic aneurysms or enlargement of the left atrium

Mechanisms of Medication-induced Esophageal Injuries

To develop effective strategies for the treatment and prevention of MIEI, it is essential to understand how medications trigger esophageal damage. These mechanisms include direct mechanical injuries, chemical injuries, and systemic effects.

Direct Mechanical Injuries: Certain characteristics of pills can directly cause esophageal injuries. Tablets or capsules may become lodged in the esophagus, leading to mechanical irritation, trauma, and tissue damage (Chen *et al*., 2009). Tetracycline antibiotics (such as doxycycline), large pills, and gelatin capsules are common contributors to MIEI (Tresca, 2024; Dağ *et al*., 2014; McGrotty and Knottenbelt, 2002).

As previously noted, capsules are generally larger than tablets, making them more prone to retention in the esophagus and more difficult to dislodge once they adhere (Jaspersen, 2000; Perkins *et al*., 1999). Experimental studies on the feline esophagus have demonstrated that local damage from doxycycline hydrochloride is more severe when administered in capsule form compared to the same salt in tablet form (Carlborg *et al*., 1983). This underscores the importance of considering the physical properties of medications when prescribing them to patients.

Chemical Injuries from Medication Components: Certain medications, particularly those with acidic properties, can directly irritate and damage the esophageal lining, causing inflammation, erosions, or ulcers. For example, acidic antibiotics, ferrous sulfate, NSAIDs, and vitamin C tablets form acidic solutions when dissolved in water or saliva (Saleem and Sharma, 2023; Zografos *et al*., 2009). Doxycycline, a tetracycline derivative with a high acidic content, can predispose patients to esophageal injury if taken with insufficient water or while lying down. Doxycycline-induced esophageal damage ranges from superficial erosions to deep ulcers (Pemmada *et al*., 2023). NSAIDs, which are acidic molecules with pKa values of 4 to 5, can be absorbed through the mucosa and may exert a direct toxic effect on the esophagus when the luminal pH falls below 4, although prostaglandin inhibition is not considered a major mechanism in NSAID-induced esophagitis (Winstead and Bulat, 2004).

Medications with alkaline properties can also cause chemical burns or caustic damage to the esophageal lining if they come into contact with the mucosa. For instance, phenytoin generates an alkaline solution when mixed with water, and alendronate can produce a caustic solution. If these pills become lodged in the esophagus, the resulting alkaline fluid can cause tissue damage and burns (Tresca, 2024; Tesic-Rajkovica and Radovanovic-Dinic, 2022). Furthermore, medications containing osmotic agents, such as potassium chloride or quinidine, can cause esophageal injury by increasing osmotic pressure, which disrupts the water balance in the esophageal tissues. The hyperosmolarity can draw water out of the esophageal tissues, leading to dehydration of the mucosa and subsequent tissue damage (Brocker *et al*., 2012; Kultz, 2004; Sasaki *et al*., 2017).

The mechanisms of mucosal toxicity from certain medications can be highly complex. For example, iron-induced injury involves the absorption of iron as ferrous iron, which is then oxidized to ferric iron. When ferric iron exceeds the binding capacity of transferrin, it causes cellular damage through two primary mechanisms. First, ferric iron inflicts direct corrosive injury to the esophageal mucosa. Second, it generates free radicals and induces lipid peroxidation, disrupting various cellular processes and leading to further damage (Ohki *et al*., 2023; Chen *et al*., 2000). A thorough understanding of these mechanisms is vital for effectively preventing and treating medication-induced esophageal injuries.

Systemic Effects: Certain medications have pharmacological properties that can indirectly affect the esophagus through systemic actions, such as altering

esophageal motility, decreasing salivation, or reducing mucosal protection, thereby increasing susceptibility to injuries (Szymanski, 2016). Anticholinergic drugs, such as atropine, dicycloverine, hyoscine butylbromide, and oxybutynin, can cause xerostomia by inhibiting acetylcholine activity, which is crucial for stimulating saliva secretion through muscarinic receptors. This inhibition reduces saliva production, leading to oral dryness. The resulting lack of adequate saliva can contribute to swallowing disorders, thereby increasing the risk of MIEI (Tesic-Rajkovica and Radovanovic-Dinic, 2022). Additionally, other systemic effects that may contribute to esophageal injury include medication-induced infections and gastroesophageal reflux (Kahrilas, 2024).

In conclusion, medications can induce esophageal injuries through a range of mechanisms, emphasizing the importance of proper administration techniques and patient education to prevent such complications. Awareness of these mechanisms enables veterinary professionals to make informed decisions when prescribing medications and implementing preventive strategies to minimize the risk of adverse effects.

