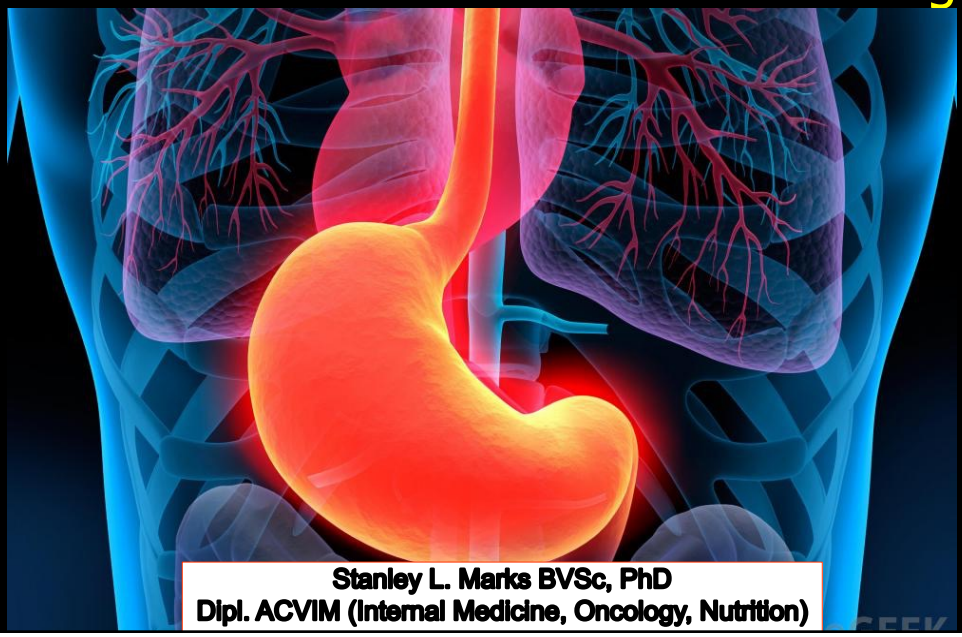
Rational Use of Gastric Protectants for Dogs & Cats



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Dipl. ACVIM (Internal Medicine, Oncology, Nutrition)

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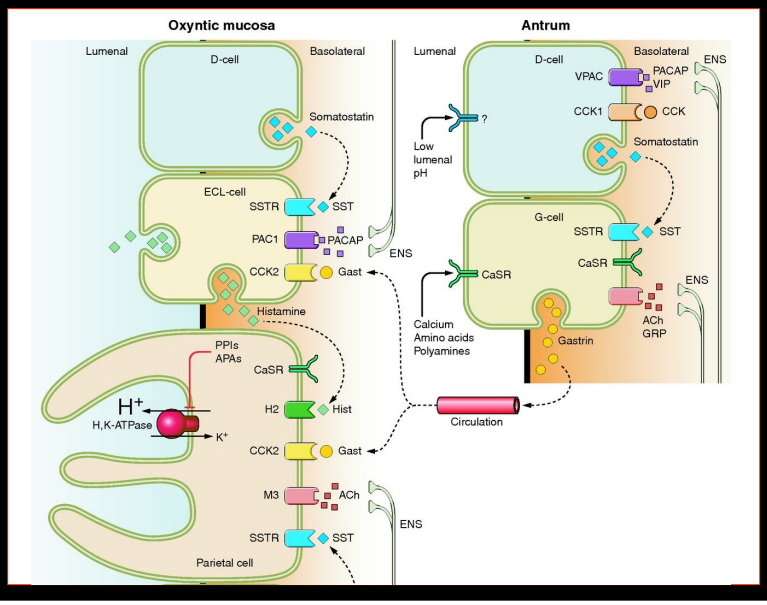
Regulation of Gastric Acid Secretion



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Antacids

- Weak base that neutralizes acid that is already secreted in the stomach
- Also inhibits formation of pepsin
  - Aluminum hydroxide
  - Magnesium hydroxide
- Duration of action
  - 30 min when taken on empty stomach
  - 2 hrs when taken after a meal

3

Side Effects of Antacids

- Al^{3+} antacids
  - Constipation
  - Relax gastric smooth muscle & delays gastric emptying
  - In renal failure – aluminum toxicity
    - Segev G, et al. JVIM 22:2008
- Mg^{2+} antacids
  - Osmotic diarrhea

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Gastric Acid Suppressants – Too Much of a Good Thing?

