Drugs Used to Treat Digestive Disorders in Pet animals

By
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I. Drugs Affecting Appetite (Monogastric)

- Disorders of appetite are very common in pet animals.
- Anorexia is a common clinical problem in sick animals.
- Obesity from overfeeding is common in companion animals

[Treatment of Anorexia]

- Appetite Stimulation
- A lack or Loss of appetite (anorexia), is often associated with many systemic diseases.
- A veterinarian suggest drug treatment to stimulate appetite for animals that cannot be coaxed to eat.
Table 1: Drugs Used to Stimulate Appetite

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Animals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stanozolol</td>
<td>Dog, cat, horse</td>
</tr>
<tr>
<td>✓ Boldenone undecylenate</td>
<td>Horse, dog, cat</td>
</tr>
<tr>
<td>✓ Cyproheptadine</td>
<td>Cats: 1–4 mg, PO, bid</td>
</tr>
<tr>
<td>✓ Prednisone / prednisolone</td>
<td>Dog, cat, horse 1 mg/kg, PO, every other day</td>
</tr>
<tr>
<td>Diazepam, Oxazepam</td>
<td>Cats: 0.005–0.4 mg/kg, IV</td>
</tr>
<tr>
<td>Megestrol acetate</td>
<td>Cats: 2 mg, PO, bid</td>
</tr>
<tr>
<td></td>
<td>Dog, cat,</td>
</tr>
</tbody>
</table>
1. **Anabolic steroids:**

- Synthetic derivatives of testosterone have enhanced anabolic effects with reduced androgenic effects.
- Anabolic steroids do not directly affect hunger, or satiety.
- Instead, they antagonize catabolic effect of glucocorticoids, illness, trauma, and aging.
- Stimulate hematopoiesis, appetite, weight gain.
- **Adverse effects:** hepatotoxicity, masculinization, and early closure of bony epiphyses in young animals.
- Contraindicated in animals with congestive heart failure because of sodium & water retention.
- **Use of anabolic steroids in performance horses is prohibited**
- **Stanozolol** *(winstrol(R))*: anabolic steroid synthetic derivatives of testosterone improve appetite; promote weight gain and increase strength, vitality in dogs & cats.
• **Boldenone undecylenate (Equipoise®):**
  - An anabolic, moderately androgenic steroid.
  - Increase protein synthesis in muscle cells & give slower but much higher quality gains in muscle.
  - Also well known to cause a dramatic increase in appetite.

2. **Cyproheptadine (Periactin®):**
   - Antihistamine (H₁-blocker) with serotonin-antagonist action used clinically in cats as an appetite stimulant.
   - promote the appetite by inhibiting serotoninergic receptors.
   - It acts as a 5-HT2 receptor antagonist
   - The hypothalamus normally excrete endogenous opiates which stimulate eating.
   - The release of opiate inhibited by serotonin →inhibit eating.
   - Cats very sensitive to changes in serotonin conc. so serotonin antagonists are very potent in cats.
3. **Glucocorticoids:**
- Increase gluconeogenesis & antagonize insulin for hyperglycemic
- Appetite is stimulated by the steroid-induced euphoria.
- Continued use of gluco.has catabolic effects because skeletal ms & collagen proteins are broken down to provide the precursors for gluconeogenesis.

4. **Benzodiazepines (diazepam & oxazepam):**
- When used as anxiolytics, benzodiazepines (BZD) became well known for their appetite stimulation effects independent of their anxiolytic activity.
- Binding of a BZD to GABA A receptors produces a strong dose-dependent increase in food consumption.
- Effective appetite stimulant in cats induced by increased release of aminobutyric acid (GABA) & by central inhibition of the satiety center in hypothalamus.
- **Diazepam** is the more effective appetite stimulant when administer IV to cats, but also cause a greater sedative effect than oxazepam.
- **Oxazepam**, a metabolite of diazepam, can be given orally to cats.
5. **Megestrol acetate:**
- A synthetic progestin, has significant antiestrogen and glucocorticoid activity, with resulting adrenal suppression.
- Used to stimulate appetite & promote weight gain in people with cancer and have a similar effect in anorectic cats and dogs.
- In cats, megestrol acetate can induce a profound adrenocortical suppression, adrenal atrophy, and diabetes mellitus.
- Toxicity is less of a problem in dogs.
- Megestrol is contraindicated in pregnant animals & in animals with uterine disease, diabetes mellitus, or mammary neoplasia.