Antibiotics: The Most Common Cause of MIEI in Veterinary Medicine

In veterinary practice, antibiotic-induced esophageal injury is the most frequently reported type of MIEI, particularly in cats. Numerous studies have documented cases where antibiotics, especially doxycycline and clindamycin, have caused significant esophageal damage in animals (Beatty *et al*., 2006; Defarges, 2022; German *et al*., 2005; McGrotty and Knottenbelt, 2002). This section explores antibiotic-induced esophageal injury in feline patients. Several cases of esophageal injury, including inflammation and stricture, have been reported in cats following antibiotic administration (McGrotty and Knottenbelt, 2002; German *et al*., 2005; Beatty *et al*., 2006). Notably, tetracycline antibiotics like doxycycline are strongly associated with MIEI, partly due to their larger capsule size (Jaspersen, 2000). The size of doxycycline capsules can vary depending on the manufacturer and dosage, typically ranging from 50 mg to 200 mg, with lengths of approximately 16-22 mm (NIH, 2021). For cats, even smaller capsules can be difficult to swallow due to their narrower esophagus compared to humans. This difficulty, combined with improper administration (e.g., without sufficient water), increases the risk of esophageal injury.

Doxycycline has been shown to concentrate within the basal layer of the esophageal squamous epithelium, suggesting an additional mechanism for local irritation (Zografos *et al*., 2009). Administering tablets and capsules to cats often impairs esophageal motility, leading to significant retention in the mid-cervical region, particularly after a dry swallow (Graham *et al*., 2000; Westfall *et al*., 2001; Ovartlarnporn *et al*., 1991). However, lesions can also develop along the entire length of the esophagus. For instance, a cat in the UK was found, through fluoroscopy, to have multiple esophageal strictures throughout the esophagus following oral administration of doxycycline and oxytetracycline. This cat recovered after successful balloon dilation, resulting in symptom resolution (McGrotty and Knottenbelt, 2002).

Clindamycin-associated esophageal injuries have been reported in five cats with no prior history of esophageal issues before the administration of clindamycin (Beatty *et al*., 2006). Various forms of clindamycin, including oral capsules and tablets, can be challenging for cats to swallow due to their relatively narrow esophagi. These anatomical characteristics make cats particularly prone to difficulties with larger pills or capsules. The esophageal injuries observed in clindamycin-treated cats may be worsened when capsules are administered without water, leading to a dry swallow. Clindamycin has also been implicated as a cause of MIEI in humans, where insufficient liquid intake during medication ingestion is considered a significant contributing factor (Rivera Vaquerizo *et al*., 2004; Sutton and Gosnold, 1977; Froese, 1979; Stanić Benić *et al*., 2016). To mitigate this risk, it is recommended to routinely provide a small amount of water to help clear the esophagus of any retained medication (Westfall *et al*., 2001; Kook, 2021).

Antibiotics can cause damage to esophageal tissues not only through direct mechanical injury but also through chemical injury. When antibiotics become trapped in the esophagus, they can lead to esophagitis and ulceration due to the irritant effects of their acidic properties on the esophageal mucosa. Common doxycycline formulations include doxycycline hyclate, doxycycline hydrochloride, and doxycycline monohydrate.

Doxycycline hyclate tablets, in particular, are known to cause esophageal ulceration and esophagitis in humans, which has led to the recommendation of drinking one or two glasses of water after ingestion (Carlborg and Farmer, 1983; Kikendall *et al*., 1983). Remarkably, antibiotic-associated injury has been reported in 11 published cases involving cats treated with doxycycline hyclate or hydrochloride (Melendez *et al*., 1998; Leib *et al*., 2001; McGrotty and Knottenbelt, 2002; German *et al*., 2005; Beatty *et al*., 2006). Doxycycline hyclate is known to create a highly acidic solution with a pH ranging from 2 to 3, unlike doxycycline monohydrate (Adami *et al*., 2011; Beatty *et al*., 2006). As a result, doxycycline monohydrate is believed to have a lower propensity to induce MIEI, as it is less irritating and safer for oral administration compared to the hyclate or hydrochloride salts (Carlborg and Farmer, 1983).

The monohydrate form of doxycycline is available in several countries, including Thailand, Australia, and Italy, and comes in tablet form as well as a palatable paste suitable for dogs and cats. Post-registration data indicate that the monohydrate formulation carries a minimal risk of causing ulcers, with only one potential case reported since its introduction in Australia in 1993, despite over two million courses of treatment being administered (Trumble, 2005; Beatty *et al*., 2006). Although doxycycline monohydrate tends to be less irritating than its hyclate or hydrochloride counterparts, it is advisable to administer any form of doxycycline with a small amount of water or just before a meal to minimize the risk of esophageal ulceration (Mohandas *et al*., 1991; Sasaki *et al*., 2017). Alternatively, using the

paste formulation further reduces this risk due to its lower likelihood of being retained in the esophagus.

