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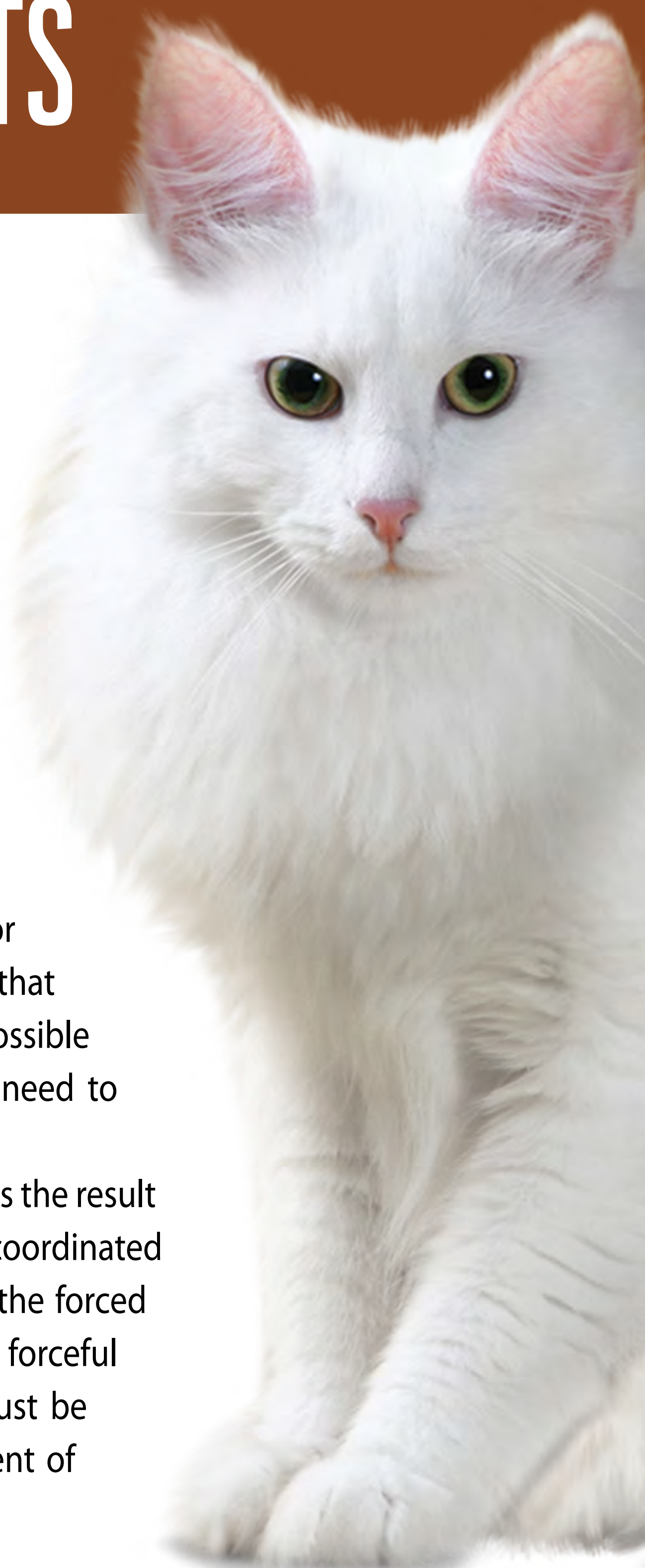
SCIENTIFIC APPROVED

CHRONIC VOMITING IN CATS

1. INTRODUCTION

The complaint of chronic vomiting is one of the most frequent and important reasons for consultation for apparently healthy or debilitated cats. This clinical sign progresses with episodes that last for more than three weeks. Cats can vomit intermittently with increasing frequency (some cats vomit once a month, others twice a week and even daily). However, it is common for owners to attribute this active reflex to the fact that the cat ingests the food very quickly, or to a possible sensitivity of the gastric mucosa, or even the need to eliminate hairballs¹.

It is known that the involuntary act of vomiting is the result of a complex pattern of response reflexes that is coordinated by the central nervous system and consists of the forced peroral expulsion of gastric contents, caused by forceful contraction of the abdominal muscles. This must be distinguished from regurgitation, a passive event of transfer of gastric contents to the pharynx⁵.



