GHENT UNIVERSITY

FACULTY OF VETERINARY MEDICINE

Academic year 2015 - 2016

SYMPTOMATIC TREATMENT OF THE VOMITING DOG

by

Hayley SLUIJTERS

Promoter: Prof. dr. S. Croubels

Literature Review as part
of the Master's Dissertation

GHENT UNIVERSITY

FACULTY OF VETERINARY MEDICINE

Academic year 2015 - 2016

SYMPTOMATIC TREATMENT OF THE VOMITING DOG

by

Hayley SLUIJTERS

Promoter: Prof. dr. S. Croubels

Literature Review as part
of the Master's Dissertation

ACKNOWLEDGEMENTS

A number of individuals have given invaluable help and advice during the preparation of my literature study, *Symptomatic Treatment of the Vomiting Dog*. I would like to extend my thanks in particular to the following people:

Thank you to Prof. dr. Siska Croubels for her professional advice, critical evaluation and improvement of my work during its compilation. Furthermore, I would like to thank my parents, Ad and Lesley Sluyters, for their continuing support and motivation during my vet school endeavours, without whom none of this would be possible. In particular, thanks to Lesley Sluyters for proofreading this literature study. I am also grateful to Ruud van den Berg for his motivation and encouragement and for the many hours of help improving my Dutch writing skills. Similarly, thanks to dr. Tina Leggett (BSc) MRCVS for her initial correspondence highlighting her personal approach as a veterinarian to my topic.

Finally, I would like to thank Patsy, Harry, William, Bella, Jessa and Dille for inspiring me to pursue this incredible career.

TABLE OF CONTENTS

ABSTRACT

Vomiting is a clinical sign commonly seen in small animal practice. It can be a challenging problem for veterinary clinicians seeing that it can be associated with a multitude of causes. Underlying disease processes can be gastrointestinal or systemic and the treatment can be simple or complex. The management of vomiting requires a rational and systematic approach with a sound understanding of the pathophysiology involved. This literature study explores the anatomical and physiological processes involved in the vomiting reflex, the consequences of emesis and the general clinical management of the vomiting dog. Particular attention is given to initial supportive and symptomatic treatment, such as fluid therapy, dietary management and anti-emetic treatment, where intensive diagnostic procedures are not yet indicated.

Key words: Anti-emetic – Dog – Emesis – Symptomatic – Vomiting

SAMENVATTING

Braken bij honden is één van de meest voorkomende symptomen waar dierenartsen mee geconfronteerd worden in de praktijk. Het onderscheid tussen een zelflimiterend proces en een proces dat verdere onderzoek en behandeling vereist, verlangt een systematische en methodologische aanpak. ‘Braken’ wordt soms fysiologisch beschouwd, namelijk bij dieren die hun maaginhoud uitbraken ten behoeve van hun nakomelingen. Dit gedrag wordt soms vertoond door bepaalde hondenrassen en er blijkt een link te zijn tussen de primitiviteit van het ras en dit gedrag. Dysfagie, regurgitatie en expectoratie kunnen verward worden met braken, maar ze verschillen van etiologie. Dysfagie en regurgitatie beperken zich tot de pathologieën in de proximale delen van het gastro-intestinaal kanaal, en expectoratie tot de luchtwegen. Zij uiten zich ook door het uitwerpen van materiaal uit de muil, maar ze missen de karakteristieke prodromale tekenen geassocieerd met braken, zoals misselijkheid, ptyalisme, kokhalzen en abdominale inspanning.

Het braakcentrum ligt ter hoogte van de *formatio reticularis* in de *medulla oblongata* van de hersenstam en ontvangt afferente informatie vanuit de verschillende lichaamsdelen. Anti-emetische geneesmiddelen richten zich op bepaalde receptoren in deze locaties en de keuze van het geneesmiddel is afhankelijk van de oorspronkelijke oorzaak van de stimulus. De chemoreceptor trigger zone, het vestibulair apparaat en het braakcentrum zelf, zijn het meest betrokken bij de braakreflex.

Honden gepresenteerd met symptomen van braken moeten een grondig lichamelijk onderzoek ondergaan. Dit dient voorafgegaan te worden door een analyse van de anamnese en signalement van de patiënt. Het diagnostisch proces moet gezien worden als een algoritme.

De oorzaak van emesis kan van gastrointestinale oorsprong zijn, zoals voedingsproblemen, maagzweren of –tumoren en infecties. Het kan ook van extra-gastrointestinale oorsprong zijn en kan verder onderverdeeld worden in intra- en extra-abdominale oorzaken. Braken door intra-abdominale pathologieën, zoals nier-, lever- en urogenitaalziekten, gaan vaak gepaard met karakteristieke symptomen en/of laboresultaten. Extra-abdominale oorzaken van braken omvatten onder andere metabole afwijkingen, intoxicaties en neurologische stoornissen zoals reisziekte.

Symptomatische behandeling van de brakende hond houdt het corrigeren van afwijkingen van de norm in. Het doel daarvan is het verlichten van ongemak en het terugkeren naar fysiologische homeostase. Wanneer geen hospitalisatie en diagnostische aanpak vereist is, dan kan niet-specifieke symptomatische behandeling geïmplementeerd worden. Dit houdt in het onthouden van voedsel voor 24-48 uur, een orale elektrolytoplossing en 24 uur anti-emetische therapie. Bij genezing, kunnen kleine porties van gemakkelijk opneembaar voedsel met een laag vetgehalte frequent gegeven worden. Bij chronisch braken kan een 'elimination-challenge' dieet toegepast worden om diëtaire discrepanties zoals voedselallergie en voedsel intolerantie uit te sluiten.

Ernstig en chronisch braken leidt meestal tot dehydratatie en verlies van elektrolyten zoals kalium, natrium en chloride. Zonder ondersteunende therapie kan aanhoudend braken zich verder manifesteren in levensbedreigende situaties, zoals hypovolemische shock en metabole acidose/alkalose. Aspiratie pneumonie en ondervoeding kunnen zich ook secundair ontwikkelen. Infuustherapie is belangrijk bij honden met dehydratatie of hypovolemie. Intraveneuze crystalloide oplossingen worden bij de meeste casussen bij voorkeur gekozen. Zodra normovolemie bereikt wordt, moet de overige vochtbehoefte berekend worden. Dit omvat een eventueel bestaand tekort, onderhoudsbehoefte en voorspeld toekomstig verlies. Elektrolytonevenwichten en zuur-base stoornissen kunnen via het infuus gecorrigeerd worden en de dosering wordt berekend op basis van bloedonderzoek. Het toepassen van anti-emetische therapie in een vroeg stadium kan verslechtering van de symptomen voorkomen, echter langdurig gebruik is tegenaangewezen tenzij er tekenen zijn van een duidelijke verbetering. Zuurremmers, maagbeschermers en geneesmiddelen toegepast bij maagzweren zoals H_2-receptor antagonisten, sucralfaat en protonpomp inhibitoren worden geïndiceerd voor de gevolgen van chronische braken of hematemesis. Ze worden dus niet noodzakelijk toegepast als onderdeel van de initiële symptomatische behandeling aangezien ze geen anti-emetisch effect hebben. Analgesie of antimicrobiële geneesmiddelen kunnen onderdeel zijn van de initiële behandeling bij bepaalde aandoeningen, bijvoorbeeld pijn bij pancreatitis, of bacteriële infecties. Onderliggende pathologieën moeten gericht behandeld worden bij diagnose en dit is vaak ook curatief voor het symptoom van braken.

Sleutelwoorden: Anti-emetica – Braken – Emesis – Hond – Symptomatisch

INTRODUCTION

The retrograde expulsion of the stomach contents is no scarcity in the canine world, and it is one of the most common reasons for pet owners to present their dogs for consultation in small animal practice. The myriad of aetiologies associated with vomiting can range from simple to complex and therefore can be potentially challenging for veterinarians. A logical and systematic approach is required to sift through the acquired information and to be able to set up a plan of action. Limiting factors such as available diagnostic test facilities and client funds should also be taken into consideration and alternative options are always expected. It is important to emphasize that vomiting is simply a *clinical sign* of an underlying process that can originate from any organ system in the body. The first problem for veterinary clinicians is identifying these processes. Therefore, they must have a sound knowledge of the anatomy and physiology involved, how this affects the patient and how components of these systems can be clinically manipulated into restoring homeostasis.

In order to start the diagnostic process, the dog first needs to be made comfortable and any symptoms causing divergence from homeostasis need to be halted. This is the basis of symptomatic treatment. In some cases it is almost impossible to truly treat the symptoms of vomiting without identifying and treating the cause. Vomiting arising from pancreatitis or dogs presenting in an Addisonean crisis for example, will not respond adequately to basic symptomatic treatment alone. These patients require specific testing (see Table 3) and treatment protocols additional to the supportive therapy. Due to the huge amount of potential underlying disease processes, these will not be studied in depth as they are beyond the scope of this literature study. The core of this document will primarily focus on the symptomatic treatment of dogs presented with either an undetermined aetiology, or symptoms of uncomplicated vomiting.

An important initial consideration before any diagnosis or treatment plan can be made is whether ‘vomiting’ forms part of a normal physiological process within the species, or an actual pathological problem that requires intervention. Furthermore, veterinary practitioners need to confirm that it is indeed vomiting that they are faced with and not symptoms associated with an entirely different disease process, such as regurgitation due to a mega-oesophagus. It is paramount that this is clarified before initiating treatment. These items will first be explored before delving into the symptomatic treatment of the vomiting dog.

LITERATURE STUDY

1 WHEN IS VOMITING CONSIDERED TO BE NORMAL?

Dogs in general have a rather low threshold for vomiting and are able to expel whatever they have ingested with relative ease (Elwood, 2003), and this does not necessarily go hand in hand with an underlying pathology. This low threshold to stimulate the vomiting reflex may be attributed to the evolution of the species. A particular behavioural trait that is still shared between the domestic dog (*Canis lupus familiaris*) and its wild canid counterparts, such as the wolf (*Canis lupus*; Mech et al., 1999), is the deliberate regurgitation of semi-digested food for the young (Elwood, 2003). Although this may be seen as a type of 'vomiting' by some dog owners, it is considered to be a normal behaviour trait retained through evolution as a means to wean pups from milk onto solid food (Malm, 1995). There are, however, indications that the trait is becoming diluted through man's rigorous selection for more desirable attributes in domesticated animals, such as cleanliness (Wilsson, 1984; Malm, 1995). An abundant supply of nutritious food also removes selection pressures. In Malm's comparative study (1995) of breeding dogs, some Spitz breeds appeared to show higher incidences of regurgitative behaviour than others. This may be attributed to the debated primitiveness of the breed (Malm, 1995). Dogs bred primarily for outdoor activities such as the Swedish Dachsbrackens also rated high in the same study. Comparatively, Wilsson (1984) did not observe any regurgitation in his study involving pure bred German Shepherd dogs. A typical example of a breed that has become a popular household pet and that is diverging more and more from its original herding purpose.

The urge to purge with such ease in dogs may have also arisen from the sheer fact that dogs are omnivorous opportunists that, in general, are not particularly selective with what they eat. In this way they could easily expel the indigestible items and move on (Elwood, 2003). Furthermore, what is considered as 'normal' when it comes to vomiting can be subjective. Elwood (2003) reports that many dog owners occasionally see individual vomiting events in their dogs, but this is not out of the ordinary in the dog's lifestyle. The observed consumption of grass before these occasional vomiting acts (Elwood, 2003) would suggest that grass may serve as a kind of emetic, and this therefore questions the 'normality' of these bouts. However, Bjone et al. (2007) could only link five instances of vomiting out of a total of 709 grass-eating events in their study investigating the grass-eating habits of domestic dogs. Due to the ambiguity of the latter sporadic type of emesis, the chance of an underlying pathology cannot be completely ruled out, and it should therefore always be included in the animal's anamnesis where relevant.