Clinical Presentation and Diagnosis

Signs and Symptoms of MIEI: Symptoms of MIEI commonly include regurgitation, dysphagia, odynophagia, drooling, chest or throat discomfort, lethargy, anorexia, and weight loss (Webb, 2014; Adami *et al*., 2011; German *et al*., 2005). Although affected animals often maintain a normal appetite, they may be able to ingest small amounts of water or liquefied food despite difficulties in swallowing. However, they typically avoid solid food, as the passage of a food bolus can cause pain. In severe cases, partial or complete esophageal obstruction may occur, preventing the passage of the food bolus through the esophagus (Kook, 2021; Stathopoulou and Liapis, 2019). A history of acute onset regurgitation in an animal patient is highly indicative of acquired esophageal obstruction, potentially due to a foreign object, such as a pill (Willard, 2011). Regurgitation, which is more passive than vomiting, is often associated with esophageal issues. Therefore, distinguishing between regurgitation and vomiting is critical. Regurgitation usually occurs shortly after eating without abdominal contractions, whereas vomiting involves more active abdominal effort (Husnik, 2022; Willard and Twedt, 2012).

MIEI in animals may be more prevalent than many veterinarians realize. Diagnosis can be challenging because MIEI, such as esophagitis, often presents with clinical signs similar to vomiting rather than regurgitation. Additionally, mild esophagitis may only cause subtle symptoms like slight regurgitation of mucus, while severe esophagitis can result in significant pain, leading patients to avoid swallowing even water or saliva (Beatty *et al*., 2006; Stathopoulou and Liapis, 2019). Due to the diverse range of clinical manifestations, pill-induced esophagitis is often overlooked as a potential differential diagnosis (Willard, 2015).

MIEI is typically transient or self-limiting. In most cases, healing occurs spontaneously within a few days after discontinuing the offending medication (Abid *et al*., 2005). Symptoms generally resolve within 7 to 10 days, particularly when not complicated by stricture formation. However, symptoms may occasionally persist for several weeks after the medication has been withdrawn. Esophageal strictures are relatively uncommon in cats (Burk *et al*., 1987). Nevertheless, MIEI can sometimes result in persistent injuries that lead to stricture formation. For example, four cases of esophageal stricture following doxycycline administration in cats have been reported (German *et al*., 2005). Additionally, in 2019, a case of esophageal stricture in a cat following the oral administration of amoxicillin/clavulanic acid film-coated tablets formulated for humans was reported (Stathopoulou and Liapis, 2019). Clinical signs of esophageal strictures typically emerge within 3 to 16 days after the onset of MIEI (Stathopoulou and Liapis, 2019; Little, 2012; Adamama-Moraitou *et al*., 2002). These manifestations include regurgitation of primarily solid foods, increased salivation, and weight loss despite a normal appetite (Willard, 2015; Zawie, 1989). The severity of symptoms often depends on the location and size of the stricture. Strictures frequently form as fibrous rings in the middle cervical esophagus and the thoracic esophagus near the heart base (Adamama-Moraitou *et al*., 2002; German *et al*., 2005).

Diagnostic Approaches: Accurate diagnosis and management are essential for preventing complications and promoting the healing of the esophageal mucosa in cases of MIEI. This is particularly critical due to the diverse range of symptoms associated with MIEI, which can easily be mistaken for other conditions. MIEI should be considered in patients presenting with odynophagia, dysphagia, or regurgitation, especially if there is a history of ingesting medications known to cause esophageal injury. Animal patients with persistent symptoms one week after discontinuation of the medication should undergo further evaluation, if not already performed, to confirm the diagnosis (Kahrilas, 2024). Diagnostic procedures include oral examination and esophageal imaging, which can help identify foreign body involvement (Abd Elkader *et al*., 2020; Nelson and Couto, 2009). Plain and contrast radiography are valuable for confirming the diagnosis, providing information not only about the location of lodgments but also about potential complications (Tyrrell and Beck, 2006; Tams, 2003). This information is crucial for determining the appropriate treatment approach.