2. MECHANISM

The vomiting center is located at the brainstem. It can be stimulated until reaching a threshold directly or receiving input from other areas, including the

chemoreceptor trigger zone (CTZ), vestibular system (inflammatory alterations and motion sickness), vagal afferent neurons (parasympathetic) or cerebral cortex and sympathetic neurons (fibers coming from genitourinary system)¹.

The area postrema, or chemoreceptor trigger zone, is located on the fourth ventricle floor, outside the blood-brain barrier, receiving stimuli predominantly via the hematogenous route, in response to circulating drugs and toxins.

Peripheral sensory receptors are present in different parts of the body such as the pharynx (via glossopharyngeal nerve), the heart and large vessels (vagus nerve); as well as visceral receptors in the stomach, small intestine, mainly duodenum, pancreas, liver, urinary tract, reproductive tract and peritoneum. These are distributed as dopamine, norepinephrine, 5-hydroxytryptamine, histamine, substance P, opioids and acetylcholine receptors and, when stimulated, lead to vomiting and nausea⁵ (Figure 1).

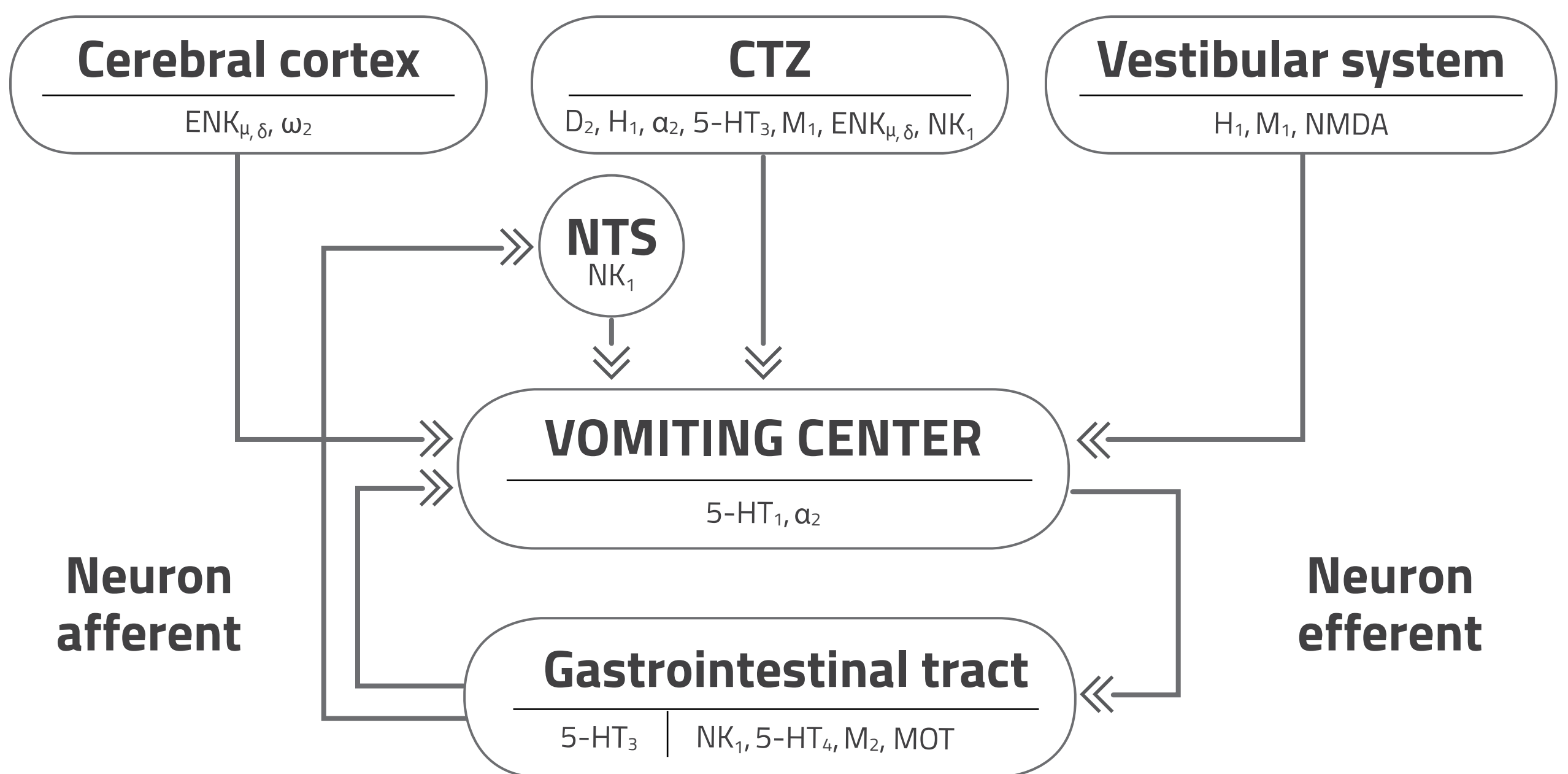


Figure 1: Mechanism and pharmacology of vomiting – neurotransmitters and receptors. A_{2,2}, adrenergic receptor α₂; D₂, dopamine receptor ₂; ENK_{μ, δ}, enkephalin receptor _{μ, δ}; H₁, histamine receptor₁; 5-HT₁ Receptor, 5-hydroxytryptamine₁; 5-HT₃ Receptor, 5-hydroxytryptamine₃; 5-HT₄ Receptor, 5-hydroxytryptamine₄; M₁, muscarinic cholinergic receptor ₁; M₂, muscarinic cholinergic receptor ₂; MOT, motilin receptor; NK₁, neurokinin receptor₁; NMDA, N-methyl D-aspartate; NTS, nucleus tractus solitarius; ω₂, benzodiazepine receptor ω₂; CTZ, chemoreceptor trigger zone (Adapted 18).

3. MAIN CAUSES OF CHRONIC VOMITING

Chronic vomiting is the symptom expression of a multiplicity of causes, with different pathophysiological mechanisms, which requires a wide and meticulous approach. For a better clinical investigation, the possible mechanisms involved in the most frequent causes of chronic vomiting in cats can be basically divided into two categories (Table 1):