2 DYSPHAGIA, EXPECTORATION, REGURGITATION AND VOMITING

Dysphagia, expectoration and regurgitation are some examples in which material may be ejected through the mouth and therefore perceived as vomiting, but symptoms surrounding these events can give an indication as to which problem is at hand. **Dysphagia** is defined as painful or difficult swallowing in which food items may be seen falling from the mouth shortly after ingestion, especially when the problem is located oropharyngeally. There are usually multiple swallowing attempts and the ejected food is undigested. Lower forms of dysphagia may however present themselves with a delayed regurgitation (Guilford, 1996). Similarly, **regurgitation** is indicative for an oesophageal problem and the dog passively ejects a 'tubular cast' of undigested food (Dunn, 1989). Usually there is no bile present and the pH of contents is usually higher than that of true vomit. For both dysphagia and regurgitation, there is no abdominal effort or signs of nausea present. **Expectoration** is the ejection of debris from the respiratory tract accompanied by forceful expiration sounds. No nausea is present and differentiation can be made via examination of the ejected material and pharyngeal inspection (Guilford, 1996). **Vomiting** is an active reflex and is often accompanied by prodromal signs of nausea, ptyalism, retching and abdominal effort. The vomitus can be partially digested with bilious staining and have a low acidic pH (Guilford, 1996; Elwood, 2003).

3 THE ANATOMY AND PATHOPHYSIOLOGY OF VOMITING

3.1 The Vomiting Reflex

In order to be able to symptomatically treat vomiting, it is necessary to possess an elementary knowledge of the canine anatomy involved, as well as of the sequence and interaction of the mechanisms that ultimately lead to the act of vomiting. Vomiting is a reflex where an organism attempts to remove potentially harmful substances from the gastrointestinal (GI) system (Elwood, 2003). The motor and sensory activities that evoke this forceful expulsion of contents from the stomach, and often from the proximal duodenum (McGrotty, 2010), are coordinated via a central pattern generator in the brain commonly known as the 'vomiting centre' (Elwood et al., 2010). The vomiting centre consists of a region of grouped neurons located in the reticular formation of the *medulla oblongata* (Fig. 1) (Devauchelle et al., 2006; Encarnación et al., 2009; Uemura, 2015). The centre is an integration zone. Neural and humoral afferent signals arrive from numerous locations in the body and synapse in the medulla. Efferent pathways leave the medulla and ultimately result in the motor events involved in the vomiting act. Furthermore, neural centres associated with other somatic systems are also located within the vomiting centre and the afferent impulses subsequently result in their co-stimulation. These centres are responsible for the control of peri-emetic respiration, salivation and swallowing (Strombeck and Guilford, 1996).

This overlap of pathways is necessary to protect the body against the mechanical effects of vomiting. For example, ptyalism (or hypersalivation), which precedes emesis, causes repeated swallowing actions. This in turn leads to the stimulation and subsequent relaxation of the gastroesophageal sphincter in preparation for the expulsion phase. Saliva also acts as a lubricant and is additionally rich in bicarbonate neutralising the low pH of the vomitus and thus shielding the oesophagus and oral cavity from gastric acid. Respiration is conversely inhibited during vomiting, necessary for the prevention of aspiration pneumonia and nasal regurgitation. This is achieved through closure of the glottis and nasopharyngeal orifice during emesis (Strombeck and Guilford, 1996; Encarnación et al., 2009).

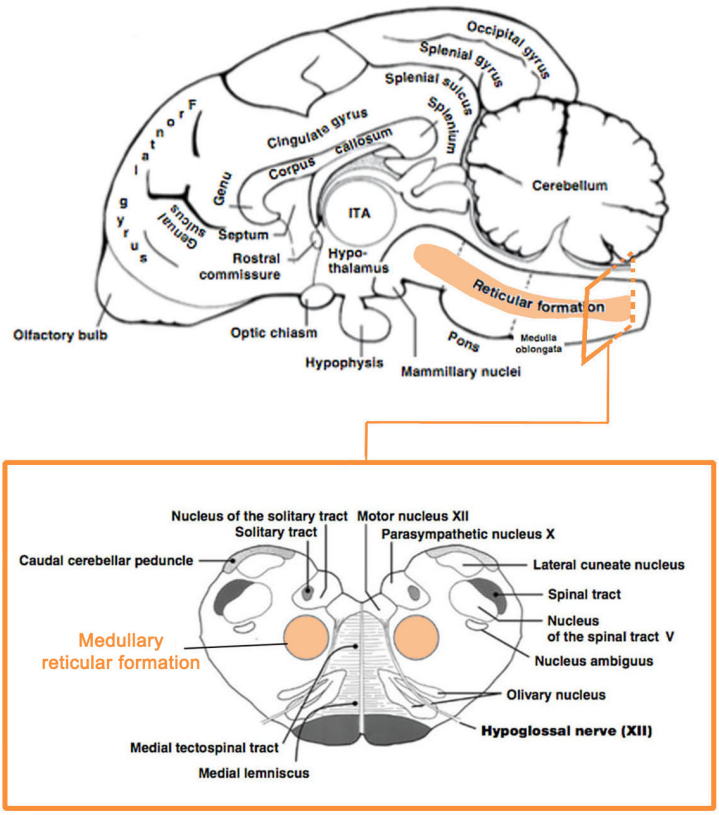

Fig. 1: Above: Midsagittal view of the canine brain. The reticular formation occupies the core of the brainstem and extends from the midbrain to the *medulla oblongata*.
Below: Transverse section of the *medulla oblongata* at the level of the vomiting centre, which is comprised of a group of neurons located within the reticular formation (adapted from Uemura, 2015)

The afferent data received by the vomiting centre is relayed from various sites in the body in response to a myriad of physiological and pathological stimuli. The main routes that orchestrate these stimuli include receptors within the abdominal viscera, namely the stomach and duodenum; the receptors in the vestibular apparatus that can be stimulated through motion or vestibular disease; higher cerebral cortical receptors that transfer psychogenic, traumatic and pain signals; and the chemoreceptor trigger zone (CTZ) responding to chemical changes in the blood and cerebrospinal fluid (CSF) (Fig. 2) (Encarnación et al., 2009; Elwood et al., 2010; Uemura, 2015).

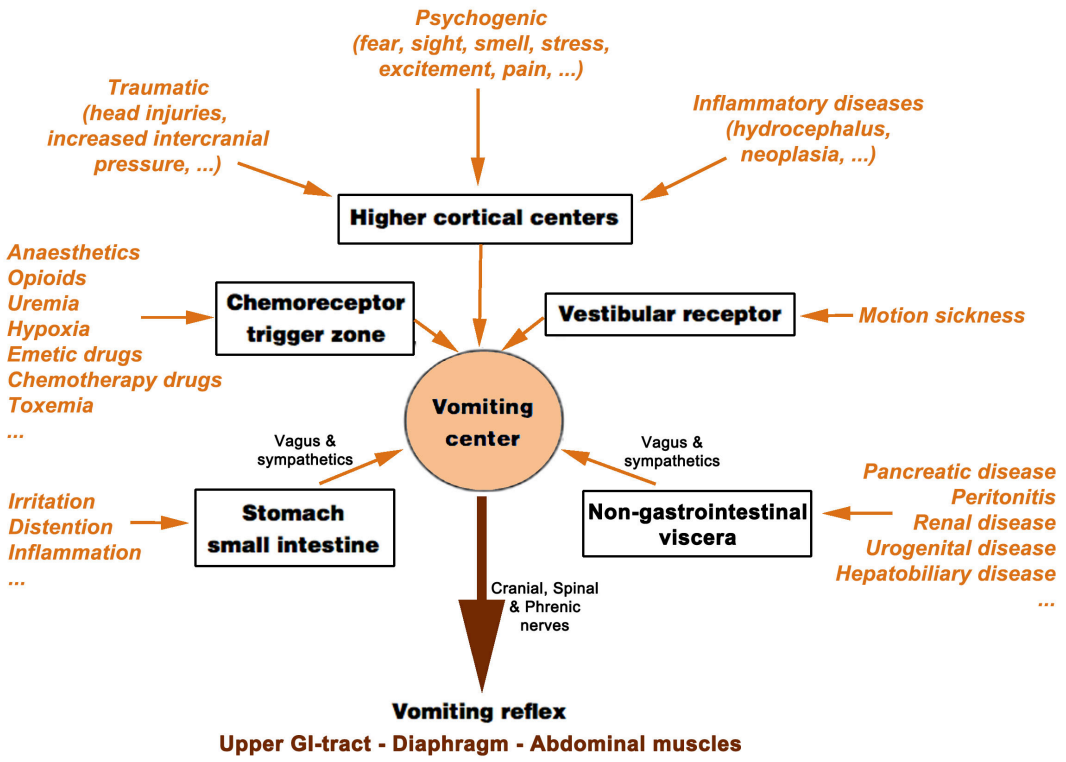

Fig. 2: Diagrammatic representation of de afferent (orange) and efferent (brown) pathways involved in the vomiting reflex. The vomiting centre is located in the medullary reticular formation and coordinates the afferent signals into a final common pathway for efferent responses that ultimately leads to the vomiting response. GI: Gastrointestinal. (Summarised and adapted from Strombeck and Guilford, 1996; Encarnación et al., 2009; Elwood et al., 2010; Uemura, 2015).

3.2 The receptors involved in the vomiting reflex

The GI system, in particular the stomach and duodenum, possesses a number of chemoreceptors, osmoreceptors and mechanoreceptors (Strombeck and Guilford, 1996; Uemura, 2015). The chemoreceptors are responsible for the detection of toxins present in the lumen of the GI-tract, and the mechanoreceptors detect stress on the tract walls caused by distension, torsion or obstruction (Uemura, 2015). Osmoreceptors present in the duodenum can induce vomiting when amplified emptying of the stomach ('gastric dumping') threatens the integrity of the intestinal mucosa (Strombeck and Guilford, 1996). The majority of the receptors in the stomach and duodenum utilize the vagal nerves for their afferent signalling pathway to the emetic centre, and any remaining receptors along the intestines use the sympathetic fibres (Fig. 2). Important receptors along this pathway are, for example, the neurokinin-1 (NK-1) receptors in the stomach and serotonin (5-HT_3) receptors along the vagal afferent fibres (Encarnación et al., 2009; Elwood et al., 2010). These receptors are stimulated by certain neuropeptides involved in the vomiting cascade and have therefore become prime targets of several anti-emetic drugs (Table 1). Table 1 shows the most important receptors engaged in the control of vomiting within the vomiting reflex, their natural neurotransmitters and some antagonistic pharmaceuticals commonly used in small animal medicine.

Table 1. Receptors in the Vomiting Reflex, their neurotransmitter agonists, receptor antagonistic drugs, doses and possible adverse effects in dogs (summarised and adapted from [a] Encarnación et al., 2009; [b] Elwood et al., 2010; and dosages from [c] Plumb D.C., 2008).