The preferred diagnostic method for suspected MIEI is endoscopy or esophagoscopy, which is among the most effective tools for assessing esophageal disease (Abd Elkader *et al*., 2020; Zoran, 2005). Numerous studies in veterinary medicine have utilized esophagoscopy to locate entrapped capsules or tablets within the esophagus. For example, Beatty *et al*. (2006) reported that lesions were predominantly found in the proximal esophagus. This finding aligns with the observations of Graham *et al*. (2000), who noted that over 50% of capsules administered to normal cats lodged in the mid-cervical esophagus. Similarly, Westfall *et al*. (2001) found that capsules given through dry swallowing tended to be retained in the cervical esophagus (88%) or the oropharynx (8%). The increased recognition of MIEI in clinical practice can be attributed, in part, to the improved accessibility of esophagoscopy (Pemmada *et al*., 2023). This procedure often reveals medication remnants and identifies ulcers. Although the histological features of MIEI, such as esophagitis, are non-specific, biopsies can help exclude infection and neoplasia, providing valuable diagnostic insights (Pusztaszeri *et al*., 2007). Esophagoscopes used in esophagoscopy are typically equipped with an operational channel, allowing the use of various instruments such as biopsy forceps and injection catheters. These tools enable veterinarians to perform both therapeutic and diagnostic procedures during endoscopic examination, including taking tissue samples, administering medications, or conducting other interventions like using balloon dilators, removing abnormal mucosal growths, or managing bleeding (Kahrilas and Hirano, 2022).

Treatment

The primary goal in treating MIEI is to address the underlying cause by discontinuing and removing the offending medication, using either surgical or non-surgical approaches to prevent further damage (Saleem and Sharma, 2023; Webb, 2014). Additionally, managing symptoms and providing supportive care are recommended. Currently, evidence is lacking to support the efficacy of specific treatments in significantly improving the prognosis of MIEI (Katzka, 2021).

Immediate Treatment: Esophageal foreign bodies are medical emergencies that require swift intervention. The initial step in managing MIEI involves discontinuing the offending medication. If a pill is lodged in the esophageal lumen, immediate removal is advised. Oral tablets and capsules that become stuck in the esophagus can erode the mucosal lining, potentially leading to stricture formation (Kahrilas, 2024; Ruaux, 2020). Three methods are available for pill removal: (1) using forceps, (2) using forceps in conjunction with endoscopy or esophagoscopy, and (3) surgical removal. Forceps-based retrieval has proven effective for managing foreign bodies in the pharynx of dogs and is widely used for removing oral foreign bodies in both dogs and cats (Cote, 2015; Gugjoo *et al*., 2012). Various retrieval devices are available for extracting esophageal foreign bodies, including long, rigid forceps such as Rochester Pean artery forceps, flexible alligator forceps, wire cages, three-pronged graspers, Foley catheters, wire loops, snares, and older biopsy forceps. Rigid forceps are especially useful with a rigid endoscope but can also be utilized with flexible endoscopy equipment (Abd Elkader *et al*., 2020; Ruaux, 2020).

Many studies recommend endoscopic extraction as an effective method for managing esophageal and upper gastrointestinal foreign bodies, with reported success rates ranging from 65% to 95% (Michels *et al*., 1995; Deroy *et al*., 2015; Abd Elkader *et al*., 2020). Endoscopy, whether rigid or flexible, serves as a highly effective first-line option for managing such cases. The ability to remove foreign bodies without surgery facilitates faster patient recovery and reduces the risk of complications such as esophageal perforation and wound reopening. However, this benefit must be balanced against the potential challenges, as endoscopic removal of delicate or slippery capsules and pills can be time-consuming and occasionally impractical. Setting a maximum duration for the endoscopic procedure is recommended before deciding to proceed with surgical intervention (Ruaux, 2020). It is reported that 15–38% of animals may require surgical intervention for the removal of foreign bodies (Binvel *et al*., 2018; Deroy *et al*., 2015).

Esophageal foreign bodies, such as pills, may require surgical intervention for several reasons:

- Failure of endoscopic removal: If attempts to remove the pill endoscopically are unsuccessful, surgical intervention may be necessary.
- Esophageal perforation: When a pill causes or poses a risk of causing an esophageal perforation, immediate surgical intervention is required to repair the damage and prevent further complications.
- Severe esophageal erosion or ulceration: Pills can lead to significant erosion or ulceration of the esophageal lining. If these conditions are severe and unresponsive to less invasive treatments, surgery may be needed to prevent further damage and facilitate healing.
- Risk of aspiration: If there is a risk that the pill could be aspirated into the airway, especially when lodged near the upper esophagus, surgical removal may be the safest approach.
- Obstruction: When a pill causes complete or significant obstruction of the esophagus, blocking the passage of food and liquids and leading to severe symptoms, surgery may be required to restore normal esophageal function.
- Presence of complications: If the pill has resulted in complications such as abscess formation, mediastinitis, or severe esophagitis that cannot be managed endoscopically, surgical intervention may be necessary to address these issues.

