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## DRUG THERAPY OF UPPER GI DISEASES

Michael S. Leib DVM, MS, Diplomate ACVIM  
Virginia Maryland Regional College of Veterinary Medicine  
Virginia Tech, Blacksburg, VA

Many drugs are available to treat the clinical signs associated with gastric diseases or to treat the disease process itself. A thorough knowledge of these drugs, including several of the newer developments, is necessary for the practitioner to effectively treat dogs and cats with gastric disease. Portions of this article are adapted from the author's chapter in Leib MS. Diseases of the Stomach, Practical Small Animal Internal Medicine. WB Saunders, Philadelphia, PA, 1997: 653-684.

### ANTIEMETICS

Antiemetics are effective in reducing the frequency of vomiting or in some cases completely eliminating it. In the outpatient, it relieves a very objectionable clinical sign for the owner. In the hospitalized patient, it reduces the severity of dehydration and electrolyte changes and allows the animal to rest. Antiemetics should be used cautiously, as continued vomiting is an important sign that the underlying condition may be progressing or that an incorrect diagnosis has been made. Masking this important parameter may give the clinician a false sense of security that the animal is improving, when actually heightened surveillance and therapy is indicated. The author is most comfortable prescribing antiemetics when a definitive diagnosis has been reached or when used for only a brief period in animals with self-limiting vomiting.

### Phenothiazines

Phenothiazines are potent centrally acting drugs that block both the vomiting center and the CRTZ. They are dopamine antagonists with antihistaminic and weak anticholinergic properties. They can not be administered until the animal has been rehydrated because they are alpha-adrenergic receptor blockers and can cause hypotension. Even at low doses they produce tranquilization, which has the benefit of promoting rest and reducing stress, but the disadvantage of interfering with monitoring the animal's attitude. They should not be used in animals with epilepsy as they may lower the seizure threshold. They can be given IM or SQ and several are available in suppository form. Recommended dosages of commonly used drugs include chlorpromazine (Thorazine) 0.2-0.5 mg/kg TID to QID and prochlorperazine (Compazine) 0.5 mg/kg TID to QID.

### Metoclopramide

Metoclopramide (Reglan) is a highly effective antiemetic with both central and peripheral effects. Metoclopramide is a dopamine antagonist that very effectively blocks the CRTZ and raises the threshold of the vomiting center. Peripherally it augments acetylcholine release from postganglionic nerves and increases the tone and amplitude of gastric contractions and increases gastroesophageal sphincter pressure. These actions oppose some of the physical events necessary for the vomiting reflex to occur. Short term side effects are uncommon and include depression, nervousness, and restlessness. Metoclopramide is contraindicated in intestinal obstructions. Dosages of 0.2-0.4 mg/kg TID SQ are often

effective. Because it has a short half life it may need to be administered by constant infusion 1.0-2.0 mg/kg/day IV.

Metoclopramide can also be used to treat esophagitis. Increasing tone of the GES helps to reduce the reflux of acid which would impede healing of the esophageal mucosa. Increasing gastric motility and emptying will help to move acid and ingesta out of the stomach into the duodenum, reducing the amount available to reflux into the esophagus. Metoclopramide's prokinetic effects are useful in treating gastric motility disorders, a group of under diagnosed conditions causing chronic vomiting (see article on gastric motility disorders).

### Ondansetron

Ondansetron (Zofran) is a serotonergic antagonist that is very effective in blocking the nausea and vomiting associated with chemotherapy. It is effective in blocking neural transmission in both the chemoreceptor trigger zone and in vagal afferent pathways. Dosages of 0.5-1.0 mg/kg PO can be given 30 minutes prior to administration of chemotherapy. It can also be used to reduce vomiting associated with GI disorders at 0.1-0.15 mg/kg slow IV BID-QID. The author has not found it necessary to use the drug in this manner, although others have found it very effective. Presently, the drug is very expensive.