1.

Primary gastrointestinal disorders, properly speaking.

2.

Non-gastrointestinal disorders that present systemic impairment without the origin of the gastrointestinal tract.

Sometimes, there may be, in some cases, an association between them and lead to a category of mixed causes⁵.

The main primary gastrointestinal disorders include inflammatory gastroenteric diseases. When the upper gastrointestinal tract becomes irritated, inflamed, or excessively distended, these stimuli trigger the vomiting reflex¹⁰.

Chronic enteritis or chronic gastrointestinal disease or chronic small intestine disease affects a large number of cats with a history of persistent and recurrent vomiting. It is very common for other clinical signs to be associated, such as hyporexia, weight loss or diarrhea. In these enteritis, it is worth stressing the idiopathic inflammatory bowel disease (IBD), which is normally responsive to steroids, food and antibiotics, and the gastrointestinal small cell lymphoma, which represents about 75% of gastrointestinal lymphomas in cats⁸. Other gastrointestinal disorders may be involved, such as infectious diseases (e.g. Histoplasmosis, FIP, FeLV, FIV); parasitic diseases (e.g. gastric parasites – *Ollulanus tricuspis*, *Physaptera spp.* and intestinal parasites – Ascarids and *Giardia spp.*); anatomical disorders (e.g. obstructive disorders by foreign bodies or trichobezoars); and also, those related to medication or nutritional causes (food allergy or food intolerance) and neoplastic causes (e.g. lymphoma, carcinoma and mastocytoma).

Among the conditions unrelated to the origin of the gastrointestinal tract that can lead to chronic vomiting attacks in cats, metabolic diseases deserve attention (e.g., chronic kidney disease, hypercalcemia); inflammatory diseases such as liver disease (cholangitis); pancreatitis (sometimes classified as gastrointestinal disease); endocrine disorders (hyperthyroidism); systemic infections (heartworm, FIP, FeLV, FIV) and neurological diseases (vestibular disease, intracranial disease), among others.