Pharmacological Interventions for Symptomatic Relief

Analgesics and Anti-inflammatory Drugs: Pain can significantly impede recovery and delay the resumption of normal functions in patients (Steagall & Monteiro, 2019; Monteiro & Steagall, 2019). Effective pain management in MIEI is vital for promoting recovery. Parenteral or liquid oral analgesics may be needed temporarily to manage acute erosive injuries (Boyce, 1998). The combination of topical anesthetics, such as lidocaine, with opioids can effectively alleviate acute pain from MIEI, including esophageal ulcers and esophagitis (Steagall *et al*., 2022). This approach allows patients to swallow without severe discomfort.

The use of nonsteroidal anti-inflammatory drugs (NSAIDs) in treating esophageal injury is generally contraindicated (Kook, 2021). The primary reasons include:

- Impaired Healing: NSAIDs inhibit cyclooxygenase enzymes, which are essential for prostaglandin production. Prostaglandins play a key role in mucosal defense and healing, and their inhibition can impair esophageal injury healing.
- Increased Risk of Complications: NSAIDs can exacerbate esophageal damage and elevate the risk of complications such as perforation and strictures.
- Gastrointestinal Toxicity: NSAIDs are associated with risks like gastric ulcers, bleeding, and perforations (Papich & Riviere, 2018), posing a particular threat to the already vulnerable esophageal mucosa.

NSAIDs have been linked to severe esophageal ulceration and bleeding, especially in the middle third of the esophagus in humans (Lees, 2018). Although NSAID-induced esophageal injury is relatively rare, it often results in hemorrhagic complications when it occurs. A review of the literature identified only 77 documented cases of NSAID-induced esophageal injury in humans. Nonetheless, aspirin and other NSAIDs accounted for nearly 50% of hemorrhagic complications in pill-induced esophageal injuries (Kikendall, 1999). Severe injuries associated with NSAID use include ulcers requiring surgical intervention, fatal hemorrhages, esophageal strictures, perforations, and the formation of multiple esophageal septa (Abid *et al*.,

2005). Given these significant risks, alternative pain management strategies, such as opioids or topical anesthetics, are often preferred for patients with esophageal injuries (Lampridis *et al*., 2020; Mubang *et al*., 2023; Lees, 2018).

Glucocorticoid use in MIEI treatment has been reported in some animal cases, with drugs like oral prednisolone or parenteral dexamethasone (McGrotty & Knottenbelt, 2002; German *et al*., 2005). However, the role of glucocorticoids in MIEI remains controversial (Beatty *et al*., 2006). Potential benefits include reducing inflammation, providing pain relief, and preventing esophageal narrowing. Glucocorticoids are believed to slow the proliferation of fibrous connective tissue and minimize scar formation; however, their efficacy is uncertain. Disadvantages include delayed wound healing, immunosuppression, and an increased risk of infection (Ferguson & Hoenig, 2018; Saleem & Sharma, 2023). Concurrent use of glucocorticoids and NSAIDs is not advised, as it significantly raises the risk of adverse reactions (Monteiro *et al*., 2023).

Acid Suppression for Preventing Additional Injury from Acid Reflux: Beyond analgesics and anti-inflammatory drugs, MIEI treatment often involves the use of proton pump inhibitors (PPIs). PPIs are effective in preventing and treating conditions associated with gastric acid, such as ulcers, by reducing acid secretion and promoting healing (Beatty *et al*., 2006; Katzka, 2021). In veterinary medicine, PPIs like omeprazole, pantoprazole, and esomeprazole are commonly used to manage gastrointestinal disorders through acid reduction (Yavuz & Arslan, 2017). They are particularly preferred for treating upper gastrointestinal bleeding or NSAID-induced injuries in dogs and cats (Tolbert, 2021). Additionally, PPIs are effective for conditions like erosive esophagitis, gastric ulcers, and other acid-related disorders in animals (Tolbert, 2021; Kook, 2021). While definitive evidence linking acid suppression to faster recovery from MIEI is lacking in veterinary patients, acid suppression remains a core component of esophagitis treatment (Kook, 2021). Standard-dose PPIs may be used until symptoms resolve, as gastroesophageal reflux disease can exacerbate or prolong pill-induced esophageal injuries (Kahrilas, 2024; Kook, 2021). Marks *et al*. (2018) suggest that twice-daily PPIs are more effective than other gastroprotectants for treating acid-related gastroduodenal ulceration and erosion (GUE). Currently, no specific PPI has been shown to be superior in treating GUE in dogs and cats (Marks *et al*., 2018). However, esomeprazole may be favored for treating erosive esophagitis, as studies in humans indicate it provides better acid suppression when administered intravenously compared to pantoprazole (Hedges *et al*., 2019). When combined with cisapride and given 12 to 18 hours and 1.0 to 1.5 hours before induction, esomeprazole effectively prevents anesthetic-induced reflux in dogs (Zacuto *et al*., 2012). It is recommended to taper PPIs in dogs and cats after prolonged use for more than 3-4 weeks to avoid rebound acid secretion (Marks *et al*., 2018).

