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Medicine on a Budget
Mini Series

Session Three: Vomiting vs Regurgitation: Is it really that easy to tell?

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Differentiating Regurgitation from Vomiting

A complete history and thorough physical examination will usually allow differentiation of regurgitation from vomiting. Asking owners to describe the episodes is helpful, as a description of abdominal contractions (retching) or bile in the vomitus is specific for vomiting. In rare instances, bile may be present in regurgitation due to reflux of bile from the stomach into the oesophagus prior to regurgitation. Additionally, vomiting is often associated with prodromal signs of nausea such as salivation or lip-smacking. With regurgitation, owners typically report that the animal simply lowers its head and material is expelled.

Other factors such as timing of the episode in relation to feeding or the amount of material produced are not distinguishing factors. Animals may vomit undigested food or regurgitate digested-appearing food. The pH of the expulsed material has been considered a possible differentiating test. Vomited material is expected to have a low pH and regurgitated material to have a more neutral or high pH. However, some animals may regurgitate stomach contents (such as in reflux esophagitis) and some may vomit bicarbonate-rich fluid refluxed from the duodenum, making pH a poor indicator.

In some instances, the owner may not have witnessed the episode, but only report finding food or fluid on the floor. In other cases, the description of the episodes may not allow obvious distinction. In these cases, the rest of the history and physical examination should be used for determining if vomiting or regurgitation is more likely. As regurgitation is uncommon in cats, episodes can most often be assumed to be vomiting in this species. If possible, having the owner record an episode on video may be helpful. While rare, simultaneous vomiting and regurgitation may be present.

Regurgitation

Regurgitation is the passive expulsion of food, fluid, or other material from the pharynx or oesophagus. It must be differentiated from expectoration, which is the expulsion of material from the respiratory tract associated with coughing. Regurgitation may be followed by a terminal retch or gag, which owners may confuse with cough, and regurgitation can lead to aspiration pneumonia resulting in a true cough.

Pathophysiology

The oesophagus is a long tubular organ bordered proximally by the upper oesophageal sphincter and distally by the lower oesophageal sphincter. The muscular composition of the oesophagus differs between dogs and cats. In dogs, the oesophageal body is fully composed of striated muscle. In the cat, the distal oesophagus is composed of smooth muscle. In both species, during swallowing, the upper oesophageal sphincter relaxes to allow passage of the food or liquid into the proximal oesophagus. A primary peristaltic wave is initiated that moves food distally to the stomach. Secondary peristaltic waves are generated as a response to intraluminal distension to clear remaining material. The lower oesophageal sphincter relaxes as the food bolus approaches, allowing passage into the stomach. Diseases that result in inflammation, obstruction, or hypomotility in the oesophagus interrupt this normal process and can result in regurgitation.

Clinical Signs

The regurgitant may include undigested food, digested food, or clear, frothy fluid. Weight loss and polyphagia may occur due to inadequate nutrition. In some cases, dilation of the cervical oesophagus may be apparent. Signs of aspiration pneumonia including lethargy, anorexia, cough, or dyspnoea may be present. A neurological examination should be performed to evaluate for deficits consistent with generalized neuromuscular dysfunction.

Diagnosis

Initial evaluation consists of cervical and thoracic radiographs to assess for generalized (megaoesophagus) or focal (vascular ring anomaly, stricture) oesophageal dilation, foreign bodies, intra- or extraluminal masses, and aspiration pneumonia. Contrast radiography (oesophagram) provides further assessment if survey radiographs are non-diagnostic. Use of video fluoroscopy is beneficial to better assess oesophageal motility. Endoscopy can confirm radiographic findings, provide treatment for foreign bodies or strictures, allow biopsy of mass lesions, and identify esophagitis.

A minimum database including complete blood count, serum biochemistry profile, and urinalysis is warranted when systemic illness or megaoesophagus is present. Adrenocorticotropic hormone (ACTH) stimulation, thyroid tests, acetylcholine receptor antibody test, and blood lead assay should be considered in cases with megaoesophagus or oesophageal hypomotility.

Treatment

Specific therapy should be used for any underlying disease as well as aspiration pneumonia if present. Management strategies to reduce frequency of regurgitation are used when primary disease is not identified or is unresponsive to therapy. Dietary management includes small, frequent meals and elevated feeding. Maintaining the patient in an upright position for 5-10 minutes after feeding may allow gravity to help oesophageal transit. A Bailey chair can be used for this purpose. Owners should experiment with different food textures such as liquids, gruels, canned, or dry foods to determine which one works best for their pet. If gastroesophageal reflux disease is present, acid reducers and prokinetics may reduce the risk of esophagitis. Cisapride (cats) and bethanechol (dogs) may improve oesophageal motility. Increasing the lower oesophageal sphincter tone can exacerbate regurgitation in some cases.