- Excessive and inappropriate use of gastric acid suppressants is rampant in human medicine
- Annual expenditure of $13.6 billion per year in the US with 113 million prescriptions written in the US in 2009
- Side-effects may be less benign in older people:
  - Community and hospital acquired pneumonia
  - Increased risk of *Salmonella*, *Campylobacter*, and *C. difficile*
  - Microscopic colitis
  - Hypomagnasemia, hypocobalaminemia, iron malabsorption
  - Osteoporotic fracture
  - Renal disease, cardiac disease?

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ACVIM American College of Veterinary Internal Medicine

CONSENSUS STATEMENT

Consensus Statements of the American College of Veterinary Internal Medicine (ACVIM) provide the veterinary community with up-to-date information on the pathophysiology, diagnosis, and treatment of clinically important animal diseases. The ACVIM Board of Regents oversees selection of relevant topics, identification of panel members with the expertise to draft the statements, and other aspects of assuring the integrity of the process. The statements are derived from evidence-based medicine whenever possible and the panel offers interpretive comments when such evidence is inadequate or contradictory. A draft is prepared by the panel, followed by solicitation of input by the ACVIM membership that may be incorporated into the statement. It is then submitted to the *Journal of Veterinary Internal Medicine*, where it is edited before publication. The authors are solely responsible for the content of the statements.

ACVIM consensus statement: Support for rational administration of gastrointestinal protectants to dogs and cats

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Survey-Based Analysis of Gastrointestinal Protectant Use Among Veterinarians in Portugal

Table 2. Evidence- and non-evidence-based therapeutic indications for use of GIPs among Portuguese GPs, taking as a reference the ACVIM consensus statement.

Evidence-Based Indications	GPs Using GIPs (*n*(%)) *n* = 124
Treatment of gastrointestinal ulceration or erosion	122 (98.3%)
Prophylactic management of reflux esophagitis	99 (79.8%)
Non-Evidence-Based Indications	
Prophylactic management in animals with non-erosive gastritis	111 (89.5%)
Prophylactic management of steroid-induced ulceration	87 (70.2%)
Prophylactic management in animals with pancreatitis	76 (61.3%)
Prophylactic management in animals with CKD	74 (59.7%)
Prevention or management of thrombocytopenia-induced gastrointestinal bleeding	38 (30.6%)
Prophylactic management in animals with hepatic disease not associated with gastrointestinal bleeding	27 (21.8%)

Baptista R, et al. Veterinary Sciences 2021

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Impact of the ACVIM Consensus Statement on Prevalence and Appropriateness of Omeprazole Prescription

UNIVERSIDAD COMPLUTENSE MADRID

- Significant increase in cases that received omeprazole q12h vs. q24h following publication of Consensus Statement
- Significant increase in cases that underwent appropriate tapering after ≥ 4 weeks of omeprazole therapy following publication of Consensus Statement
- Significant increase in the appropriateness of prescription following publication of Consensus Statement

  - Frontiers in Veterinary Science – Under Review Sainz Rodriguez A, et al. 2024

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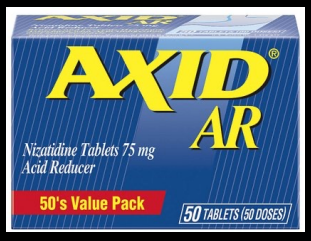
Histamine H_2 Receptor Antagonists

- Reversible competitive inhibitors of H_2 receptor
- Highly selective, no action on H_1 or H_3 receptors
- Effective in inhibiting nocturnal acid secretion
- Modest impact on meal stimulated acid secretion



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Histamine H2-Receptor Antagonists

	Cimetidine	Ranitidine	Famotidine	Nizatidine
Relative Potency	1	5-10	32	10
Half-life (hrs)	1.5-2.3	1.6-2.4	2.5-4	1.1-1.6
Duration of action (hrs)	6	8	12	8
Inhibition of CYP 450	1	0.1	0	0