TABLE 1- MAIN CAUSES OF CHRONIC VOMITING IN CATS

**PRIMARY GASTROINTESTINAL
DISORDERS**

- Inflammatory bowel disease
- food allergy or food intolerance
- Infectious diseases
(viral, bacterial and parasitic)
- Neoplasms
- Motility disorders
(mechanical or functional obstruction)
- Foreign bodies/trichobezoars
(incomplete obstruction)
- Gastric ulcerations

**NON-GASTROINTESTINAL
DISORDERS**

- Pancreatitis
- Hyperthyroidism
- Chronic kidney disease
- Liver disease
- Heartworm (*Dirofilaria immitis*)
- Neurological disease
- Drugs (chemotherapy)
- Hypercalcemia



It is worth remembering that the disorders that cause gastrointestinal dysmotility contribute to hair stagnation in cats². This alteration in motility can be triggered by neoplasms, intestinal parasitism, pancreatitis, inflammatory bowel disease, chronic kidney disease and *mellitus* diabetes. The aforementioned conditions cause the myenteric plexus imbalance. The major consequence is a reduction in physiological peristalsis designed to push the bolus from the stomach to the colon. Currently, it is suggested that the significant absence of the interdigestive migrating motor complex (MMC) presents itself as a physiological characteristic in the feline species. There is a relative lack of “cleansing contractions” during the fasting period, which hinders the passage of non-digestible material from the stomach in the aboral sense. This could justify the greater propensity of cats to form trichobezoar »»

» in the stomach. In most species, MMC begins with the stomach emptying, however, in cats it is only observed the presence of this action from the ileum. Any abnormalities in this mechanism can cause a slow passage of the bolus through the gastrointestinal tract. Free or tangled hairs eliminated by vomiting usually cause gastritis and secondary esophagitis to the influx of gastric juice⁵. The medical complications of trichobezoars in cats are usually noticed by the owner when the vomiting interval occurs in a short period, frequently and accompanies lack of appetite, prostration and weight loss. Thus, it proves to be an important alert to investigate some hidden condition. The risks associated with a trichobezoar that was not expelled by vomiting or feces present through partial and total gastrointestinal obstructions (Figure 2A – D).