Vomiting

Vomiting is one of the most common reasons dogs and cats are presented to a veterinarian for evaluation. It is an active expulsion of ingesta from the stomach and sometimes duodenum through the mouth. In contrast to regurgitation, vomiting involves a centrally mediated reflex with coordinated closure of the nasopharynx and glottis to protect the airway, reducing the risk of aspiration pneumonia. Like regurgitation, it must be differentiated from expectoration.

Vomiting evolved as protection against the ingestion of toxic or noxious substances, which explains its activation by both neural and humoral stimuli. It is most often associated with primary gastrointestinal (GI) disorders, but may also occur due to non-GI diseases such as metabolic or neurological disorders. Severe or prolonged vomiting can have significant consequences including volume depletion, acid-base and electrolyte derangements, aspiration pneumonia, and esophagitis.

Pathophysiology

Vomiting is a complex reflex initiated by the emetic center, which is composed of a group of nuclei located in the medulla oblongata of the brainstem. Within this area are serotonergic ($5HT_1$) and adrenergic ($alpha_2$) receptors. In addition, neurokinergic (NK_1) receptors are located in the adjacent nucleus tractus solitarii, which can stimulate the emetic center. Activation of these receptors may occur indirectly by humoral pathways via the chemoreceptor trigger zone (CRTZ) or directly through neural pathways from the GI tract, cerebral cortex, or vestibular system.

The CRTZ is located in the area postrema in the floor of the fourth ventricle and it lacks a blood-brain barrier, allowing it to sample chemical stimuli in the blood. Stimulants include endogenous (uremic or hepatoencephalopathic toxins) and exogenous substances (drugs, toxins). Dopaminergic (D_2), histaminergic (H_1), adrenergic ($alpha_2$), serotonergic ($5HT_3$), cholinergic (M_1), enkephalinergic ($ENK_{\mu,\delta}$), and neurokinergic (NK_1) receptors are present in the CRTZ, but there are species differences. Apomorphine (D_1 and D_2 agonist) is a potent stimulator of emesis in dogs but it has little to no effect in cats, suggesting a lack of D_2 receptors in this species. However, xylazine ($alpha_2$ agonist) is an effective emetic in cats, signifying that $alpha_2$ receptors may be more important. Visceral rather than central $5HT_3$ receptors appear to be more important in cisplatin-induced emesis in the dog.

Neural stimulation of the emetic center occurs via afferent vagal, sympathetic, vestibular, and cerebrocortical pathways. Gastrointestinal diseases can directly cause vomiting by stimulating release of serotonin from enterochromaffin cells that binds to $5HT_3$ receptors on afferent vagus nerves (dog) or the CRTZ (cat). Vestibular stimulation feeds into the CRTZ before activating the emetic centre in the dog, but appears to act directly on the emetic centre in the cat.

Clinical Approach

The initial approach starts with a thorough history. A description of the vomiting episodes is essential to differentiate them from coughing or regurgitation. The owner should be asked to describe the frequency, duration, relation to eating or drinking, and the character of the vomitus. Vomiting may be acute or chronic (>1-2 weeks in duration). In some cases, vomiting may be sporadic, making it difficult to determine if it is chronic versus intermittent acute disease. Vomiting food more than 8 hours after ingestion suggests delayed gastric emptying due to either gastric outflow obstruction or gastric hypomotility, while the presence of bile suggests patency of the gastric outflow tract. The presence of either fresh or digested blood ("coffee grounds") indicates GI erosions or ulcers.

A complete dietary history should be obtained, including past and current diets for planning possible diet trials. Recent diet changes or opening a new bag or can of food may be the cause of vomiting. Medication history must include asking about drugs, supplements, nutraceuticals, and alternative therapies that could be associated with vomiting. The owner should also be questioned about the animal's possible exposure to toxins or foreign body ingestion. Vaccination status, travel history, and exposure to other animals are important for determining risk of infectious diseases, which are more common in young animals.

Physical examination should start with an overall assessment of patient demeanor. Oral exam may reveal ulcers associated with uraemia or toxin ingestion, or lingual linear foreign bodies (particularly in cats). Icteric mucous membranes suggest liver disease. Cardiac arrhythmias can indicate metabolic derangements or toxin ingestion. The abdomen should be palpated for evidence of pain (pancreatitis, obstruction), effusion (peritonitis), gas distension (obstruction, gastric dilation-volvulus), or organomegaly. Rectal exam may reveal evidence of melena, constipation, or material consistent with foreign body ingestion.