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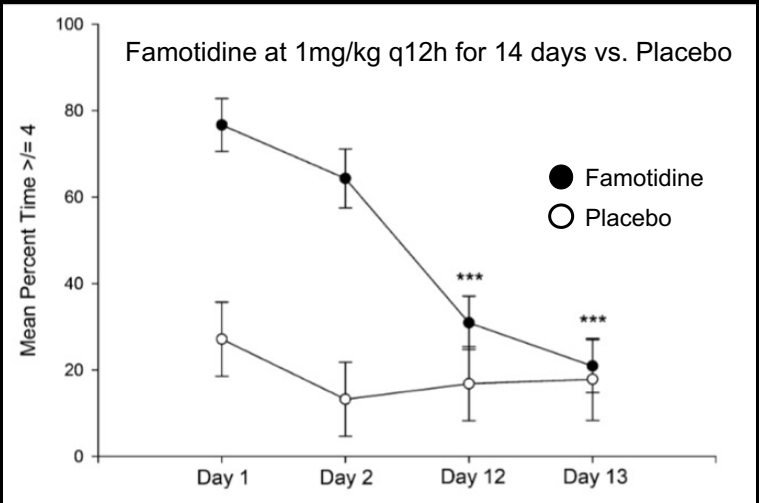
Repeated Oral Famotidine Administration Results in Diminished Effect on Gastric pH in Dogs & Cats



Tolbert MK, et al. JVIM, 31:2017

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Rebound Hypersecretion and Discontinuation of Gastric Acid Suppressants

- Upregulation of the H2-receptor to histamine
- Diminished antral D-cell release of somatostatin
- Increased G-cell release of gastrin
  - Rebound hypersecretion after H_2RAs occurs within 2-3 days after 4 weeks of therapy, and lasts 10 days
  - Rebound hypersecretion after PPIs can last for 2-4 weeks after 4 or 8 weeks of PPIs, respectively

Hunfeld NG, et al. Aliment Pharmacol 2007
Gould, et al. JVIM 2016

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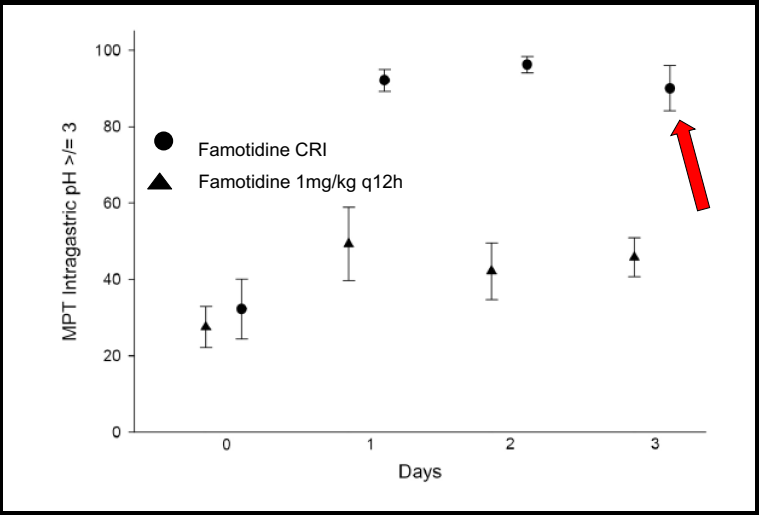
Comparison of IV Bolus Administration of Famotidine vs. Famotidine CRI on Gastric pH in Dogs



Hedges K, et al. JVIM, 2019

1 mg/kg q12h vs. 1 mg/kg IV bolus followed by 8 mg/kg/24h for 3 days

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Proton Pump Inhibitors

- Most effective and potent acid suppressants
- Irreversible inhibitor of H^+ K^+ ATPase
- Prodrugs requiring activation in acid environment
  - Give 30-60 min before meals because it requires acid for activation
  - Other acid suppressing agents should not be co-administered

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Effects of H2RAs and PPIs on Intragastric pH in 12 Healthy Beagles

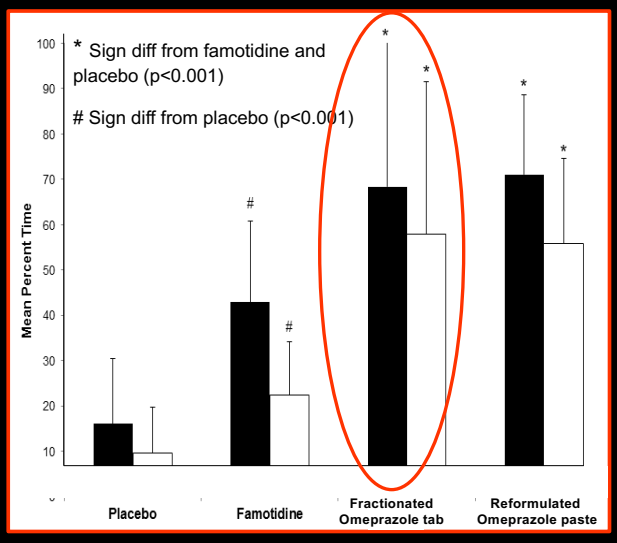
Treatment	MPT pH ≥3 Day 6
Saline	29%
Ranitidine 1 mg/kg q12h IV	37%
Famotidine 1 mg/kg q12h IV	60%
Pantoprazole 1 mg/kg q24h IV	59%
Omeprazole Tablet 1 mg/kg q24h PO	70%
Omeprazole suspension 1 mg/kg q12h PO	91%