Receptor	Site of Action	Receptor Agonists	Receptor Antagonists	Dosage dogs[a,b,c]	Adverse effects[b,c]
α_2-Adrenergic	CTZ[§] Emetic Centre	Norepinephrine	Prochlorperazine	0.1-0.5 mg/kg SQ/IM q6-8h	Sedation, hypotension
			Chlorpromazine	0.1-0.5 mg/kg SQ/IM/IV q6-8h	
			Yohimbine	0.25-0.5 mg/kg SQ/IM q12h	
			Acepromazine[§]	0.01-0.05 mg/kg SQ/IM; 1-3 mg/kg PO	
D_2-Dopaminergic	CTZ Vagal Efferents	Dopamine	Metoclopramide	0.1-0.4 mg/kg PO/SQ/IM q6h 1-2 mg/kg/day constant rate infusion	Constipation, behaviour changes, extrapyrimidal signs
			Trimethobenzamide	3 mg/kg IM q8-12h	Allergic reactions
			Chlorpromazine	0.1-0.5 mg/kg SQ/IM/IV q6-8h	Sedation, hypotension
			Prochlorperazine	0.1-0.5 mg/kg SQ/IM q6-8h	
			Acepromazine	0.01-0.05 mg/kg SQ/IM; 1-3 mg/kg PO	
			Butyrophenones	2-5mg per dog q8h	
$ENK_{\mu,\delta}$-Enkephalinergic	CTZ	Met-enkephalin Leu-enkephalin	Butorphanol	0.2-0.4 mg/kg IM ½ hour prior to cisplatin treatment	Sedation, ataxia, anorexia, diarrhoea
Glucocorticoid	Emetic Centre	Dexamethasone	-	0.1 mg/kg SQ or IV before chemotherapy	GI ulceration
H_1-Histaminergic	CTZ[§] Vestibular App.[❖]	Histamine	Diphenhydramine	2-4 mg/kg PO/IM q8h	Sedation, GI effects
			Dimenhydrinate	4-8 mg/kg PO q8h	
			Meclizine	4 mg/kg PO q24h	Sedation, xerostomia, tachycardia
			Prochlorperazine	0.1-0.5 mg/kg SQ/IM q6-8h	Sedation, hypotension
			Chlorpromazine	0.1-0.5 mg/kg SQ/IM/IV q6-8h	
			Acepromazine[§]	0.01-0.05 mg/kg SQ/IM; 1-3 mg/kg PO	
			Diazepam[❖]	0.1-0.2 mg/kg PO q6h	Sedation
Motilin	Vagal Efferents	Erythromycin	-	0.5-1.0 mg/kg IV q8h	Rarely allergic reactions

Table 1 (cont.). Receptors in the Vomiting Reflex, their neurotransmitter agonists, receptor antagonistic drugs, doses and possible adverse effects in dogs

Receptor	Site of Action	Receptor Agonists	Receptor Antagonists	Dosage dogs[a,b,c]	Adverse effects[b,c]
M_1-Cholinergic	CTZ, NTS Vestibular App.	Acetylcholine	Propantheline	0.25 mg/kg PO q8h	Xerostomia, tachycardia, Ileus, GI retention
			Isopropamide	0.2-0.4 mg/kg PO q8-12h	
			Prochlorperazine	0.1-0.5 mg/kg SQ/IM q6-8h	Sedation, hypotension
M_2-Cholinergic	Vagal Efferents	Acetylcholine	Chlorpromazine	0.1-0.5 mg/kg SQ/IM/IV q6-8h	Sedation, hypotension
			Acepromazine	0.01-0.05 mg/kg SQ/IM; 1-3 mg/kg PO	
NK-1	CTZ, Stomach Emetic Centre Vest. App., NTS Vagal Afferents	Substance P	Maropitant	1 mg/kg SC q24h up to 5 days 2 mg/kg PO q24h up to 5 days Motion sickness: 8 mg/kg PO 2 hours prior to travel and q24h max 2days	Swelling/pain at injection site High dose for motion sickness: pre-travel vomiting, ptyalism
5-HT_{1A}-Serotonergic	Emetic Centre	Serotonin	Diphenhydramine	2-4 mg/kg PO/IM q8h	Sedation, GI effects
			Dimenhydrinate	4-8 mg/kg PO q8h	
			Meclizine	4 mg/kg PO q24h	Sedation, xerostomia, tachycardia
5-HT_3-Serotonergic	CTZ Vagal Afferents	Serotonin	Ondansetron	0.1-0.2 mg/kg IV q6-12h 0.1-1 mg/kg PO q12-24h	Well tolerated; (Constipation, arrhythmia, hypotension)
			Dolasetron	0.5-0.6 mg/kg IV/PO/SQ q24h	Well tolerated
			Mirtazapine	0.6 mg.kg PO q24h (max. 30 mg/day)	Sedation, vocalisation, tachycardia
			Metoclopramide	0.1-0.4 mg/kg PO/SQ/IM q6h 1-2 mg/kg/day constant rate infusion	Constipation, behaviour changes, extrapyrimidal signs
			Granisetron	0.1-0.5 mg/kg PO/IV q12h	Tolerated well; (headaches)
5-HT_4-Serotonergic	Vagal Efferents	Cisapride	-	0.1-0.5 mg/kg PO q8h	(Cardiac arrhythmia)

Abbreviations: CTZ, Chemoreceptor Trigger Zone; NK, Neurokinin; 5-HT, 5-hydroxytryptamine; SQ, subcutaneous; IM, Intramuscular; IV, Intravenous; PO, per os; q, every; GI, Gastrointestinal; NTS, *Nucleus tractus solitarii*; [§] CTZ only; [❖] Vestibular Apparatus only; Brackets: adverse effects reported in humans that may be relevant in veterinary patients[c]

The CTZ is an emetic chemoreceptor and is located in the *area postrema*. This is a small area situated immediately adjacent to the obex in the wall of the fourth ventricle on the dorsal surface of the *medulla oblongata* (Miller and Leslie, 1994; Uemura, 2015). An important feature of the CTZ is its lack of a 'blood-brain barrier'. This can be illustrated using electron microscopy where the presence of fenestrated blood vessels and an absence of tight junctions (*zonulae occludentes*) can be seen (Miller and Leslie, 1994). It also possesses free nerve endings that make direct contact with the cerebrospinal fluid and therefore the CTZ can respond to many emetic stimuli and humoral substances that affect the blood or CSF, such as anaesthetic drugs, emetic agents such as apomorphine, chemotherapeutic substances, electrolyte imbalances, acid-base irregularities etc. (Miller and Leslie, 1994; Encarnación et al., 2009).

Many anti-emetic pharmaceuticals act on different receptors within the CTZ and are thus targeted primarily at the humoral pathway, for example metoclopramide, which is a potent D_2-dopaminergic antagonist (Encarnación et al., 2009). More recent drugs, such as maropitant, an NK-1 receptor antagonist, are thought to have advantages over the other drugs because they may be effective on both the humoral and neural pathways (Ramsey et al., 2008). The target receptor and the cause of the vomition are of utmost importance when choosing an anti-emetic drug. Drugs specific for vomiting elicited by one cause, do not necessarily inhibit vomiting from another cause, even if the involved receptors share the same location. For example, 5-HT_3-serotonergic and H_1-histaminergic receptors can both be found in the CTZ, but antagonism of 5-HT_3 receptors to control chemotherapy- and radiation-induced sickness, is ineffective against nausea induced by motion sickness. Similarly, antihistaminic (H_1-receptor) drugs for the treatment of motion sickness have a very weak potency against the cancer-therapy sickness (Uemura, 2015). As mentioned before, Table 1 shows some antagonistic pharmaceuticals commonly used in small animal medicine.

4 CLINICAL PRESENTATION AND INITIAL ASSESSMENT

The initial assessment of any patient allows the veterinarian to identify the severity of the case and to choose an initial treatment plan. For the identification of life-threatening cases, such as gastric dilation-volvulus or septic shock, treatment should be immediately applied before other procedures are carried out (McGrotty, 2010). For all cases, a history and clinical examination are the first steps in the diagnostic procedure.

4.1 Signalment

Vomiting cases can roughly be differentiated into those in which the problem is self-limiting and no treatment is required, those where symptomatic treatment will suffice and cases that require specific treatment or further diagnostic intervention (Elwood et al., 2010).

The signalment of the patient helps to assess the likelihood of certain predisposed disorders known to induce vomiting. For example, puppies and young dogs are more susceptible to infectious and parasitic diseases such as parvovirus (Desario et al., 2005), and consideration should be given to foreign body ingestion due to the inquisitive nature of this age (Elwood, 2003). Other diseases are more common in older dogs, such as gastric neoplasia, and as highlighted in one study (Gualtieri et al., 1999), age is not the only signalment at play: the prevalence of gastric adenomas has a gender-bias towards the male population, and a breed predisposition has also been reported for gastric carcinomas for the Rough Collie, Staffordshire Bull Terrier and Belgian Shepherd (Gualtieri et al., 1999). Similarly, it is not uncommon to witness regurgitation and vomiting in brachycephalic dog breeds due to their anatomical conformation. This may further lead to swallowing disorders and result in respiratory distress. Aerophagia resulting in chronic distension of the GI-tract, and congenital or acquired pyloric hypertrophic gastropathy are also commonly described in the same breeds (Lecoindre and Richard, 2004).

4.2 Anamnesis

A detailed and accurate history is essential and in particular the veterinarian must differentiate between true vomiting and clinical problems that owners may perceive as vomiting, such as regurgitation (Dunn, 1989; Guilford, 1996; Leib, 1999; Elwood et al., 2010), expectoration or dysphagia (Guilford, 1996) (see Chapter 2). A diet history should be sought with details about frequency of feeding, quantity given, recent dietary changes and any relation between eating or drinking and the vomiting events (Dunn, 1989). In some cases a highly digestible diet for 3-4 weeks can often resolve the problems (Leib, 1999).

Information about the onset and duration of the vomiting is also crucial. Quite often, acute vomiting can be handled symptomatically, however this is not exclusive and can be indicative for processes which require further intervention, such as metabolic disturbances, foreign body ingestion, pancreatitis or toxin exposure etc. Emesis with a chronic, intermittent or refractory behaviour can be associated with a process that is not self-limiting, such as a chronic GI disease (e.g. chronic gastritis or inflammatory bowel disease (IBD) (Elwood, 2003)). This would again require further diagnosis and treatment (Elwood et al., 2010). Details of the vomitus itself, such as quantity, colour and consistency, are also helpful. The vomiting of bile on an empty stomach can indicate gastric irritation, whereas the purging of undigested food may allude to pyloric obstructions such as a stenosis or the presence of a foreign body (Elwood, 2003). Under normal circumstances, the ingesta should have left the stomach within 6-8 hours (Dunn, 1989). Haematemesis requires more vigorous attention and may present itself as undigested red blood, or as a digested ‘coffee-grounds’ aspect. The former is indicative for a loss of gastric mucosal integrity, often observed with gastric ulcers and tumours, but can also be associated with the trauma of the vomiting act itself (Elwood, 2003).