Diagnostic Approach

The diagnostic approach differs based on classification of the vomiting as acute or chronic. Acute vomiting with mild clinical signs is often self-resolving. As such, a minimalistic approach is usually appropriate. Faecal examination may identify parasitic causes of vomiting. Abdominal radiographs are performed if there is a clinical suspicion of surgical disease (e.g., suspected foreign body ingestion) or if vomiting does not resolve with initial therapy.

Conversely, severe or life-threatening signs indicate a more thorough evaluation should be done. Complete blood count, serum biochemistry profile, and urinalysis allow identification of systemic or metabolic diseases. Metabolic alkalosis is suggestive of gastric outflow or proximal duodenal obstruction and is often associated with hyponatremia, hypokalaemia, and hypochloraemia. Abdominal radiographs +/− abdominal ultrasound are used for evaluating for surgical diseases such as foreign body, obstruction, gastric dilation-volvulus, or intussusception.

Chronic vomiting requires further investigation so definitive therapy can be prescribed. Complete blood count, serum biochemistry profile, and urinalysis should be performed. In addition, cats should be tested for feline leukaemia and feline immunodeficiency viruses and those over 5 years of age should be evaluated for hyperthyroidism with a serum total T4 assay. If a cause is not found, additional diagnostic testing including ultrasonography, heartworm testing (cats), bile acids profile, pancreatic lipase testing, and ACTH stimulation testing should be considered. If a non-GI cause for the vomiting is not identified with such testing, further evaluation of the GI tract is needed. Contrast radiography may be helpful, particularly if ultrasonography is not available or the stomach is poorly visualized during ultrasonography due to intraluminal gas. Diet trials should be considered in stable animals to exclude diet-responsive disease prior to more invasive testing. Endoscopic or surgical biopsy is required to identify inflammatory disease such as chronic gastritis, *Helicobacter* gastritis, or inflammatory bowel disease.

Treatment

Initial treatment should be aimed at the primary disease, which often results in resolution of vomiting. Acute, self-limiting vomiting usually resolves with fluid replacement and fasting for 12-24 hours. Acute cases with protracted or severe vomiting may benefit from antiemetic therapy. Caution should be used, as antiemetics may mask underlying disease that has not yet been identified. Chronic cases are best treated by identifying the underlying cause. Antiemetic therapy can be considered for improving comfort and nutrition, and prevent excessive fluid losses.

Common Causes of Vomiting

Metabolic Diseases

1. Renal disease
2. Hepatobiliary disease or failure
3. Electrolyte derangements
4. Acid-base derangements
5. Endotoxaemia

Endocrine Diseases

1. Hypoadrenocorticism
2. Hyperthyroidism

Toxins/Drugs

1. Heavy metals
2. Ethylene glycol
3. Nonsteroidal anti-inflammatory drugs (NSAIDs)
4. Antibiotics
5. Chemotherapy agents

Dietary Causes

1. Indiscretion
2. Allergy
3. Intolerance

Abdominal Diseases

1. Pancreatitis
2. Peritonitis
3. Neoplasia

Gastric Diseases

1. Gastritis
2. Parasites
3. *Helicobacter*
4. Foreign bodies
5. Obstruction
6. Gastric dilation-volvulus
7. Motility disorders
8. Neoplasia

Small Intestinal Diseases

1. Inflammatory bowel disease
2. Neoplasia
3. Obstruction
4. Parasites
5. Infections

Large Intestinal Diseases

1. Constipation
2. Colitis

Inflammatory Bowel Disease in Small Animals

Idiopathic inflammatory bowel disease (IBD) constitutes a group of GI diseases characterized by persistent clinical signs and histologic evidence of inflammatory cell infiltrate of unknown etiology. The various forms of IBD are classified by anatomic location and the predominant cell type involved. Lymphocytic-plasmacytic enteritis is the most common form in dogs and cats, followed by eosinophilic inflammation. There are occasional reports of inflammation with a granulomatous pattern (regional enteritis). A neutrophilic predominance in the inflammatory infiltrate is rare. A mixed pattern of cellular infiltrate is described on many occasions. Certain unique IBD syndromes occur more often in some breeds, such as the protein-losing enteropathy/nephropathy complex in Soft-coated Wheaten Terriers, immunoproliferative enteropathy of Basenjis, IBD in Norwegian Lundehunds, and histiocytic ulcerative colitis in Boxers.