Clinical GOAL in people for medical treatment of ulcerative disease: pH ≥ 3 for ≥ 75% of the day

Bersenas, et al. AJVR 66: 2005

15

Omeprazole Formulations in 6 Cats Approached Human pH Goals



n =6 cats/crossover treatment

Parkinson,, et al. JVIM 2015

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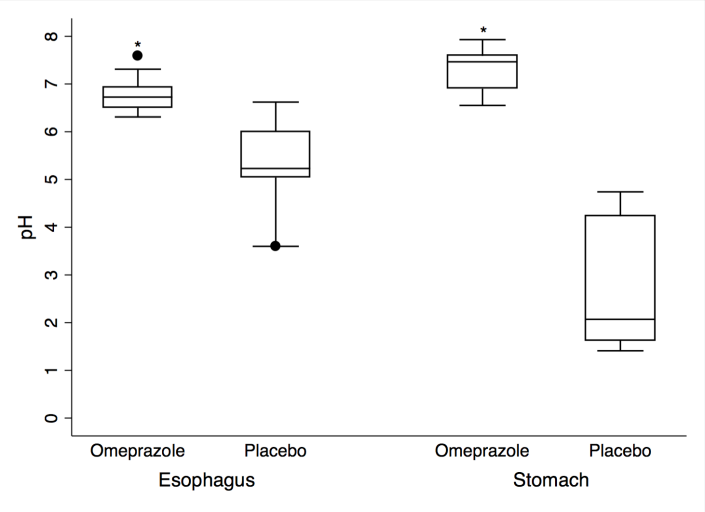
Effect of 2 Oral Doses of Omeprazole Administered Within 24hrs to Cats



Garcia R, et al. J Vet Intern Med 2017

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Acid Suppression for Renal Disease

- Hypergastrinemia, gastritis, and gastric ulceration are common complications of end-stage renal disease (ESRD) in humans
- Acid suppression is recommended for humans with ESRD and uremic gastritis
- Gastric mucosal erosion and ulceration are <u>not</u> complications of CKD in dogs and cats

McLeland SM, et al. JVIM 2014, Peters RM, et al. JVIM 2005

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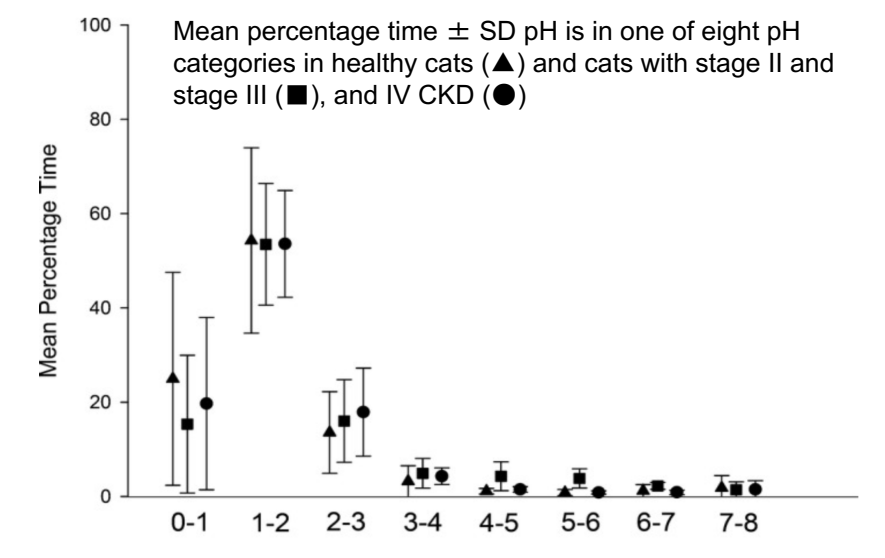
Gastric pH in Cats with CKD