### EROSION AND ULCER THERAPY

Erosion and ulceration of the gastric and duodenal mucosa commonly occur in chronic gastritis and gastric-duodenal ulcer disease. Back-diffusion of acid across a damaged mucosa leads to further damage and retards healing processes. Reduction of gastric acid secretion, protection of ulcerated mucosa, or augmentation of cytoprotection promotes healing of erosions and ulcers.

### H-2 Receptor Blockade

Drugs such as cimetidine (Tagamet), ranitidine (Zantac), famotidine (Pepsid), and nizatidine (Axid) block the H-2 receptor on the gastric parietal cell and dramatically decrease acid production. Cimetidine (5-10 mg/kg QID) and ranitidine (2 mg/kg BID-TID) have been used most commonly in veterinary medicine. Both can be given orally or parenterally and have not been commonly associated with adverse effects. Cimetidine can inhibit hepatic cytochrome P-450 enzymes, potentially interfering with the metabolism of other drugs. Famotidine, 0.5 mg/kg SID-BID, and nizatidine, 5 mg/kg SID (this dosage has not been well established), have not been used as frequently in veterinary medicine, but are also effective. All four of these drugs are now available over the counter in smaller dosage forms than prescription strength, making treatment of cats and small dogs easier. Elixirs are available for cimetidine, ranitidine, and famotidine.

### Sucralfate

Sucralfate (Carafate) is a sulfated disaccharide that forms an adherent gel and binds to an ulcer crater, protecting it from acid and pepsin. It also stimulates the synthesis of prostaglandin, increases mucosal cytoprotection, and binds epithelial growth factor at the ulcer, where it stimulates cellular proliferation. It has been shown to be as effective as H-2 receptor blockers in healing ulcers in humans. Because sucralfate can bind other drugs, medications should be given 1-2 hours prior to sucralfate administration. The recommended dose is 1 gm/25 kg TID-QID in dogs and

0.25 gm TID in cats. Because absorption is minimal, toxicity is uncommon. Long-term use may lead to constipation because of its aluminum content. There is no evidence to support that combination therapy with an H-2 receptor antagonist provides added benefit compared to therapy with either sucralfate or an H-2 blocker alone.

Sucralfate is also effective to treat esophagitis because of its ability to coat ulcerated mucosa. The suspension form is necessary for this indication.

### Misoprostol

Misoprostol (Cytotec) is a synthetic prostaglandin that prevents or heals ulcers associated with NSAID administration by directly increasing mucosal cytoprotection. The suggested dose is 3µg/kg TID. The most common side effect is diarrhea although it can also cause abortion. Its major indication is preventing GI mucosal injury in dogs with arthritis that require long-term NSAID therapy. It can also be used to treat cases of GDUD caused by NSAIDS.

### PROTON PUMP INHIBITORS

Omeprazole (Prilosec) inhibits action of the proton pump at the apical portion of the parietal cell that exchanges H<sup>+</sup> for luminal K<sup>+</sup>, thus preventing secretion of acid. As a weak base it accumulates in the acid compartment of the parietal cell, necessitating only SID administration. The recommended dose is 0.7 mg/kg SID. The enteric-coated granules (20 mg) are packaged in gelatin capsules to resist degradation by gastric acid. If less than one capsule is to be administered (20 mg), the granules should be repackaged in gelatin capsules. Omeprazole also inhibits hepatic p-450 enzymes. Prolonged use may induce mucosal hyperplasia and tumor formation in laboratory species. Omeprazole is indicated if GDUD is unresponsive to therapy with H-2 blockers or sucralfate or in gastric acid hypersecretory conditions such as systemic mast cell disease.

### HELICOBACTER

Many treatments have been shown to be effective in humans with *Helicobacter* infection. Little is known regarding effective treatments in dogs and cats. See The Role of *Helicobacter* proceedings for additional information. My current therapy is two weeks of omeprazole 0.7 mg/kg SID (or an H2 blocker), amoxicillin 15 mg/kg BID, metronidazole 10 mg/kg BID, and Pepto Bismol 1/4 - 2 tablet BID. Other suggestions include omeprazole with either azithromycin 10-20 mg/kg SID in dogs and 5 mg/kg SID in cats or clarithromycin 7.5 mg/kg BID.

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