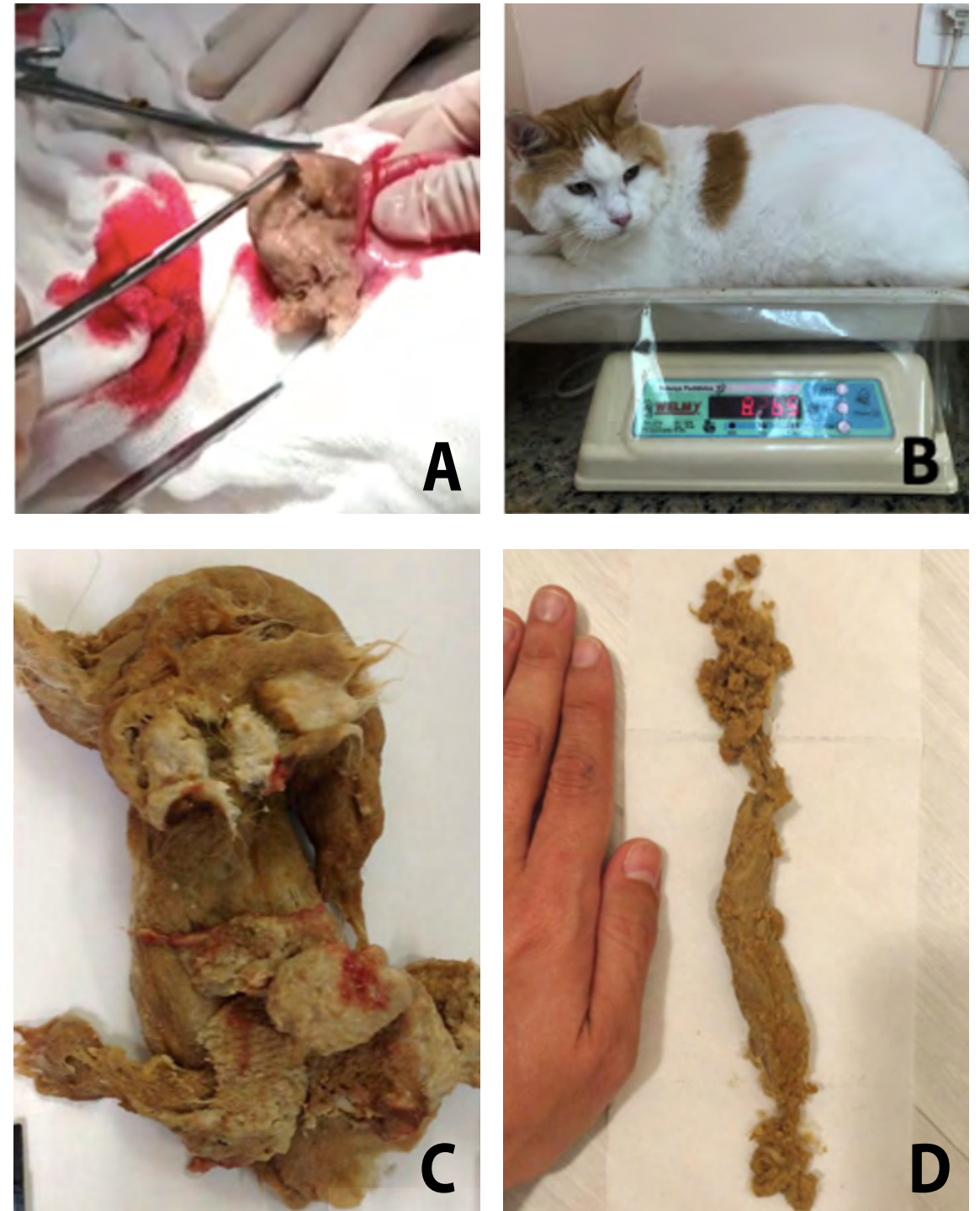


Figure 2: Cat Che, castrated male, of the Maine Coon breed, with three years old, weighing 6,820 kg, with a history of chronic vomiting of hairball (Fig D - trichobezoar), prostration and lack of appetite. The animal had a condition of chronic inflammatory enteritis (submucosa layer with slight chronic inflammatory infiltrate and muscle hyperplasia) and dysmotility. It was submitted to a gastrotomy to remove a large amount of hair (Figs A and C).



4. APPROACH DIAGNOSIS

The broad spectrum of potential causes of chronic vomiting in cats increases the difficulty of establishing a definitive diagnosis. However, it is important to carefully consider each of the potential differential diagnoses through a detailed clinical history and a good anamnesis, which should include: onset of symptoms; type of food (dry and/or wet diet), frequency and quantity of food supply; changes in feeding; presence of pruritus; feces consistency (if diarrheal) and frequency; use of medications and supplements; appearance and frequency of vomiting; if hair balls are present in the expelled material; and the moment of vomiting in relation to feeding can be useful, as the stomach must be emptied in six to eight hours after the meal; thus, vomiting eight hours after a meal may suggest motility or retention disorders¹.

Physical examination should always assess the cat's body and muscle score, whether there has been weight loss, the presence of jaundiced or dyed mucous membranes, the degree of hydration and whether there are electrolyte disorders. On abdominal»

» palpation, observe whether there is thickening of the intestinal loops (chronic enteropathies) or a feeling of mass formation (pancreatitis), an increase in viscera and lymph nodes or the presence of discomfort or pain. In cats over seven years old, palpate the thyroid glands and, especially in kittens and young adults, inspect the lingual frenulum to check for the possible presence of a linear foreign body. Also assess alterations in pacing or walking in a circle.

Supplementary tests are necessary, mainly, to take into account the findings in laboratory tests such as: complete blood count, serum biochemical (urea, creatine, phosphorus, total proteins and fractions, alanine aminotransferase (ALT), alkaline phosphatase (ALP), Gama glutamil transferase (GGT), bilirubin, total Ca), in addition to iCa, total thyroxine (T4), urinalysis and screening test for FIV/FelV.

Additional special tests may be required. **SNAP fPL[®]** and **Spec fPL[®]** are used in the investigation of pancreatitis, although some cases have results within the normal range. DGGR Lipase is also an option for the diagnosis of feline pancreatitis. FTLI should be measured in cats with suspected exocrine pancreatic insufficiency¹¹. And the assessment of serum cobalamin and folate levels is useful in intestinal diseases and/or pancreatic disease.

The ultrasonography imaging is a very effective diagnostic tool. It helps in the detection of foreign bodies, it shows regional thickening in the small intestine wall^{4, 9,10}, the presence of mesenteric lymphadenitis, tumor lesion, inflammation of the pancreas, liver and gallbladder. Radiological tests can be used to assess intestinal obstruction or the presence of a foreign body, abdominal/thoracic effusion or organomegaly.