H2 blockers (H2 antagonists), including cimetidine, famotidine, and ranitidine, inhibit histamine activity at the H2 receptors on parietal cells in the stomach, reducing stomach acid production and alleviating acid reflux, which can lead to esophagitis (Baumer, 2017). However, the use of H2 blockers has declined with the introduction of more effective and longer-lasting proton pump inhibitors (PPIs) (Papich, 2018). Studies have demonstrated that PPIs are significantly more effective than H2 blockers in increasing gastric pH, as well as in preventing and healing acid-related tissue injuries in dogs and cats (Tolbert, 2021). The American College of Veterinary Internal Medicine (ACVIM) consensus (Marks *et al*., 2018) states that H2 blockers administered once daily are not effective for treating gastroduodenal ulceration or reflux esophagitis in dogs and cats. Even when given twice daily, H2 blockers are less effective than PPIs taken at the same frequency. Moreover, combining H2 blockers with PPIs does not enhance ulcer healing and may actually diminish the efficacy of PPIs (Papich, 2018; Tolbert, 2021). Given the superior efficacy of PPIs over H2 blockers, current clinical guidelines favor PPIs for managing acid-related disorders in veterinary medicine. As a result, the role of H2 blockers has become more limited, typically reserved for situations where PPIs are contraindicated or unavailable.

Prostaglandin Analogs: Prostaglandins are crucial for maintaining the integrity of the gastrointestinal mucosal barrier. They stimulate the secretion of bicarbonate-rich mucus, enhance mucosal blood flow, and support epithelial repair (Papich, 2018). In veterinary medicine, misoprostol—a prostaglandin E1 analog—is the most commonly used agent in this class. The current consensus indicates that while misoprostol effectively reduces gastric lesions in dogs treated with high doses of aspirin, its effectiveness in preventing gastroduodenal ulceration (GUE) related to other NSAIDs in dogs and cats remains uncertain (Marks *et al*., 2018). Furthermore, misoprostol has limited efficacy in treating already established gastric ulcers (Papich, 2018). Given these uncertainties, the role of misoprostol in managing MIEI is not well defined. Further research is needed to clarify its potential benefits in this specific context.

Coating Agents for Mucosal Protection: Ulcer-coating agents, such as sucralfate, are commonly used in the management of MIEI (Guo *et al*., 2019; German *et al*., 2005; Frowde *et al*., 2011). Sucralfate acts by forming a protective barrier over ulcers and irritated areas within the gastrointestinal tract, including the esophagus. This barrier adheres to damaged tissues, shielding them from further irritation caused by stomach acid, bile salts, and digestive enzymes (Kudaravalli *et al*., 2024). Sucralfate has demonstrated cytoprotective effects in experimental models of feline esophagitis and helps to create a protective layer in acidic environments (Clark *et al*., 1987). However, opinions on its use for managing esophagitis or gastroduodenal ulceration (GUE) are mixed (Marks *et al*., 2018; Schmulewitz and O'Connor, 2002). Evidence supporting sucralfate's effectiveness in preventing or treating esophageal injury is limited, with few studies exploring its analgesic properties in cases of esophagitis. Additionally, there is no clear evidence suggesting any benefit or interaction when sucralfate is used alongside PPIs. Combining sucralfate with PPIs or H2 blockers for gastrointestinal ulcer treatment is not

recommended, as PPIs are generally more effective. Due to these limitations and the lack of strong evidence, the role of sucralfate in managing MIEI remains uncertain and warrants further study.

Antibiotics to Prevent Infection: Antibiotics in liquid, paste, or parenteral forms should be administered when there is significant esophageal mucosal ulceration (Mubang *et al*., 2023). Additionally, if esophageal perforation is suspected, the treatment protocol should address the condition as sepsis, necessitating the use of antibiotics alongside fluid therapy (Lampridis *et al*., 2020; Schmulewitz and O'Connor, 2002). This approach ensures effective infection control and helps to minimize complications.