The aetiology of IBD is unknown. Several factors may be involved, such as GI lymphoid tissue (GALT); permeability defects; genetic, ischemic, biochemical, and psychosomatic disorders; infectious and parasitic agents; dietary allergens; and adverse drug reactions. IBD may also be immune mediated.

The intestinal mucosa has a barrier function and controls exposure of antigens to GALT. The latter can stimulate protective immune responses against pathogens, while remaining tolerant of harmless environmental antigens (eg, commensal bacteria, food). Defective immunoregulation of GALT results in exposure and adverse reaction to antigens that normally would not evoke such a response. Although dietary allergy is an unlikely cause of IBD (except in eosinophilic gastroenteritis), it may contribute to increased mucosal permeability and food sensitivity.

Current evidence supports the likely involvement of hypersensitivity reactions to antigens (eg, food, bacteria, mucus, epithelial cells) in the intestinal lumen or mucosa. More than one type of hypersensitivity reaction is involved in IBD. For example, type I hypersensitivity is involved in eosinophilic gastroenteritis, whereas type IV hypersensitivity is likely involved in granulomatous enteritis. The hypersensitivity reaction incites the involvement of inflammatory cells, resulting in mucosal inflammation that impairs the mucosal barrier, in turn facilitating increased intestinal permeability to additional antigens. Persistent inflammation may result in fibrosis.

There is no apparent age, sex, or breed predisposition associated with IBD; however, it may be more common in German Shepherds, Yorkshire Terriers, Cocker Spaniels, and purebred cats. The mean age reported for development of clinical disease is 6.3 yr in dogs and 6.9 yr in cats, but IBD has been documented in dogs <2 yr old. Clinical signs are often chronic and sometimes cyclic or intermittent. Vomiting, diarrhea, changes in appetite, and weight loss may be seen. In a retrospective study of cats with lymphocytic-plasmacytic enterocolitis, weight loss, intermittent vomiting progressing to more frequent vomiting on a daily basis, diarrhea, and anorexia were seen most often. Vomiting, melena, and cranial abdominal pain are often seen with gastroduodenal ulceration and erosion. Weight loss, vomiting, diarrhea, ascites, and peripheral edema can be seen in the cases of protein-losing enteropathy. Pulmonary thromboembolism is a rare complication; however, it can occur if there is severe intestinal protein loss (loss of antithrombin III). Clinical signs of large-intestinal diarrhea, including anorexia and watery diarrhea, are not uncommon.

There are no specific abnormalities on CBC, biochemical evaluations, or radiographs.

Hypoproteinemia due to reduced dietary intake and malabsorption or increased loss via the GI tract may be seen. Hypocalcemia and hypocholesterolemia may be attributed to malabsorption. Increases in serum amylase as a consequence of bowel inflammation have been reported. Hypokalemia secondary to anorexia, potassium loss from vomiting and diarrhea, and mild increases in serum levels of liver enzymes can be expected. Low serum levels of folate and cobalamin because of malabsorption are also documented.

Eosinophilia may be associated with eosinophilic enteritis; however, this is not a sensitive parameter. Microcytic anemia may be present with loss of iron, associated with chronic loss of blood. Nonresponsive anemia, if present, likely reflects anemia of chronic or inflammatory disease.

Erythrocytosis, associated with fluid loss from vomiting and diarrhea, and a stress leukogram may be seen. Radiographic changes may include gas or fluid distention of the stomach and increased total diameter of small-intestinal loops. Contrast films may show diffuse or focal mucosal irregularities suggestive of infiltrative disease. Loss of contrast can be related to ascites.

Fecal examination is important to exclude other causes of mucosal inflammation, such as nematodes, *Giardia* infection, and bacterial infection. *Giardia* may be difficult to detect because of intermittent shedding, and empirical treatment with fenbendazole is recommended in all cases.

Abdominal ultrasonography can be used to assess all abdominal organs, examine the entire intestinal tract, and measure wall thickness (although the latter measurement is of no significant value in IBD diagnosis). Small-intestinal hyperechoic mucosal striations are frequently associated with mucosal inflammation and protein-losing enteropathy.

Ultrasonography also helps eliminate the possibility of disease in other organs, localize the disease, and determine whether endoscopy would allow biopsy of the site.