Table 2. Potential Causes of Vomiting in the Dog (Summarised and adapted from Guilford, 1996; Elwood, 2003; Chandler, 2010; Elwood et al., 2010)

Gastrointestinal

- Dietary indiscretion
- Allergy
- Eating too rapidly
- 'Garbage gut'
- Gastritis (Eosinophilic; Lymphoplasmacytic; Granulomatous; Acute)
- Gastroenteritis
- Gastric ulceration (NSAIDs; neoplasia*; Metabolic; hypergastrinaemia; irritants)
- Gastric/ intestinal neoplasia*
- Gastric/ intestinal entrapment*
- Gastric dilatation-volvulus*/ intestinal volvulus*
- Hiatal hernia*
- Pyloric stenosis*
- Polyp*
- Gastric/ intestinal foreign body*
- Inflammatory Bowel Disease (IBD)
- Intussusception*
- Motility disorders

Infection/Infestation

- Canine Parvovirus
- Canine Distemper virus
- Canine Corona virus
- Campylobacteriosis
- Leptospirosis
- Salmonellosis
- Toxoplasmosis
- Giardiosis
- Babesiosis
- Leishmaniasis
- *Ollulanus tricuspis*
- Helicobacteriosis
- Hookworms/ Roundworms (*Toxocara canis*)

Extra gastrointestinal

Intra-abdominal

- Hepato-biliary disease
- Obstructed/ruptured biliary tree*
- Portosystemic shunt*
- Renal disease
- Splenic disease
- Pancreatic disease
- Urogenital disease
  - Pyometra*
  - Endometritis
  - Prostatitis
  - Urolithiasis
- Peritonitis*
- …

Extra-abdominal

Metabolic

- Hypoadrenocorticism
- Ketoacidosis
- Uraemia
- Hypercalcaemia
- Hypokalaemia
- Hyper/hyponatraemia
- Septicaemia
- …

Intoxications

- Ethylene glycol
- Heavy metals (Pb, As, Zn, Fe, Tl, …)
- Theobromine
- Ethanol
- Grapes
- Herbicides
- Molluscicides
- Pesticides (e.g. Strychnine, …)
- Rodenticides
- Mycotoxins (vomitoxin)
- ...

Toxic plants

- Daffodil
- Rhododendron
- …

Drugs

- Chemotherapeutics
- Corticosteroids
- Apomorphine
- Digoxin
- Erythromycin
- Opiates
- Overexertion
- Heat stroke
- …

Neurological

- Motion sickness
- Encephalitis
- Meningitis
- Intracranial pressure
- Vestibular disease
- Trauma
- Hydrocephalus
- Extreme pain
- …

Abbreviations: NSAIDs, Non-steroidal anti-inflammatory drugs; Pb, Lead; As, Arsenic; Zn, Zinc; Fe, Iron; Tl, Thallium
*Critical conditions that require immediate surgery or surgery after the patient has been stabilised

The co-presence of any other ailments may give more specific detail as to what is at hand. For example, a malodourous vaginal discharge may indicate a pyometra or mucometra (Pretzer, 2008); diarrhoea could suggest intestinal disease, pancreatitis or infection (Elwood et al., 2010); weight loss is often associated with chronic tumours (Gualtieri et al., 1999); cranial abdominal pain is often evident with pancreatitis (Watson, 2004), and so forth. Table 2 summarises some of the most common causes of vomiting in dogs, and a detailed history together with a thorough physical examination (see chapter 4.4) can help to rank the rule-out list.

4.3 Intoxication

Another point to consider is the potential access to any toxic substances. Toxicity as a result of the ingestion of certain garden and household plants may not account for the majority of calls to poison centres (Campbell, 1998; Berny et al., 2010; Vandenbroucke et al., 2010), but often have vomiting as a major symptom. Daffodils (*Narcissus* genus), for example, contain alkaloids and glycosides, which have emetic properties. The highest concentrations lie in the bulbs and ingestion mostly leads to the rapid onset of clinical symptoms with GI upset predominating, however, ingestion of amounts exceeding 15g of daffodil bulb may be fatal in dogs (Campbell, 1998). Some plant toxicities may also coincide with yearly holidays such as Christmas where toxic plants are brought indoors for decorative purposes. Some popular examples include mistletoe (*Viscum album*), holly (*Ilex aquifolium*) and poinsettia (*Euphorbia pulcherrima*), all of which can elicit emetic symptoms after ingestion (Severino, 2009).

Comparatively, a ten-year review of animal poisonings in Belgium revealed that most calls to the Belgian Poisons Centre regarded agrochemical intoxication in dogs with the since-banned carbamate insecticides, aldicarb and carbofuran (Vandenbroucke et al., 2010). Vomiting is the foremost symptom of aldicarb toxicosis and this is reflected in the retrospective study conducted by Anastasio et al. (2011) where 93% of affected dogs presented with emesis as one of their symptoms.

Food items intended for human consumption may also pose a risk. Ingestion of grapes, currants, raisins and sultanas (*Vitis vinifera*) causes acute renal failure in dogs, but general GI signs are also often present. It is important to promptly administer an emetic if the patient has not yet purged, as their use appears to be particularly effective in reducing the severity of the toxicity (Sutton et al., 2009). Chocolate toxicity in dogs is attributed to the canine's relatively slower biotransformation rate of the chemical compound theobromine in comparison with that of humans. This means that intoxication occurs at low doses of theobromine and poisoning may persist for up to 72 hours. Symptoms such as vomiting and diarrhoea can already be present in mild cases, but this can escalate with severity to cardiac arrhythmias, epileptogenic convulsions, internal bleeding and sometimes death (Ahlawat et al., 2014).

Ethylene glycol is an alcohol present in many household products such as antifreeze and de-icers. It bears no colour or odour and is palatable, making it a common candidate for accidental (or deliberate) intoxication in dogs. Within the initial 12 to 24 hours post-ingestion, symptoms such as vomiting, listlessness and neurological effects can be observed. Here, vomiting results from the rapid uptake of the toxin into the GI tract. Purging is essential for the removal of excess toxin and the dog's survival, although fatal doses are often retained. After 24 to 72 hours, dogs develop renal insufficiency where further vomiting is then attributed to the ensuing uraemia (Herd, 1992).

4.4 Physical examination

The objective of a physical examination is to determine deviations from the norm through a systematically conducted assessment and to identify the aetiology of the vomiting. The examination should always begin with observation of the **unrestrained patient** at floor level. The dog's weight, posture, gait, alertness, mentation and behaviour can be observed whilst the dog is still relatively calm (Guilford, 1996).

Inspection of the oropharynx and palpation of the neck and throat area can reveal any foreign bodies or trauma. The presence of characteristic tooth abrasion, for example, can identify 'rock-chewers'; these animals may swallow stones making them possible candidates for GI obstruction (Chandler, 2010). Halitosis is usually associated with dental disease (Guilford, 1996), but may also allude to stagnant food particles present, such as in the case of a mega-oesophagus, or necrosis resulting from a foreign body, tumour or salivary gland necrosis (Guilford, 1996; Elwood et al., 2010). Alternatively, ketone (acetone) breath is an odour commonly associated with diabetic ketoacidosis and is often accompanied by vomiting and dehydration (Koenig, 2013). Dehydration can be identified by tacky mucus membranes, skin-tenting and sunken eyes (Elwood, 2003; Chandler, 2010), and hypovolaemia through the presence of pale membranes, an increased capillary refill time, tachycardia and a weak pulse. Contradictory findings of a low or normal heart rate together with hypovolaemic indications may be a hint for hypoadrenocorticism (Addison's disease) (Elwood, 2003).

Palpation of the abdomen is a key point in the assessment of vomiting dogs. This is best carried out in a methodological fashion with the clinician situated directly behind the standing patient. Beginning craniodorsally and continuing to a caudoventral position (Elwood, 2003), the veterinarian can assess the abdomen for evidence of fluid undulations, irregular densities such as abdominal masses or foreign objects, intussusception, organomegaly and focal or general responses to pain or discomfort (Chandler, 2010). For the palpation of the more cranially located organs, such as the stomach, it may be helpful to raise the dog's forepaws to allow the organs to be subjected to gravity (Guilford, 1996; Elwood, 2003).

To elicit a pain response in the case of pancreatic of biliary disease, a deeper palpation may be necessary in the right cranial abdomen (Elwood, 2003). This is not pathognomonic as abdominal pain is also often present in, but not limited to, acute gastritis or gastroenteritis, acute hepatitis, pyelonephritis, foreign bodies, intussusception and peritonitis. Conversely, abdominal pain is a less consistent symptom associated with hypoadrenocorticism (Dunn, 1989). Fluid within the abdomen can often be detected on the contralateral side of a percussed abdomen, but this may not always be evident at the time of consultation. For example, in the case report conducted by Van Israël et al. (2002) of an entire Labrador Retriever bitch presenting predominately with acute vomiting and lethargy, no abdominal fluid was detected in the initial clinical and imaging work-ups, however cranial abdominal pain was present. After 12 hours of treatment, ultrasonography was repeated and a moderate amount of peritoneal fluid was detected, aspirated via abdominocentesis and submitted for culture. Septic peritonitis was diagnosed. Subsequently, large amounts of pyo-haemorrhagic free fluid were observed at the time of surgery. The ultimate diagnosis was a unilateral pyometra with ovarian bursal abscessation with secondary septic peritonitis (Van Israël et al., 2002).

Auscultation of the abdomen may reveal an increase or a decrease in the amplitude, duration or frequency of borborygmus in the stomach, small intestine and colon. The presence of gas increases the amplitude and frequency of the sounds, and fluid increases the number of sounds in the small intestine. There must be a loss in GI motility in order for gas and fluid to accumulate, although some movement must remain for the generation of sounds between the various mediums. Therefore, paradoxically, an increase in the sounds is usually linked to partial loss of contractility (Guilford, 1996). This is the case, for example, with acute enteritis, toxins and acute obstruction (Chandler, 2010). A complete loss of motility, or adynamic ileus, however, will result in fewer borborygmi, and is suggestive of peritonitis, ileus and chronic obstruction (Guilford, 1996; Chandler, 2010). Tympanic sounds upon percussion and auscultation of a distended, painful abdomen may be indicative for a gastric dilatation-volvulus and is more common in large deep-chested dog breeds (Monnet, 2003).

A digital **rectal examination** allows the veterinarian to inspect the perianal structures, such as the anal glands, pelvis, rectum and prostate, for inconsistencies and irregularities. A fresh stool sample may also be evaluated for abnormalities in the colour and consistency. The presence of melena, for example, indicates that blood has been retained in the GI tract for some time and is more indicative for upper GI problems. In humans it is estimated that blood must be present in the intestinal tract for at least eight hours before visible melena can form, and in dogs at least 350 mg of haemoglobin per kilogram body weight is also required. Forty-six dogs with gastic neoplasia were compared in a study by Gualtieri et al. (1999). Of the 42 dogs with a gastric carcinoma, 41 showed persistent vomiting as a main symptom, and six of the dogs also had melena (Gualtieri et al., 1999). Hematochezia is more suggestive for lower colon haemorrhages (Guilford, 1996).

Physical examination of the prostate gland in male dogs is accomplished by simultaneous external pressure of the prostate through the abdomen caudally towards the pelvic canal, together with a digital rectal examination. Size, shape, consistency, symmetry, mobility and pain can be assessed for the presence of prostatic disease (Williams and Niles, 1999).