Parasitological stool tests can be performed to detect *Giardia spp.* or *Platynosomum concinnum* eggs. When necessary, PCR (faecal pathogen panels that include, e.g. *Tritrichomonas foetus*) can be performed.

Laparotomy biopsies provide a sample of the total depth of the intestinal wall for histopathological assessment of chronic enteropathies. They also help to elucidate liver and pancreas disorders. And the endoscopic examination assists in the inspection and collection of material for biopsy of the duodenum, colon and stomach and it allows the collection of samples for *Helicobacter* identification.



5. BASIC THERAPEUTIC GUIDELINES IN CHRONIC VOMITING

Vomiting should always be seen as a symptom, trying to understand its pathophysiology and diversity of causes. Specific treatment should be carried out in cases where the etiology is identified, whether it is a gastrointestinal or systemic condition.

6. DIET

..... Dietary modifications are employed to assist in the control of chronic vomiting. In many, if not in most cases of vomiting without complications or due to the type of food, the best approach is to offer a high-digestible diet or change the diet to one with less additives, flavorings or other substances that may be associated with food intolerance¹⁹. Food intolerance reactions are variable, usually dose-dependent, and can occur at any age. The signs can appear at any time, sometimes several hours or days after consuming the offensive food, and it can last for hours or days. High-digestible diets have a wide variety of formulations: different sources of proteins and carbohydrates, varying levels of fat and different types of additives designed to promote intestinal health (fructo-oligosaccharides (FOS), mannan-oligosaccharides (MOS), omega 3 fatty acids, antioxidant vitamins, soluble fiber etc.). If a high-digestible diet has been used for at least two weeks with minimal response, then it is reasonable to try another diet from a different source or a completely different dietary strategy (e.g. new protein/carbohydrates or hydrolyzed protein). The diagnosis of food allergy or food intolerance is based on a screening with an elimination diet, formulated with hydrolyzed proteins¹⁷. The main difference between these two types of adverse reactions to food is the time it takes from the diet to get a response (cats with a food allergy need 6 to 12 weeks on the elimination diet before an improvement is observed). As for cats that have food intolerance, the signs remedy usually occurs within a few days after the change in diet, 10 to 14 days is a reasonable expectation.

In most cats with food allergies, avoiding the offending food is the most effective therapy and it will result in complete remedy of the signs. Due to the large number and variety of protein sources in commercial diets, it is always difficult to identify the exact food allergen. A study demonstrated that adverse food reactions (skin lesions and signs of gastrointestinal manifestations) were associated with diets that contained beef, dairy or were fish-based⁵. Not only the type of diet, but the amount of food provided must be considered. Commercial moist food for cats with moderate levels of fat facilitates gastric emptying (especially if vomiting occurs immediately after a meal). If this type of diet is not an option, dry food should be offered in smaller and more frequent >>



» meals for cats with altered gastric motility or reflux.

The key is to remember that food management is a process of trial and error - there is no single diet that benefits all cats in all situations¹⁶.



7. NON-SPECIFIC SUPPORT THERAPIES

Supportive and symptomatic treatment modalities are often necessary to control vomiting, which generates comfort and well-being for the patient. We often see cats with acute vomiting for two to four days (almost always several times a day), that have history reports of chronic vomiting. These exacerbations in chronic vomiting are seen, mainly, in animals with chronic enteropathy and/or chronic pancreatitis. In these cases, the therapeutic objective is to maintain the feline's hemodynamics with hydroelectrolytic replacement, correction of metabolic disorders, acid-base imbalance and minimize losses. Depending on the degree of the cat dehydration, the use of fluids with crystalloid solutions intravenously is recommended, however subcutaneous administration may be useful. The fluid volume to be administered should be calculated based on the animal's weight, maintenance rate and continuous losses. The use of isotonic fluids, such as lactated Ringer's solution, is recommended, and potassium supplementation is usually necessary, because of prolonged anorexia and increased fluid therapy-induced diuresis¹⁷.

8. ANTIEMETICS AND PROKINETICS

Antiemetics and prokinetics are used to control or prevent vomiting through interaction between specific receptors mediated at the central or peripheral nervous system level. They are used when the hydroelectrolytic state is compromised, when there is a lot of discomfort or if there is a risk of aspiration pneumonia. They are contraindicated in cases of gastrointestinal obstruction.