Supportive Care: Since most cases of MIEI are self-limiting, mild or uncomplicated conditions can be managed through patient monitoring and supportive care (Juniarta and Nyoman Wibawa, 2019). Supportive care for patients with MIEI includes intravenous fluid therapy, maintaining electrolyte balance, providing nutritional support, and administering oxygen for those showing signs of airway compromise. The environment for hospitalized animals should be dry, calm, quiet, and comfortable (Antunes and Sharma, 2023). For animals experiencing severe weight loss, nutritional support through a gastrostomy tube is recommended to ensure adequate intake. Avoiding dietary triggers such as acidic or irritating foods can help mitigate symptoms associated with esophageal ulcerations caused by medication use (Johnson-Arbor, 2023). For animals with odynophagia that can still eat, dietary modifications are advisable. Feeding a soft, blended, or liquefied convalescent diet can provide time for esophageal healing (Antunes and Sharma, 2023; German *et al*., 2005).

In summary, appropriate pharmacological interventions for MIEI include discontinuing and removing the offending medication, managing pain and inflammation, suppressing acid, preventing infection, and providing supportive care. These strategies enable veterinary professionals to make informed decisions when managing cases of MIEI.

Potential Complications and Their Management

MIEI can result in complications such as inflammation, esophageal stricture, perforation, and aspiration pneumonia, though the overall complication rate remains relatively low (Abd Elkader *et al*., 2020; German *et al*., 2005; Schiele *et al*., 2015). However, severe outcomes can occur in some cases. In instances of severe esophagitis, surgical intervention may be necessary to address ulcers, bleeding, or scar tissue formation (Beatty *et al*., 2006). Managing complications such as esophageal stricture or stenosis may require endoscopic dilation (Antunes and Sharma, 2023). In a series of case reports (Stathopoulou and Liapis, 2019), three feline cases of esophageal stricture following antibiotic administration were documented. Diagnosis was achieved through standard or contrast-enhanced radiographic evaluation, and confirmed by esophagoscopy, which pinpointed the stricture in the cranial intrathoracic esophagus in all three cases. Balloon dilation was performed to treat the esophageal stricture, resulting in positive outcomes for two cats. However, in the third case, the severity of the stricture led to unsuccessful dilation, necessitating euthanasia.

MIEI Prevention Strategies

Prevention and pet owner education are essential components in managing MIEI, as they can significantly reduce the risk of complications. Veterinarians should emphasize the importance of these preventive measures and actively educate pet owners. Preventing esophageal retention is relatively simple and can be accomplished by using proper pill administration techniques and informing pet owners about the importance of careful medication administration when done at home. For a summary of the prevention strategies discussed below, please refer to Table 3.

Table 3 MIEI Prevention Strategies.

MIEI Prevention Strategies.
• Drink an adequate amount of water with each pill.
• Sit upright during and for at least 30 minutes after taking pills.
• Avoid large pills when possible.
• Do not administer pills at bedtime.
• Avoid using sustained-release formulations when possible.
• Avoid using the offending medication in elderly or bedridden patients and those with esophageal dysmotility.
• Educate pet owners on proper pill administration techniques and the symptoms of MIEI.

Drink Adequate Amounts of Water with Each Pill: Administering water after giving medication is not a common practice for companion animals like cats and dogs, which can increase the risk of pills becoming lodged in the esophagus (Graham *et al*., 2000). A study of normal cats (Westfall *et al*., 2001) demonstrated that dry swallowing tablets or capsules led to prolonged esophageal retention compared to swallowing with water. To prevent medication-induced esophagitis or stricture formation, it is recommended to provide a small amount of water after administering oral tablets or capsules (Gaschen, 2016; Westfall *et al*., 2001; McGrotty and Knottenbelt, 2002). This practice aids in esophageal clearance, prevents mucosal injury, and enhances the dissolution and absorption of the medication. Veterinarians can achieve this by administering water orally using a syringe immediately after giving the pill. Additionally, using a single-step pill gun with flavored liquid or a pill delivery treat has proven helpful for cats (Bennett *et al*., 2010). Applying a butter or other viscous coating to tablets or capsules can also reduce the likelihood of esophageal retention (Griffin *et al*., 2003).

Maintaining Animals in an Upright Position: Keeping animals in an upright position aids the movement of pills through the esophagus into the stomach, thereby reducing the risk of esophageal retention (Bennett *et al*., 2010; Geagea and Cellier, 2008). For pets, this can be accomplished by holding them upright or encouraging them to remain standing for about 30 minutes after medication administration. This practice is especially

important for medications known to cause esophageal irritation if retained. Additionally, elevating the head and neck of bedridden animals can facilitate medication administration and decrease the likelihood of MIEI (Anderle *et al*., 2018).