5 DIAGNOSTIC APPROACH

Table 3: Diagnostic tests used in the investigation of dogs with emesis (Reproduced from Elwood et al., 2010)

Diagnostic test	Indication	Sought information
Complete blood count	Criteria for concern (see Table 6)	Dehydration, hemoconcentration, leucopenia, polycythaemia, anaemia, microcytosis, eosinophilia
Total protein, albumin	Diarrhoea, ascites	Hypoproteinaemia
Liver enzymes, bile acids	Jaundice, chronic emesis	Hepatobiliary disease
Blood glucose	Diarrhoea in toy breeds, seizures	Hypoglycaemia
Calcium	Polyuria/ polydipsia	Hypercalcaemia, Hypocalcaemia
Pancreatic enzymes (cPLI)	Abdominal pain	Pancreatitis
ACTH-stimulation test	Bradycardia, hyperkalaemia, dehydration, polyuria, weakness, lack of stress leukogram, hypocholesterolaemia	Hypoadrenocorticism (Addison's disease)
Coomb's test	Pale mucous membranes, jaundice	Immune-mediated haemolytic anaemia
Electrolytes	Dehydration, dysrhythmias, bradycardia, fluid therapy	Electrolyte disturbances that need correction by fluid therapy
Culture of bile	Liver enzyme activity increases, abnormal gall bladder content on ultrasound	Bacterial cholecystitis
Ultrasonography	Abdominal mass, increases in liver enzyme activity, free fluid in abdomen	Hepatobiliary disease, foreign bodies, neoplasia, urinary tract disorders, mucometra, pyometra, pancreatitis
Radiography	Very frequent acute vomiting, vomiting large volumes (especially if food has been withheld), vomiting contents of a foetid nature	Foreign body, gastric position and size, peritonitis, ilieus, intestinal entrapment
Electrocardiography	Dysrhythmias, bradycardia	Hyperkalaemia
CT	Abdominal organomegaly, focal pain	Evaluation of abdominal organs
MRI	Abdominal organomegaly, focal pain, neurological signs	Evaluation of abdominal organs, evaluation of CNS disease
Liver biopsy	Increases in liver enzyme activity and/or bile acid concentration, abnormal appearance of liver on ultrasound	Hepatobiliary disease
Endoscopy	Ingestion of foreign body, chronic emesis and/or diarrhoea	Visualisation of mucosa, gastric and intestinal biopsies
Faecal examination	Diarrhoea	Parasitic disease
Urinalysis	Signs of urinary tract disease (dysuria, haematuria)	Urolithiasis, urinary tract inflammation and/or infection
Parvovirus antigen test	Diarrhoea, haematochezia	Parvoviral enteritis

Abbreviations: cPLI, canine pancreatic lipase immunoreactivity; ACTH, adenocorticotropic hormone; CT, computed tomography; MRI, magnetic resonance imaging; CNS, central nervous system

Following the initial consultation, a plan of action should be made to either continue treating symptomatically, or resort to more specific treatment based on laboratory findings (Elwood, 2003). The results of these tests help sculpt the rule-out list. A myriad of tests are available to diagnose specific aetiologies, the most common of which are listed in Table 3. Further detail regarding each test and disease process is beyond the scope of this literature study and shall not be discussed in detail.

6 THE CONSEQUENCES OF VOMITING

Intractable vomiting often has systemic repercussions. Regardless of the underlying cause, the loss of GI fluid and electrolytes (together with less water intake) often leads to dehydration and electrolyte imbalances, such as hypokalaemia. This is accentuated if diarrhoea is also present, which is often the case with many GI ailments. Further manifestations, such as hypovolaemic shock and disturbances in the acid-base homeostasis resulting in metabolic acidosis/alkalosis, can be life threatening (Boag et al., 2005; Elwood, 2010). It is important to note that anti-emetic therapy is directed against the symptoms. Quite often this is a short-term therapy and a search for a definitive diagnosis should be made so that long-lasting success can be achieved (Strombeck and Guilford, 1996). When vomiting is seen intermittently, the associated fluid and electrolyte imbalances can quite often be corrected without further use of anti-emetic pharmaceuticals. Aspiration pneumonia is a secondary complication that results from the inhalation of oropharyngeal or GI contents into the respiratory tract. In a retrospective case study conducted by Kogan et al. in 2008, vomiting and oesophageal disease were by far the most common cause of aspiration pneumonia, scoring respectively 34 and 35 out of the 88 dogs compared. Early diagnosis and treatment is here paramount in order to prevent further damage to the integrity of the respiratory mucosa caused by the ensuing chemical, bacteriologic and immunologic mechanisms (Kogan et al., 2008). Chronic vomiting can also prevent the normal intake of food and water, with malnutrition and protein loss as a result (Elwood, 2010).

7 MANAGEMENT OF VOMITING

Deciding if the emesis should be treated, or opting to wait and see if the symptoms resolve by themselves, depends on the individual case and the balance between the risks and benefits of the treatments (Elwood et al., 2010). In a survey of dog owners registered at veterinary practices, 19.9% of 772 evaluated questionnaires revealed vomiting episodes with their dogs. Of these, 89% of the cases resolved by themselves within 2 days. Overall, only 5% of the vomiting dogs were actually seen for veterinary support (Hubbard et al., 2007).

7.1 Nutritional therapy

7.1.1 Acute vomiting

Acute gastroenteritis is the most commonly seen ailment in practice that is associated with vomiting. It is often self-limiting and if the dog is not showing signs of systemic distress, supportive treatment alone may be sufficient. Abstinence from food for 24 to 48 hours is effective in giving the stomach and intestines a rest (McGrotty, 2010). In acutely inflamed stomachs, even minor distension could be sufficient to elicit the vomiting reflex (Strombeck and Guilford, 1996). Residual food particles in the bowel can also lead to osmotic diarrhoea and withholding food can not only alleviate these symptoms, but also reduce antigenic stimulation of the GI mucosae. When symptoms have resided, a bland, low-fat, readily absorbable diet can be reintroduced, ideally in small amounts given frequently. As mild dehydration is often present, oral rehydration may be administered (McGrotty, 2010).

7.1.2 Chronic vomiting

Chronic vomiting and diarrhoea may arise from adverse food reactions (AFR). **Food allergy**, or dietary hypersensitivity, is an over-exaggerated immune response to a specific food substance; in dogs this is usually a protein. **Food intolerance** is a non-immunologic response to a foodstuff and may have numerous causes (Gaschen and Merchant, 2011). The most well known is a deficiency in the digestive enzyme lactase leading to lactose intolerance (Webb and Twedt, 2003). Dietary idiosyncrasies, such as gluten-sensitive enteropathy, is another example, and Irish Setters are here predisposed (Gaschen and Merchant, 2011). Animals suspected of having an AFR should undergo an elimination-challenge trial where a hypoallergenic diet replaces the dog's current diet for a minimum period of two weeks. In AFR cases, the allergic symptoms should (partially) resolve, followed by recrudescence of the symptoms when the dog is 'rechallenged' with its original food (Guilford, 1996; McGrotty, 2010). Since proteins are mostly responsible for discrepancies, constituents of an elimination diet are usually sourced from foods not commonly included in the animal's usual diet, and are thus novel proteins (e.g. rabbit, venison, duck, etc.). There is still controversy in the choice of novel protein diet. Commercially prepared diets eliminate nutritional faults that could arise with home-prepared meals, and are also less labour intensive. However, in a study of four different over-the-counter hypoallergenic dog foods commercialised as appropriate for elimination trials, traces of common pet food proteins such as beef and soy were detected using enzyme-linked immunosorbent assay (ELISA) (Raditic et al., 2011). This raises concerns as to whether allergens are reconfigured during the heat and extrusion process (Gaschen and Merchant, 2011). Hydrolysed protein diets are another option for elimination trials. These proteins are miniscule and their molecular weight is not detectable by the immune system, making them ideal candidates (McGrotty, 2010).

7.2 Fluid therapy

Fluid choice in the vomiting patient can be complex. Careful attention must be given to the physical examination to assess dehydration status (see chapter 4.4) and the dog's electrolyte and acid-base balance in order to select the correct fluid therapy. There are numerous routes of administration possible. **Oral rehydration therapy** is best used in mild to moderate dehydration cases, and never for hypovolaemic patients. The co-uptake of sodium and glucose initiates the secondary retention of water via the jejunum. **Subcutaneous** fluid therapy is indicated for patients that cannot be hospitalised, but may benefit from rehydration. The injectable fluid must be a crystalloid isotonic solution that is sterile. The use of isotonic or hypertonic solutions may cause skin necrosis via this route. **Intravenous** (IV) fluid therapy is standard for severely dehydrated and hypovolaemic patients and both crystalloid and colloid fluids may be used. It is also the best route for electrolyte and acid-base corrections. For hypovolaemic puppies, an IV route may be technically difficult and an **intraosseous** infusion of isotonic crystalloids and dextrose could prevent fatalities (Brown and Otto, 2008).

The goal of the fluid therapy determines the choice of fluid solution. In most cases of dehydration an IV crystalloid solution is used and can rapidly lead to equilibrium between the intravascular and interstitial compartments. Hypovolaemic patients presenting with shock need to be catheterised immediately with a short large-gauge catheter to reinstate circulating volume (Brown and Otto, 2008). Once normovolaemia is achieved, the amount and rate of infusion is calculated. This calculation includes: recovery of the interstitial hydration status within the following 24 to 48 hours (the fluid deficit), subsequent maintenance therapy and any estimated future losses (Humm et al., 2008) (Table 4).

Table 4. Dosage and infusion rates of crystalloid fluids in dogs (Summarised and adapted from [a]Brown and Otto, 2008 and [b]Humm et al., 2008)

	NaCl 0.9% / LRS (Hartmann's solution) fluids
Hypovolaemic shock - Moderate[b] - Severe[b]	 20 mL/kg over 20 – 60 minutes 60 – 90 mL/kg over 20 – 60 minutes
Dehydration[b]	Deficit to be replaced over 24-48 hours. Estimate deficit: $Fluid\ deficit\ (L) = \frac{\%\ dehydration}{100}\ x\ bodyweight\ (kg)$
Maintenance[a,b]	1 - 2.5 mL/kg/hour + KCl supplementation if needed (see Table 5)
Potential future losses	Estimated by collecting and weighing vomitus, diarrhoea and blood lost (rarely necessary in practice)[b] E.g. vomiting 10 times/day with estimated volume of 50 mL = 500 mL/day[a]

Abbreviations: NaCl, sodium chloride; LRS, lactated Ringer's solution; KCl, potassium chloride

7.3 Correction of acid-base and electrolyte abnormalities

Acidotic patients as a result of hypoperfusion can additionally benefit from a buffered electrolyte solution. The dosage of isotonic crystalloids for mild hypoperfusion is calculated at 20-30 mL/kg, and for severe hypoperfusion at 70-90 mL/kg with additional colloids. The latter is because aggressive crystalloid therapy can lead to a decreased colloid osmotic pressure (Brown and Otto, 2008). Hartmann's solution, or lactated Ringer's solution (LRS), is a slightly hypotonic crystalloid fluid. It contains lactate, which uses hydrogen ions during metabolisation in the liver and thus produces bicarbonate. This has an alkalising effect, which makes LRS a suitable fluid for patients with metabolic acidosis due to vomiting that is accompanied with intestinal losses. It is also useful for lactic acidosis arising from secondary hypovolaemia. The metabolic alkalosis in dogs with pure gastric vomiting is usually attributed to GI chloride loss. A suitable fluid choice for these dogs is physiological saline solution, or 0.9% sodium chloride (NaCl). This is not only to replace lost chloride ions, but also because it lowers plasma bicarbonate levels through increased secretion and decreased absorption of bicarbonate in the renal tubules. It therefore has an acidifying effect (Humm et al., 2008).