Tolbert MK, et al. JVIM 2017

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Acid Suppression for Gastritis

- Benefits of gastric acid suppression not evaluated in canine or feline idiopathic gastritis to date
- Rationale for acid suppression extrapolated from human medicine
  - Cornerstone in the treatment of *Helicobacter pylori* gastritis
- *Helicobacter pylori* gastritis not present in dogs and cats

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Acid Suppression for Hepatic Disease

- Widely assumed that dogs with hepatic disease have gastric ulceration
- Prevalence of upper GI bleeding in dogs and cats with liver disease is unknown; published evidence is scarce[14,15]
- Acid suppression not considered effective in humans with portal hypertensive gastropathy[18]
- Acid suppression (omeprazole SID) decreased GI bleeding in dogs undergoing endovascular intrahepatic shunt attenuation[19]

[14]Murray et al. Vet Rec 1972; [15]Stanton, et al. 1989; [16]Silen, et al. Surgery 1963;
[17]Mazaki-Tovi, Vet Rec 2012; [18]Gjeorgjievski, et al. World J Hepatol 2016;
[19]Weisse, et al. JAVMA 2014

21

Acid Suppression for Pancreatitis

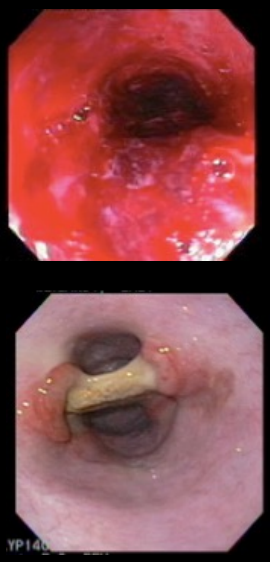
- Weak and conflicting evidence for gastric acid suppression in humans with acute pancreatitis[20,21]
- Pantoprazole ameliorated inflammation in rodent model of pancreatitis[22]
- Recent placebo-controlled pilot study in people with acute pancreatitis failed to show any benefit on clinical outcome with pantoprazole[23]

[20]Burdan, et al. J Physiol Pharmacol 2000; [21]Cai, et al. In Vitro Cell Dev Biol Anim 2007;
[22]Hackert, et al. Life Sci 2010; [23]Yoo, et al. Korean J Gastroenterol 2012

22

Oesophagitis

1. Secondary to anesthesia
   - Median 7.5 days post-anesthesia
   - Presumed GER
2. Pill-induced esophagitis
   - Doxycycline
   - Clindamycin
3. Vomiting gastric contents
4. Secondary to foreign body injury
5. Secondary to ingestion of caustic material



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Oesophagitis Secondary to GER in Dogs

- Incidence of GER in dogs during anesthaesia varies from 16-55%
- Reduction of LES pressure
  - Morphine, atropine, acepromazine, thiopentol, xylazine, isoflurane
  - Large-breed dogs (> 40kg; orthopedic surgery procedures)
- Transient lower esophageal sphincter relaxations (TLESRs)

- Wilson DV, et al. AJVR 67:2006
- Tak J. Curr Opin Gastroenterol 21:2005
- Lamata C, et al. Vet Anesth Analg 39;2012

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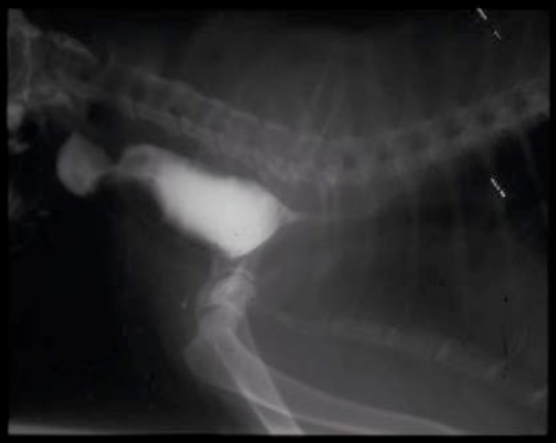
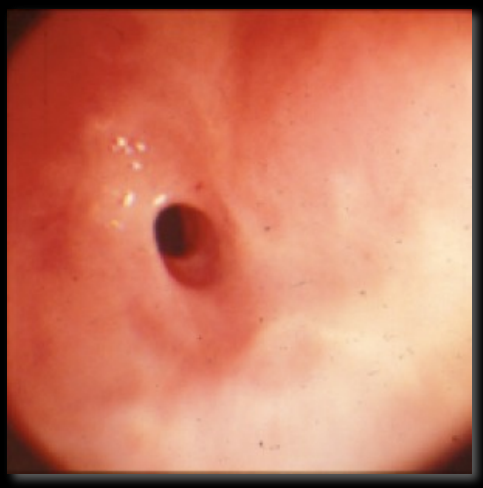
Benign Oesophageal Strictures