9. ANTIACIDS

Antacids are useful medications for frequent and cyclic vomiting to minimize possible lesions in the gastric and/or esophageal mucosa resulting from the action of gastric juice and they help in the healing of gastric ulcerations.

TABLE 2 - NON-SPECIFIC SUPPORT THERAPIES

DRUG	RECEPTOR	ACTION LOCATION	DOSE	NOTES
Antiemetic and prokinetic agents				
Maropitant ^{6, 14}	Neurokinin antagonist ₁ (NK ₁)	Vomiting center, CTZ, GIT	1 mg/kg OA, SC, IV q. 24h	It also prevents visceral pain ³ and reduces itching in hypersensitivity dermatitis not induced by fleas and food ⁷
Ondansetron ¹³	5 HT ₃ Serotonin antagonist	CTZ and afferent GIT	0,5-1,0 mg/kg OA, SC, IV q. q. 8-12h	SC half-life greater than OA and IV
Dolasetron	5 HT ₃ Serotonin antagonist	CTZ and afferent GIT	0,5-1,0 mg/kg OA, IV q. 24h	Study did not detect the drug after 12h when applied via SC
Metoclopramide ^{5, 14, 17}	D ₂ Dopamine antagonist	CNS, GIT	0,2-0,5 mg/kg OA, SC, IM q. 6-8h 1-2 mg/kg IV continuous infusion	Before use, discard intestinal obstruction
Antacids				
Omeprazole ^{16, 17}	Proton-pump inhibitor		1 mg/kg OA q. 12h	After prolonged use, perform weaning. There is a rebound effect of acid hypersecretion after abrupt interruption.
Famotidine ^{16, 17}	H ₂ Histamine antagonist	GIT	0,5-1,0 mg/kg OA q. 12-24h	For chronic use, administration of the drug q. 24h instead of q. 12h. is recommended.
Sucralfate	Binds itself to ulcerated tissue and aids in healing ulcers	GIT	250mg/cat OA q. 12h	May act as a cytoprotector (via prostaglandin synthesis)
Appetite stimulant				
Mirtazapine ^{12, 15}	Action mechanism is not fully understood. It involves acting as a 5 HT _{2c} serotonin antagonist and as an H ₁ histamine antagonist	-	1.88 mg/cat OA, transdermal q. 48h	It also has an antiemetic effect due to its action as a HT ₃ serotonin antagonist in the CTZ and afferent GIT

Abbreviations: CNS, central nervous system; GIT, gastrointestinal tract; CTZ, chemoreceptor trigger zone; OA, oral administration; SC, subcutaneously; IV, intravenously.



10. FINAL NOTES

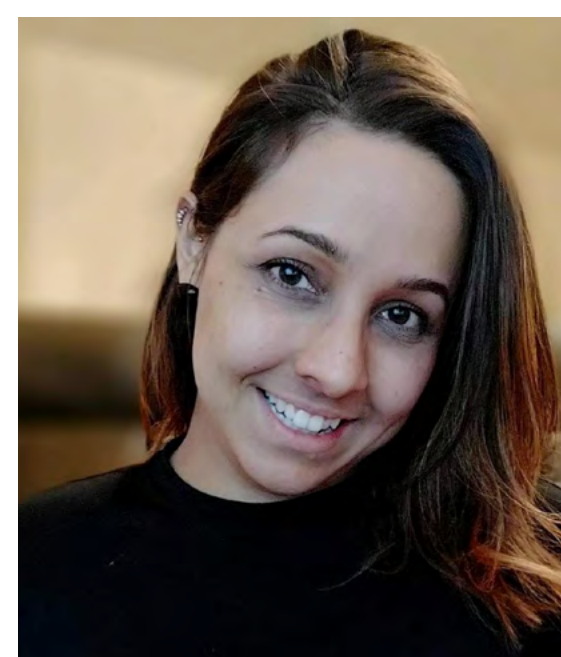
One of the great challenges in the treatment of cats that have chronic vomiting is to introduce the most appropriate therapy directed to the underlying cause. A careful individualized diagnostic approach for each patient is essential, starting with the health check with emphasis on history, anamnesis and physical examination, with the help of supplementary tests so that a definitive diagnosis can be determined and the treatment can be directed.



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