Vomiting dogs presenting with hypovolemia and an inappropriate low heart rate may be a hint for an underlying hypoadrenocorticism. Fluid and electrolyte losses via the GI tract, along with an impaired adrenal aldostrone production, lead to significant fluid loss with hypovolaemia and hypoperfusion as a result. Subsequently, the aldosterone impairment decreases sodium and water retention at the renal cortical collecting tubules, and potassium and hydrogen ion secretion is hampered. Hyponatraemia, hyperkalaemia and ultimately metabolic acidosis ensue. An obvious fluid choice here is 0.9% NaCl because it can increase the sodium levels and has an absence of potassium. Calcium and/or dextrose or insulin can be added to protect the cardiac function and reduce the extracellular potassium excess. The disadvantages of 0.9% NaCl solution in Addison's dogs are that the correction of metabolic acidosis is less efficient than with a balanced isotonic crystalloid solution, and that infusion rates of sodium need to be administered slowly (Brown and Otto, 2008). Sudden increases in sodium tonicity in hyponatraemic dogs can lead to delayed central pontine myelinolysis, where the myelin sheaths of the pons neurons are damaged (Carron et al., 2015). Effects can be permanent and therefore the increase rate must not exceed 0.5 mmol/litre/hour (Humm et al. 2008). Supplemental potassium is often required in chronic vomiting cases, even when the serum potassium levels are within normal limits. This is because total body potassium is often deficit in these cases (McGrotty, 2010). In hypokalaemic patients, supplemental potassium can be added to IV fluids, but the rate of infusion of the fluid-potassium solution must never exceed 0.5 mmol/kg/hour as toxicity and death may occur. Potassium is usually added as potassium chloride (KCl) and the dosage is dependant on the dog's serum potassium levels (Table 5). It is important to reduce the dosage of KCl accordingly when spiking fluids that already contain potassium, such as LRS (Strombeck and Guilford, 1996; Humm et al., 2008).

Table 5. Potassium supplementation of intravenous fluids (Summarised from Guilford, 1996; Brown and Otto, 2008 and Humm et al., 2008)

Serum potassium (mmol/litre)	**KCl to add to NaCl 0.9% fluids** (mmol/litre)	**KCl to add to LRS (Hartmann's solution)** (mmol/litre)	**Maximum infusion rate*** (mL/kg/hour)
< 2.0	80	75	6
2.1 – 2.5	60	55	8
2.6 – 3.0	40	35	12
3.1 – 3.5	28	23	16

*Maximum must not exceed 0.5 mmol/kg/hour
Abbreviations: KCl, potassium chloride; NaCl, sodium chloride; LRS, lactated Ringer's solution

Some patients, such as puppies with Canine Parvovirus Enteritis, can benefit from spiking LRS with 5% dextrose. Puppies are usually anorexic due to the severe GI symptoms, and this together with the concurrent sepsis, hypermetabolism and impaired liver function, can lead to hypoglycaemia (Strombeck and Guilford, 1996; Humm et al., 2008).

7.4 Management of intoxication

When presented with a poisoning case, there are four main lines of treatment to consider. Firstly, **further absorption of the ingested toxin should be prevented**. This can be achieved with a saline lavage of the stomach of the anaesthetised dog. Alternatively, an emetic can be administered to hasten elimination. Apomorphine is extremely effective in dogs, but the disadvantage is its prolonged working time. Emetics are not suitable where corrosive toxins are suspected, ingestion is not recent or with collapsed animals where the risk of aspiration pneumonia is high (Anonymous, 1990a). Adsorbent substances, such as activated charcoal can be used to bind organic toxins and retard their further absorption. They are not effective against inorganic and metal poisons and their efficacy is debateable for water-soluble substances, such as the carbamate pesticides. However, they are often used in combination with a cathartic, such as sorbitol, in order to encourage faster passage through the GI tract. This is particularly useful when parasympatholytics, such as atropine, have been administered to tackle muscarinic symptoms (Anonymous, 1990a; Anastasio and Sharp, 2011). As many toxins are excreted via the kidneys, **increasing the removal rate of the circulating toxin** can be achieved with the use of IV fluid therapy. Diuretics are contraindicated as patients are usually dehydrated from GI water loss. Similarly, toxins and metabolite excretion can be encouraged with the use of alkalising or acidifying drugs, prompting the toxins to enter the urine. Amphetamines, for example, are alkalis and their hastened removal can be promoted with urine-acidifying substances such as ammonium chloride. Similarly, acidic toxins, such as acetylsalicylic acid (aspirin), can be persuaded into the urine with sodium bicarbonate (Anonymous, 1990a). **Antidotes** are available for some poisonings, but diagnosis would indeed need to be affirmed. Lead, for example, can be chelated in a non-ionisable, soluble complex rendering it non-toxic and ready for excretion.

The calcium salt, sodium calcium-EDTA (ethylenediamine tetraacetate), is still widely used as its antidote, although its use is limited due to its own toxicity and inconvenience of parenteral administration (Anonymous, 1990b). Succimer (meso-2,3-dimercaptosuccinic acid or DMSA) is less toxic and more efficient in the clinical treatment of heavy metal poisoning and its availability in oral capsules facilitates administration (Aaseth et al., 2015). The product is registered for human use only and is therefore used extra-label in dogs at a dosage of 10 mg/kg PO every 8 hours (Plumb, 2008). It is available in Belgium from the Belgian poison control centre (Belgisch Antigifcentrum). Finally, **supportive treatment** should be applied with all patients. Fluid therapy is essential to prevent circulatory collapse and correct the fluid imbalance. Electrolyte and acid-base irregularities should be corrected accordingly and the correct body temperature should be monitored and sustained via environmental changes. Care should be taken with the use of hot water bottles as localised vasodilatation may accentuate shock. Hyperpyrexia can be treated with ice packs and cold enemas (Anonymous, 1990a).

7.5 Anti-emetic drugs

Antiemetic drugs are targeted at specific receptors within the vomiting reflex (Table 1) and are effective at reducing the frequency of vomiting events and in some instances the complete elimination of the act (Leib, 2005). Their use should only be applied where the underlying cause of emesis has been identified, or for short-term use only. An initial course of 24 hour anti-emetic therapy would be an appropriate time frame as an initial symptomatic treatment, unless the emesis is considered beneficial to the patient, for example for the expulsion of ingested toxins where continued retention would have adverse effects (Devauchelle et al., 2006). Many of the anti-emetics currently used in small animal practice also have a prokinetic effect on the GI-tract and thus the use of these drugs is not indicated where there is suspicion of GI obstruction, as perforation can occur (Elwood, 2010; McGrotty, 2010).

There are several classes of anti-emetic drugs as indicated in Table 1. Some of the more commonly used drugs will be further discussed, and information about their licensing, registration and uses in Belgium in particular have been sourced from the Belgian veterinary medicine register ‘Gecommentarieerd Geneesmiddelen-Repertorium voor Diergeneeskundig Gebruik’ (Anonymous, 2015). The first class is the **phenothiazines** including chlorpromazine, prochlorpromazine and ace(tyl)promazine (ACP). ACP is the only phenothiazine available in Belgium and is registered for use in dogs as a neuroleptic and anti-emetic. These compounds are potent drugs that act centrally antagonising emetic stimuli in the emetic centre and the CTZ. They also have weak anticholinergic properties. The phenothiazines also block peripheral α-adrenergic receptors leading to arteriolar vasodilatation and hypotension. Their use in dehydrated and hypovolaemic patients is thus discouraged or continual fluid therapy is advised (Encarnación et al., 2009).

Due to their central interference, they are effective against most causes of vomiting but are nowadays being succeeded by more potent and licensed anti-emetics (Strombeck and Guilford, 1996; McGrotty, 2010).

In dogs, **antihistaminic drugs** interrupt the vomiting stimulus derived in the vestibular apparatus and to a lesser extent at the level of the CTZ. Interestingly, cats do not possess H_1-receptors in the CTZ and antihistaminic drugs do not control vomiting in this species (Encarnación et al., 2009). Some examples are diphenhydramine, dimenhydrinate and meclizine, which are drugs that are registered for human use only, and are thus administered extra-label in veterinary medicine. Due to their selectivity, they are mainly utilized for the prevention of motion sickness (Strombeck and Guilford, 1996; Encarnación et al., 2009), however newer drugs such as maropitant now take precedence over the antihistamines for the treatment of motion sickness in dogs. In Belgium, maropitant is registered for both species and ailment, and therefore ranks highest on the veterinary cascade system outlined in articles 230, 231 and 232 of the Belgian Royal Decree (Koninklijke besluit) from 14 December 2006.

One of the most frequently used anti-emetics in small animal medicine is metoclopramide, under the class of the **antidopaminergics**. It is licensed for veterinary use and has both a central effect by inhibiting signals in the CTZ and by raising the vomiting centre threshold, as well as a peripheral effect. Here it stimulates post-ganglionic acetylcholine release that subsequently increases gastric contractions and pressure at the gastroesophageal sphincter (Leib, 2005). It is therefore indicated in animals with gastroesophageal reflux, oesophagitis, delayed gastric emptying and motility disorders (McGrotty, 2010). It is a particularly useful drug against vomiting and ileus when used as a continuous infusion for puppies recovering from parvo-virus. Due to its prokinetic effect, it is contraindicated where GI obstruction is suspected (Hall, 2002).

Serotonin antagonists such as ondansetron and dolasetron are licensed for emetic patients that are receiving radiation and chemotherapy in human medicine, but seem to also have a good response in veterinary medicine (extra-label use). They are however ineffective for emesis caused by motion sickness (Encarnación et al., 2009). The limiting factor for the use of these drugs is the high cost (McGrotty, 2010).

As mentioned above, a more current anti-emetic drug which is extremely effective and licenced for veterinary use in dogs with emesis, is maropitant, commercially sold under the trade name of Cerenia®. It selectively blocks **NK-1 receptors**, which are located centrally and peripherally throughout the body (Table 1) and is thus effective against a wide range of emetic stimuli (Trepanier, 2015). Its efficacy has been demonstrated with only one or two administrations in cases such as dietary indiscretion, pancreatitis, parvoviral enteritis and non-specific gastritis (Ramsey et al., 2008).

Further studies have also shown its efficacy against motion sickness, as well as its prevention of vomiting in dogs caused by emetogens such as apomorphine, cisplatin and syrup of ipecac (Benchaoui et al., 2007). It is contraindicated in puppies less than 16 weeks of age as bone-marrow hypoplasia has been reported. Painful injection sites can be avoided by refrigerating the product before administration (Trepanier, 2015).

7.6 Gastric mucosal protectants

Intermittent vomiting and hematemesis can be diagnostic features of gastric ulceration. In this instance, symptomatic treatment centres around treatment of the primary cause (Strombeck and Guilford, 1996). **Sucralfate** is a sulphated disaccharide that has a local effect by reacting with hydrochloric acid in the stomach and forming a gel-like precipitate that shields the lesions from future damage (Bovens, 2013). It also binds to epithelial growth factor sites in the ulcers and promotes cellular proliferation, increases mucus-, bicarbonate- and prostaglandin release (McGrotty, 2010), as well as inactivates pepsin and binds to refluxed bile acids. As it binds to gastric mucosa, it should be administered before food and 1-2 hours apart from other drugs where its presence can cause their decreased absorption. Sucralfate is not registered for use in dogs, but is accepted to be a safe off-label product (Hall, 2002).

7.7 Antacids

Cimetidine, ranitidine and **famotidine** are H_2-receptor antagonists that competitively block histamine-induced gastric acid secretion (Hall, 2002). None of the three antacids are registered for use in dogs in Belgium (Anonymous, 2015), although cimetidine is licensed for dogs in some neighbouring EU countries (Bovens, 2013). Cimetidine is the least potent and therefore needs to be administered 3-4 times daily. Its main disadvantage is its inhibiting activity on hepatic cytochrome-P450 (CYP450) enzymes and thus can interfere with the metabolism of other drugs. Ranitidine and famotidine are more potent than cimetidine, and only require administration 1-2 times a day; they also do not interfere with CYP450. Furthermore, ranitidine also posses an anticholinesterase activity and therefore has a prokinetic effect, which can be beneficial to reduce vomiting (McGrotty, 2010; Bovens, 2013).