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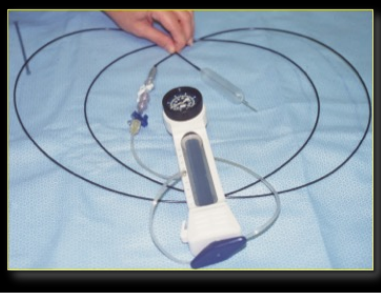
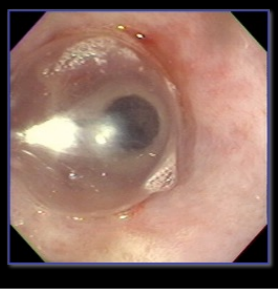
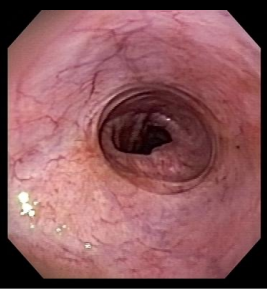
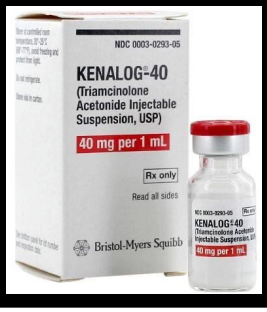
Oesophageal Balloon Dilation

- Success rate of 70-88%
  - Median of 2-4 dilation procedures
  - Triamcinolone injected in 4 quadrants or Mitomycin C









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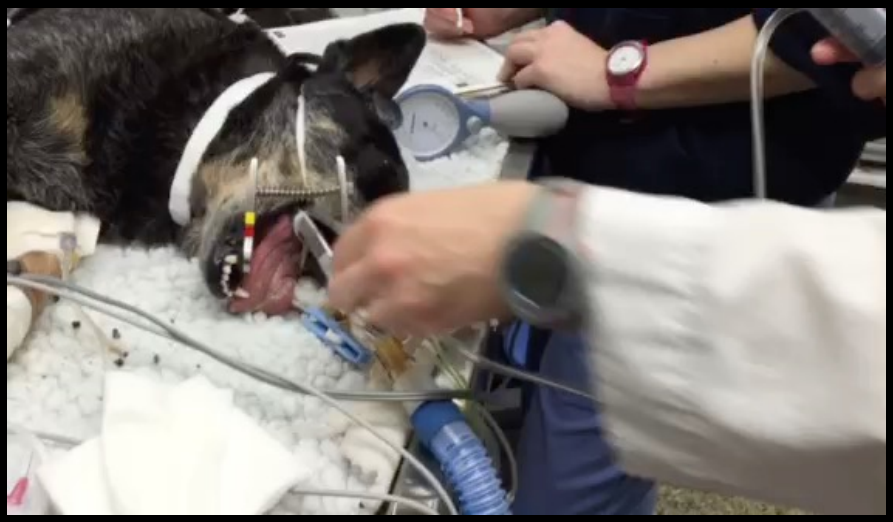
Can One Prevent Oesophagitis Intraoperatively?



- Suctioning fluid from esophagus using 12 Fr control valve suction catheter (Safe-T-Vac)