Endoscopy allows examination of the oesophagus, stomach, duodenum, and sometimes the jejunum, depending on the size of the animal. Colonoscopy allows exploration of the colon. In some cases, gross mucosal lesions may be seen endoscopically, including erythema, friability, enhanced granularity, erosion, and ulceration. In many cases, the endoscopic appearance is normal. However, biopsy samples should always be taken, because the macroscopic and microscopic appearance of the intestinal mucosa are poorly correlated. At least six biopsies of each segment of the GI tract are recommended. Endoscopy is the easiest way to collect biopsy samples, but such samples are superficial and usually can be collected only from the proximal small intestine. One study suggested that ileal biopsies can reveal lesions not apparent in the duodenum and, therefore, should be performed routinely. More specifically, feline lymphoma was much more likely to be found in the ileum than the duodenum. In some cases, exploratory celiotomy and full-thickness biopsy are necessary to reveal histopathologic changes at the level of the mucosa (eg, dilation of the lacteals in lymphangiectasia). However, wound healing can be compromised if there is severe hypoproteinemia or if urgent steroid treatment is needed. For this reason, most clinicians choose to perform endoscopic biopsies unless biopsies of other abdominal organs are required.

Small populations of lymphocytes, plasma cells, macrophages, eosinophils, and neutrophils are normal components of intestinal mucosal tissue. Increased numbers of plasma cells, lymphocytes, eosinophils, and neutrophils in the lamina propria are seen in IBD. However, these morphologic features may also be seen with other causes of GI disease (eg, *Giardia*, *Campylobacter*, *Salmonella*, lymphangiectasia, lymphosarcoma). Although histopathologic assessment of intestinal biopsy material remains the gold standard for diagnosis of many IBDs, it has marked limitations. Specimen quality can vary, pathologic diagnoses are inconsistent, and differentiation between normal specimens and those showing IBD and even lymphoma can be difficult. Biopsy must always be considered in relation to clinical signs, and the animal treated accordingly.

The goals of therapy are to reduce diarrhea and vomiting, promote appetite and weight gain, and decrease intestinal inflammation. If a cause can be identified (eg, dietary, parasitic, bacterial overgrowth, drug reaction, etc), it should be eliminated.

Dietary manipulation by itself may be effective in some cases (eg, in chronic colitis); in other cases, it can enhance the efficacy of concurrent medical therapy, allowing for the drug dosage to be reduced or for drug therapy to be discontinued once clinical signs are in remission. Corticosteroids, azathioprine, sulfasalazine, tylosin, and metronidazole are among the drugs most often used in management of IBD.

Unless the animal is debilitated, it is better to institute therapeutic modalities sequentially. The frequency and nature of clinical signs should be monitored, and therapy adjusted as needed. Treatment should begin with anthelmintic/antiparasitic medication (eg, fenbendazole at 50 mg/kg/day, PO, for 3–5 days). This is followed by dietary modification (preferably with an antigen-limited or hydrolyzed protein diet) for 3–4 wk, then a 3- to 4-wk antibacterial trial (usually tylosin 10 mg/kg, PO, tid, or metronidazole 10 mg/kg, PO, bid), and finally trial immunosuppressive therapy (initially prednisolone, 1 mg/kg, PO, bid).

In refractory cases, adding an immunosuppressive drug to corticosteroid therapy may be beneficial. Azathioprine (for dogs) and chlorambucil (for cats) can be used. The dosage of azathioprine is 2.2 mg/kg/day, PO. Adverse effects include myelosuppression, pancreatitis, and hepatotoxicity. The dosage of azathioprine can be tapered after several weeks. Typically, the prednisone is tapered first (by 25% every 2–3 wk). After prednisone has been tapered to 0.5 mg/kg every other day without a relapse, then azathioprine is given every other day. If response to steroids is poor, even if combined with azathioprine, cyclosporine can be added at 5–10 mg/kg/day, PO, for at least 8–10 wk. No study has been done to compare cyclosporine and azathioprine.

However, one recent study suggested that the combination of chlorambucil-prednisolone was more efficient to treat chronic enteropathy with concurrent protein-losing enteropathy in dogs than the azathioprine-prednisolone protocol.

Azathioprine is not recommended in cats because of sensitivity to adverse effects. Instead, cats are treated with a combination of prednisone and chlorambucil (0.1–0.2 mg/kg or 1 mg/cat). Clinical signs typically improve in 3–5 wk, although 4–8 wk of treatment may be needed. A CBC should be done every 2 wk to monitor for evidence of myelosuppression.

The response rate to treatment of IBD is variable. Quality of life tends to be poor, and prognosis is guarded. Hypoalbuminemia is a negative prognostic sign. Prognosis is worse in cases with severe histologic lesions, mucosal fibrosis, eosinophilic enteritis, protein-losing enteropathy, or hypereosinophilic syndrome. Relapses occur and are most often precipitated by dietary indiscretion.