7.8 Proton pump inhibitors

Omeprazole is a proton pump inhibitor that irreversibly prevents acid secretion from gastric parietal cells, making it more potent than cimetidine and ranitidine, with a longer duration of activity (McGrotty, 2010). In Belgium it is only registered for veterinary use in horses and therefore is used off-label in dogs (Anonymous, 2015). It is the drug of choice for dogs with sever GI erosions and ulceration, particularly with patients also presenting with hematemesis and melena (Bovens, 2013).

There is some debate as to whether chronic use of omeprazole can lead to histological changes in the gastric mucosa. In rat studies, lifelong high doses were shown to lead to reflex hypergastrimaemia and the subsequent development of enterochromaffin-like (ECL) cell carcinoids. The ECL cell changes seen in human patients did not lead to carcinomas (Klinkenberg-Knol et al., 2000), however treatment is not recommended for longer than eight weeks unless necessary. It is prudent to apply the same guidelines for dogs (Bovens, 2013).

7.9 Other treatments

Dogs may have pain caused by processes that develop secondary to vomiting, for example, from oesophagitis, gastric inflammation or ulceration. The pain may also be attributed to the cause of the emesis, such as with pancreatitis. An example of **analgesia** suitable for use in vomiting dogs, and registered in Belgium (Anonymous, 2015), is opioids such as buprenorphine and methadone. Other analgesics such as NSAIDs are contraindicated in patients with GI symptoms as any gastric ulceration may be exacerbated. Steroid use should be avoided unless the underlying cause is diagnosed as some diseases can be masked, such as IBD and gastric lymphoma.

Infectious agents also need to be tackled where indicated. **Antibiotics** are not usually indicated for vomiting dogs, although they may be considered where gastric biopsies of dogs with chronic inflammatory processes in the stomach reveal the presence of *Helicobacter spp.* (Bovens, 2013). It is a debated treatment choice because it is well known that *Helicobacter pylori* can cause chronic gastritis and ulceration in humans. However, other species of *Helicobacter* (but not *H. pylori*) are frequent residents in more than 80% of canine stomachs, in both healthy and vomiting patients (Webb and Twedt, 2003). **Antiparasitic** drugs such as the benzimidazoles have a broad-spectrum use in dogs. They are licensed for the eradication of several internal parasites that often induce symptoms of diarrhoea and vomiting. Some examples are *Giardia sp.*, hookworms and *Toxocara canis* (Fisher, 2001). Conversely, viral infections can only be treated symptomatically and not curatively, although **antiviral** treatments are available for some conditions and have shown good results. In a comparative study of dogs with canine parvovirus infection, the mortality of infected dogs treated with feline interferon-ω preparations was significantly lower than those in the control group, where only 19.9% of the animals succumbed to their illness in comparison to the 61.9% of dogs without this treatment (Minagawa et al., 1999).

It goes without saying that the **underlying cause** of the vomiting should be treated if a definitive diagnosis is made. Surgical correction, for example, is often curative as far as vomiting is concerned, although any symptoms leading up to and subsequent to the definitive treatment can be supported using the aforementioned methods.

DISCUSSION

After reviewing several literature sources on the topic of emesis in dogs, it is clear that the treatment of these patients should be conducted systematically, prioritising stability of the patient and tackling the symptoms of discomfort and distress. With this in mind, the next question may then be posed: what is systematic? There is a definite consensus between some authors on the order in which the treatment of a vomiting dog should be approached. When there is no indication of intoxication, hematemesis or other criteria for concern, symptomatic treatment is initially applied in all cases. In the majority of surveyed literatures, authors concurred that this primary symptomatic treatment should initially entail anti-emetic therapy for 24 hours, fluid therapy and dietary management. For cases of concern, diagnostic tests are then indicated to begin a rule-out list and specific treatment based on these results can be applied at an earlier stage additional to the symptomatic treatment (Devauchelle et al., 2006; Elwood et al., 2010; Nelson and Couto, 2014). Fig. 3 shows an algorithm incorporating several approaches recommended in numerous literatures (Devauchelle et al., 2006; Elwood et al., 2010; McGrotty, 2010; Nelson and Couto, 2014). This allows the reader to visualise the systematic approach to symptomatic treatment of the vomiting dog.

This then raises the question: what criteria would elicit concern? Table 6 lists the most important criteria that warrant immediate further investigation.

Table 6: Criteria for concern justifying further investigation of vomiting in dogs (Summarised from Elwood, 2003 and Devauchelle et al., 2006)

Persistence of symptoms despite initial treatment	Chronicity (>3-4 weeks)
Marked malaise, weight-loss or abdominal pain	Abdominal swelling/ free fluid
Haematemesis	Associated polyuria/polydipsia
Severe dehydration, hypovolaemia or shock	Inability to retain food in the stomach
Bradycardia relative to volume status	Gastrointestinal obstruction
Fever	Vaginal discharge

Presence of any of these criteria is an important pivot point in the clinical examination, and the Pandora's box of possible pathologies can turn a simple vomiting case into a challenging intervention. However, they are usually the minority of the presented vomiting cases.

Hubbard et al. (2007) recorded a 19% frequency of dogs that showed vomiting acts, but it is important to note that 89% of these did not require veterinary assistance as their symptoms subsided within 48 hours. Only 5% of the vomiting animals were physically seen by veterinarians, which means that there is another 5% with vomiting lasting beyond 48 hours that were also not brought in for assessment.

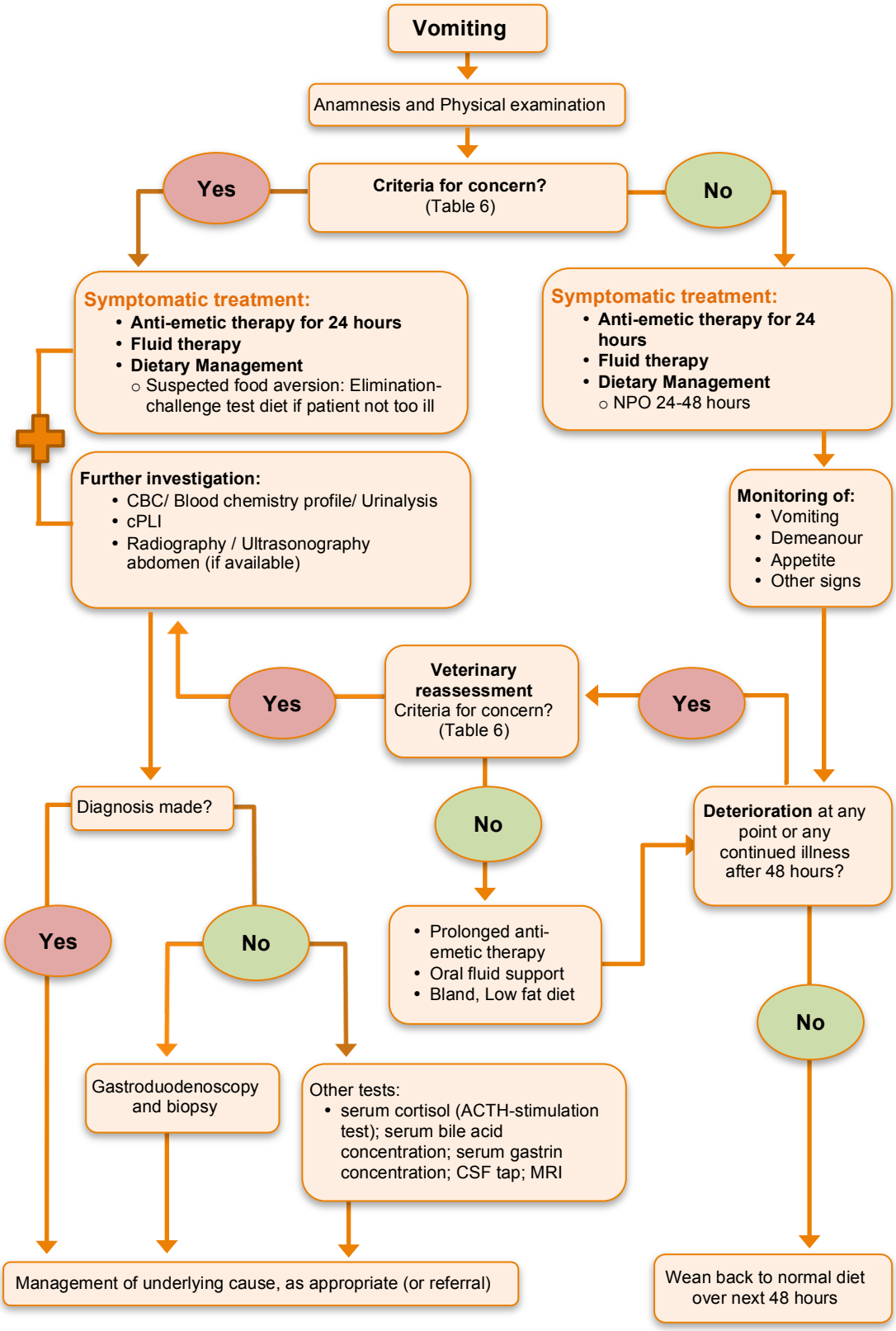

Fig. 3: Algorithm to guide the approach to managing emesis in the dog (Summarised and adapted from Devauchelle et al., 2006; Elwood et al., 2010; McGrotty, 2010; Nelson and Couto, 2014).
Abbreviations: NPO, nil per os; CBC, Complete blood count; cPLI, canine pancreatic lipase immunoreactivity; ACTH, Adenocorticotropic hormone; CSF, cerebrospinal fluid; MRI, magnetic resonance imaging.

The survey only related to the prevalence of vomiting acts within a two-week period and so owners would not have referred to incidences before or after this period. Similarly, the explanation on the pet-owner survey was rather broad as to what one would consider as a vomiting event. This could lead to some confusion with pet owners, especially if their dog was showing symptoms with similar characteristics, such as regurgitation or dysphagia (see Chapter 2).

An interesting observation is that gastric mucosal aids such as proton-pump inhibitors, antacids, anti-ulcer medication and mucosal barriers are considered to be superfluous at the early stage of pure symptomatic treatment. This is because they contain no direct anti-emetic properties. They are however included in most of the articles surveyed as chronic cases often require extra support to restore the integrity of the gastric mucosa (Devauchelle et al., 2006; Chandler, 2010; Elwood et al., 2010; McGrotty, 2010; Bovens, 2013).

An important turning point in the recent history of the treatment protocols of emetic dogs is the arrival of maropitant. Its veterinary use in Europe was approved in 2006 and there is a definite shift towards maropitant being the anti-emetic of choice in the literature after this date. This is predominantly due to its broad-spectrum activity. Before the introduction of maropitant into veterinary medicine, the selection of anti-emetic drug would have to depend on the origin of the emetic stimuli. Peripheral emetic stimuli, for example, would primarily be treated with anti-emetics such as ondansetron, and drugs such as metoclopramide and chlorpromazine were more directed at centrally initiated stimuli. Because of the wide distribution of substance P throughout the body, maropitant has a broad spectrum of efficacy, both centrally and peripherally. Additionally, it is also effective against motion sickness and the benefit here is that it does not elicit the same sedative side effect as its earlier alternatives (e.g. ACP and dimenhydrinate) (Trapanier, 2015).