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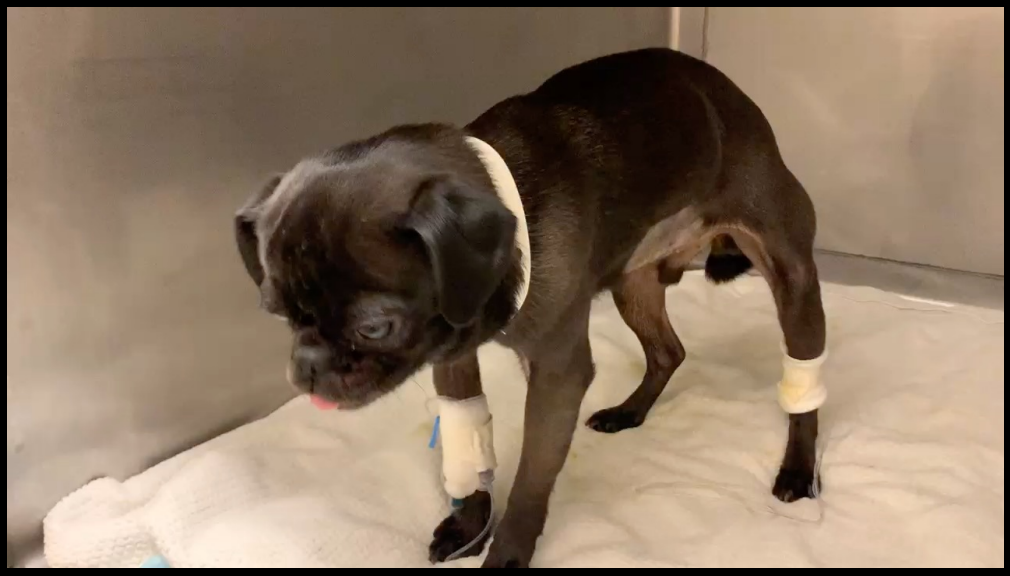
Recognition of Hard Swallowing is Important!



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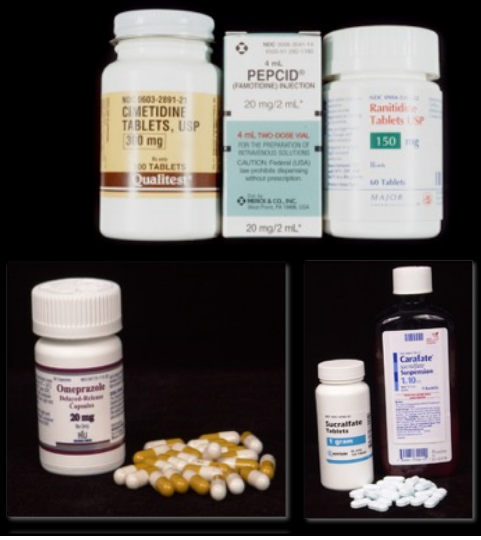
Management of Oesophagitis in Dogs

- **Gastric acid suppressants**
  - **Proton pump inhibitors**
  - H2-receptor antagonists
- +/- Sucralfate
- **Prokinetics**
  - Cisapride
  - Metoclopramide CRI
- **Dietary fat restriction**
- PEG tube?



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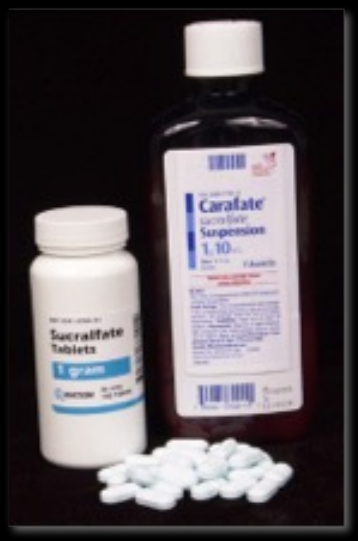
Management of Oesophagitis
Sucralfate

- Sulfated sucrose + polyaluminum hydroxide
  - Binds to proteins electrostatically
  - Stimulates PG production
  - Adsorption of bile salts
  - Inactivation of pepsins
- Adverse effects:
  - Constipation
  - Inhibit absorption of other drugs



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Management of Oesophagitis

Cisapride

- Increases LES sphincter tone (smooth muscle)
- Stimulates gastric emptying
- Stimulates distal oesophageal motility in cats, humans, guinea pigs

✓ Gastroesophageal reflux

✓ Oesophagitis

– Contraindicated in dogs with megaoesophagus!

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Summary

1. PPIs are superior to H2RAs for the treatment of acid-related disorders
   - Gastroduodenal ulceration/erosion and Reflux Esophagitis
2. PPIs are more effective when dosed q12h
3. Combination therapy with omeprazole and famotidine is not recommended
4. PPIs and misoprostol are effective at reducing NSAID-induced peptic ulcers
5. Taper PPIs and H2RAs over the course of 2-3 weeks
6. Prevent reflux during anesthesia and treat proactively and aggressively

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