Alternative Dosage Forms and Formulations: Veterinarians should proactively ask pet owners about any challenges they face when administering medication to ensure proper adherence. If difficulties are reported, a switch to a more appropriate alternative should be considered. Liquid drug formulations may be a safer option than solid forms like tablets or capsules (Grissinger, 2013). Alternatively, medications can be compounded by crushing and dissolving them into a liquid form. However, it is important to note that some oral solutions and suspensions contain excipients, such as suspension agents, sweeteners, gums, and stabilizers. These additives can increase the viscosity and osmolality of the solution, potentially leading to complications like esophageal clogging or incomplete medication delivery, as well as side effects like diarrhea (Grissinger, 2013; Reeves *et al*., 2011).

Avoid Large Pills: Large pills can increase the likelihood of esophageal retention, which may cause irritation and damage to the esophageal lining (Boyce, 1998). Opting for a liquid formulation or breaking the pill into smaller pieces can help reduce this risk. However, splitting pills is generally not recommended and should only be considered if no other suitable alternatives are available. Veterinary professionals should evaluate the size and form of the medication to ensure it is appropriate for the patient's size and health condition.

Do Not Administer Pills at Bedtime: Giving pills at bedtime raises the risk of the medication becoming lodged in the esophagus, as the swallowing reflex diminishes during sleep, leading to prolonged contact with the esophageal mucosa and potential irritation or injury. Additionally, lying down soon after taking medication can impede the pill's passage into the stomach, resulting in delayed movement through the esophagus. Administering pills at least 30 minutes to an hour before allowing the animal to lie down can help minimize the risk of esophageal retention and injury (Graham, 2000).

Avoid Using Sustained-Release Formulated Pills When Possible: Sustained-release pills are designed to dissolve gradually, which can extend their contact time with the esophageal lining if they become lodged. This prolonged exposure may worsen irritation or injury to the esophagus (Katzka, 2021). Choosing alternative formulations, such as liquid medications or immediate-release pills, is preferable because they pass through the esophagus more quickly, reducing the risk of mucosal damage (Juniarta and Wibawa, 2020). Selecting the appropriate formulation is particularly important for patients with a predisposition to esophageal issues.

Avoid Using the Known Offending Medication in Elderly or Bedridden Patients and Those with Esophageal Dysmotility: Elderly or bedridden animals, as well as those with esophageal dysmotility, are at an increased risk for MIEI due to diminished esophageal motility (Kappelle *et al*., 2016). This reduction in motility can cause difficulties in swallowing and elevate the likelihood of medication retention in the esophagus (Juniarta and Wibawa, 2020). It is critical to avoid these medications in such patients. If their use is unavoidable, alternative formulations like liquid solutions, which are easier to swallow and less likely to cause esophageal injury, should be considered. Alternatively, administration through a different route, such as topical applications, is recommended (Schmulewitz and O'Connor, 2002).

Educating Pet Owners: Educating pet owners about proper pill administration techniques and the symptoms of MIEI is vital for prevention (Maddison *et al*., 2021). It is especially important to inform pet owners about administering water after giving medications to ensure that the medication reaches the stomach quickly. Additionally, owners should be advised to keep their pets in an upright position and avoid allowing them to lie down immediately afterward, particularly if esophageal dysmotility is suspected. Educating owners about the signs of MIEI, such as difficulty swallowing, drooling, or discomfort after medication administration, can be crucial. Providing clear instructions and demonstrations enables owners to administer medications safely and recognize early signs of esophageal injury, allowing for prompt veterinary intervention.

Conclusion

This review article provides a thorough exploration of MIEI in veterinary medicine, emphasizing its significance, mechanisms, and management. It starts by highlighting the importance of MIEI and detailing the esophagus's structure and function. The article then discusses the epidemiology and etiology of MIEI, focusing on various susceptibility factors and the mechanisms of injury. Antibiotics are identified as the primary cause of MIEI in veterinary medicine. Additionally, the review outlines the clinical presentation, diagnostic approaches, and treatment strategies for MIEI, covering both immediate interventions and long-term management. Supportive care and potential complications, such as esophageal stricture and perforation, are also addressed. The article underscores the importance of prevention and the role of pet owner education, emphasizing how veterinarians can prevent esophageal retention through proper medication administration techniques and client guidance. Overall, this review aims to enhance the understanding of MIEI, with the goal of improving diagnosis, treatment, prevention, and the overall well-being of animal patients.

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