Many underlying causes of vomiting may be linked to specific dog breeds. Some examples mentioned earlier include: gastric-dilatation volvulus in large deep-chested breeds, congenital or acquired pyloric hypertrophic gastropathy in brachycephalic breeds, and gastric carcinomas in the Rough Collie, Staffordshire Bull Terrier and Belgian Shepherd. It is also known that some breeds, such as the Labrador retriever, tend to scavenge more than other breeds, which can inevitably lead to ‘garbage gut’ (Hubbard et al., 2007). With this in mind, there is an obvious correlation between numerous ailments and particular breeds. Perhaps a take-home message would be to encourage dog owners and breeders to adhere to responsible breeding practices and eradicate the need to breed for aesthetic reasons that carry dysgenic factors with them.

REFERENCES

Aaseth J., Skuag M.A., Cao Y., Andersen O. (2015). Chelation in metal intoxication – Principles and paradigms. Journal of Trace Elements in Medicine and Biology, 31, 260-266

Ahlawat A.R., Ghodasara S.N., Dongre V.B., Gajbhiye P.U. (2014). Chocolate toxicity in a dog. Indian Journal of Veterinary and Animal Sciences Research, 43 (6), 452-453

Anastasio J.D., Sharp C.R. (2011). Acute aldicarb toxicity in dogs: 15 cases (2001-2009). Journal of Veterinary Emergency and Critical Care, 21 (3), 253-260

Anonymous. (1990a). Poison Series: Principles of treating suspected poisoning cases. In Practice, 12 (1), 33

Anonymous. (1990b). Poison Series: Lead. In Practice, 12 (2), 53

Anonymous. (2015). Gecommentarieerd Geneesmiddelen-Repertorium voor Diergeneeskundig Gebruik. Belgische Centrum voor Farmacotherapeutische Informatie v.z.w. Gent

Benchaoui H.A., Cox S.R., Schneider R.P., Boucher J.F., Clemence R.G. (2007). The pharmacokinetics of maropitant, a novel neurokinin type-1 receptor antagonist, in dogs. Journal of Veterinary Pharmacology and Therapeutics, 30, 336–344

Berny P., Caloni F., Croubels S., Sachana M., Vandenbroucke V., Davanzo F., Guitart R. (2010). Animal poisoning in Europe. Part 2: Companion animals. The Veterinary Journal, 183, 255-259

Bjone S. J., Brown W. Y., Price I. R. (2007). Grass eating patterns in the domestic dog, *Canis familiaris*. Recent Advances in Animal Nutrition in Australia, 16, 45-49

Boag A.K., Coe R.J., Hughes D., Martinez T.A. (2005). Acid-Base and Electrolyte Abnormalities in Dogs with Gastrointestinal Foreign Bodies. Journal of Veterinary Internal Medicine, 19, 816-821

Bovens C. (2013). Therapeutics in canine GI disorders: part one – treatment of vomiting. Veterinary Times, June 24, 2013, 22-24

Brown A.J. and Otto C.M. (2008). Fluid Therapy in Vomiting and Diarrhea. Veterinary Clinics of North America: Small Animal Practice, 38 (3), 653-675

Campbell A. (1998). Poisoning in small animals from commonly ingested plants. In Practice, 20 (10), 587-591

Carron M., Meneghetti M., Gagliardi G., Ori C. (2015). Severe hyponatremia: a physicians's nightmare. International Journal of Case Reports and Images, 6 (11), 694-697

Chandler M. (2010). Vomiting in dogs and cats - is it medical or surgical? In Practice, 32, 82-89

Desario C., Decaro N., Campolo M., Cavalli A., Cirone F., Elia G., Martella V., Lorusso E., Camero M., Buonavoglia C. (2005). Canine parvovirus infection: Which diagnostic test for virus? Journal of Virological Methods, 126, 179-185

Devauchelle P., Elliot J., Elwood C., Freiche V., German A., Gualtieri M., Hall E., Den Hertog E., Neiger R., Peeters D. and Roura X. (2006). Approach to the management of emesis in dogs. Current guidelines to best practice from the European Emesis Council, Pfizer Animal Health, Sandwich, Kent, UK

Dunn J. (1989). The vomiting dog. Part 1: Pathophysiology, diagnostic approach and differential diagnosis of acute vomiting. In Practice, 11, 184-192

Elwood C. (2003). Investigation and differential diagnosis of the vomiting dog. In Practice, 25 (7), 374-386

Elwood C., Devauchelle P., Elliott J., Freiche J., German A.J., Gualtieri M., Hall E., Den Hertog E., Neiger R., Peeters D., Roura X. and Savary-Bataille K. (2010). Emesis in dogs: a review. Journal of Small Animal Practice, 51, 4-22

Encarnación H.J., Mears E., Parra J. (2009). Vomiting. Compendium: Continuing Education for Veterinarians. 31 (3) E8, 122-131

Fisher M. (2001). Endoparasites in the dog and cat. 1. Helminths. In Practice, 23, 462-471

Gaschen F.P. and Merchant S.R. (2011). Adverse Food Reactions in Dogs and Cats. Veterinary Clinics of North America: Small Animal Practice, 41 (2), 361-379

Gualtieri M., Monzeglio G., Scanziani E. (1999). Gastric neoplasia. Veterinary Clinics of North America: Small Animal Practice, 29 (2), 415-440

Hall E. (2002). Rational selection of gastrointestinal drugs for cats and dogs. In Practice, 24, 242-249

Herd P. (1992). Poison: Ethylene glycol. In Practice, 14, 298-299

Hubbard K., Skelly B.J., McKelvie J., Wood J.L.N. (2007). Risk of vomiting and diarrhoea in dogs. Veterinary Record, 161 (22), 755-757

Humm K., Goggs R., Hughes D. (2008). Fluid therapy in small animals: 2. Crystalloid solutions. In Practice, 30 (2), 85-91

Klinkenberg-Knol E.C., Nelis F., Dent J., Snel P., Mitchell B., Prichard P., Lloyd D., Havu N., Frame M.H., Romàn J., Walan A, Long Term Study Group. (2000). Long-term Omeprazole Treatment in Resistant Gastroesophageal Reflux Disease: Efficacy, Safety, and Influence on Gastric Mucosa. Gastroenterology, 118, 661-669

Koenig A. (2013). Endocrine emergencies in dogs and cats. Veterinary Clinics of North America: Small Animal Practice, 43 (4), 869-897

Kogan D.A., Johnson L.R., Sturges B.K., Jandrey K.E., Pollard R.E. (2008). Etiology and clinical outcome in dogs with aspiration pneumonia: 88 cases (2004-2006). Journal of the American Veterinary Medical Association, 233 (11), 1748-1755

Lecoindre P. and Richard S. (2004). Digestive disorders associated with the chronic obstructive respiratory syndrome of brachycephalic dogs: 30 cases (1999-2001). Revue de médecine vétérinaire, 155 (3), 141-146

Leib M.S. (1999). Chronic vomiting in dogs and cats. A practical diagnostic approach. Proceedings of the North American Veterinary Conference 1999, Orlando, Florida, 13, 305-308

Leib M.S. (2005). Drug Therapy of Upper GI Diseases. Proceedings of the North American Veterinary Conference 2005, Orlando, Florida, p. 364-365

Malm K. (1995). Regurgitation in relation to weaning in the domestic dog: a questionnaire study. Applied Animal Behaviour Science, 43, 111-122

McGrotty Y. (2010). Medical management of acute and chronic vomiting in dogs and cats. In Practice, 32 (10), 478-483
Mech D., Wolf P.C., Packard J.M. (1999). Regurgitative food transfer among wild wolves. Canadian Journal of Zoology, 77 (8), 1192-1195

Miller A.D. and Leslie R.A. (1994). The Area Postrema and Vomiting. Frontiers in Neuroendocrinology, 15, 301-320

Minagawa T., Ishiwata K., Kajimoto T. (1999). Feline interferon-ω treatment on canine parvovirus infection. Veterinary microbiology, 69, 51-53

Monnet E. (2003). Gastric dilatation-volvulus syndrome in dogs. Veterinary Clinics of North America: Small Animal Practice, 33 (5), 987-1005

Nelson R.W. and Couto C.G. (2014). Small Animal Internal Medicine, Fifth Edition. Mosby Elsevier, St. Louis, Missouri, 373-374

Plumb D.C. (2008). Plumb's Veterinary Drug Handbook, 6th Edition. Blackwell Publishing Professional, Ames, Iowa

Pretzer S.D. (2008). Clinical presentation of canine pyometra and mucometra: a review. Theriogenology, 70, 359-363

Raditic D.M., Remillard R.L., Tater K.C. (2011). ELISA testing for common food antigens in four dry dog foods used in dietary elimination trials. Journal of Animal Physiology and Animal Nutrition, 95 (1), 90-97

Ramsey D.S., Kincaid K., Watkins J.A., Boucher J.F., Conder G.A., Eagleson J.S., Clemence R.G. (2008). Safety and efficacy of injectable and oral maropitant, a selective neurokinin$_1$ receptor antagonist, in a randomized clinical trial for treatment of vomiting in dogs. Journal of Veterinary Pharmacology and Therapeutics, 31, (6), 538–543

Severino L. (2009). Toxic plants and companion animals. CAB Reviews: Perspectives in Agriculture, Veterinary Science, Nutrition and Natural Resources, 4 (008), 1-6

Strombeck D.R. and Guilford W.G. (1996). Vomiting: Pathophysiology and Pharmacologic Control. In: Guilford W.G., Centre S.A., Strombeck D.R., Williams D.A., Meyer D.J. Strombeck's Small Animal Gastroenterology, 3rd edition. W.B. Saunders Company, Philadelphia, London, p. 52-62, 70, 256-271, 436-437, 900-913

Sutton N.M., Bates N., Campbell A. (2009). Factors influencing outcome of *Vitis vinifera* (grapes, raisins, currants and sultanas) intoxication in dogs. Veterinary Record, 164, 430-431

Trepanier L.A. (2015). Maropitant: Novel Antiemetic. NAVC Clincian's brief, February 2015 Nutrition Focus, p. 75-77

Uemura E.E. (2015). Fundamentals of Canine Neuroanatomy and Neurophysiology. First Edition. John Wiley & Sons, Inc., Ames, Chichester, Oxford, p. 42, 207, 238-242

Van Israël N, Kirby B.M., Munro E.A.C. (2002). Septic peritonitis secondary to unilateral pyometra and ovarian bursal abcessation in a dog. Journal of Small Animal Practice, 43, 452-455

Vandenbroucke V., Van Pelt H., De Backer P., Croubels S. (2010). Animal poisonings in Belgium: a review of the past decade. Vlaams Diergeneeskundig Tijdschrift, 79, 259-268

Watson P. (2004). Pancreatitis in the dog: dealing with a spectrum of disease. In Practice, 26 (2), 64-77

Webb C. and Twedt D.C. (2003). Canine gastritis. Veterinary Clinics of North America: Small Animal Practice, 33 (5), 969-985

Williams J. and Niles J. (1999). Prostatic disease in the dog. In Practice, 21 (10), 558-575

Wilsson E. (1984). The social interaction between mother and offspring during weaning in German Shepherd Dogs: Individual differences between mothers and their effects on offspring. Applied Animal Behaviour Science, 13, 101-112

LEGISLATION

Royal decree (Koninklijke besluit) Belgium, 14 December 2006. Articles 230, 231 and 232