6. **Mirtazapine:**
- Antidepressant used to treat depression in people.
- **MOA:** antagonist of presynaptic $\alpha_2$-adrenergic receptors, plus is a potent antagonist of postsynaptic 5-HT2 receptors.
- Clinically, it is effective appetite stimulant & antiemetic for cats with chronic kidney disease. Typically given once a day to dogs and twice a week to cats.
[Treatment of Obesity]

Appetite Suppression

- **Dirlotapide**: A microsomal triglyceride transfer protein (MTP) inhibitor.
- Developed specifically for weight loss in dogs.
- After oral admin., dirlotapide has in vivo selectivity for intestinal MTP.
- **Mechanism of weight loss**: Dirlotapide reduces fat absorption and sends a satiety signal from lipid-filled enterocytes.
- Dirlotapide also decreases appetite in a dose-dependent manner.
- The decrease in food intake is responsible for most of the weight reduction effect.
- Absorbed dirlotapide metabolized in liver & secreted in the bile.
- Effectiveness of dirlotapide has linked to drug concs. in the gut.
- Initial dosage of 0.5 mg/kg is doubled after 14 days.
- Dosages as high as 10 mg/kg administered to dogs without severe adverse effects in safety studies.
II. Drugs that Control or Stimulate Vomiting

Emetic drugs [Treatment of oral poison, toxin]

- Used to cause vomiting & given in emergency after a pet has eaten a poison.
- They generally remove about 80% of the stomach contents.

- Table 2: Emetic Drugs that cause vomiting in dog & cat:

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Animals</th>
</tr>
</thead>
<tbody>
<tr>
<td>✓ Salts (sodium chloride 5%)</td>
<td>Dog, cat</td>
</tr>
<tr>
<td>Apomorphine</td>
<td>Dogs: PO, or SC</td>
</tr>
<tr>
<td>Xylazine</td>
<td>Cats: 0.4–0.5 mg/kg, IV or IM</td>
</tr>
<tr>
<td>Hydrogen peroxide</td>
<td>Dogs: 5–10 mL, PO</td>
</tr>
<tr>
<td>Syrup of Ipecac</td>
<td>Dog, cat</td>
</tr>
</tbody>
</table>
- **Sodium chloride** (salt)
  - Act locally by irritating gastric mucosa & reflex stimulate vomiting cent
  - Sodium chloride either used as solid placed on the back of tongue, or as a sol. 5% (1-2 tea spoonfuls in a half cup of water) cause vomiting within 15 mins.

- **Apo morphine** :
  - An opioid alkaloid drug derived from morphine, act as a potent central dopamine agonist to directly stimulate the CRTZ.
  - It is less effective in cats than in dogs.
  - It can administer PO, IV, or SC; the IM route is not as effective.
  - It can also applied directly to conjunctival membrane, using the tablet formulation, which easily removed once emesis is initiated.
  - Vomiting usually occurs in 5–10 min. Although apomorphine directly stimulates CRTZ, it has a depressant effect on emetic C.
  - Therefore, if the first dose does not induce emesis, additional doses are not helpful.
  - Excitement result in cats treated with opioid antagonist **Naloxone**.
Xylazine (Rompun®):

- α₂-adrenergic agonist used primarily for its sedative, analgesic action.
- It is a reliable emetic, particularly in cats, it stimulate the CRTZ.
- Xylazine produce profound sedation & hypotension.

Hydrogen peroxide (3%)

- Applied to the back of pharynx → stimulate vomiting via 9th cranial nerve.
- Small doses (5–10 mL) of hydrogen peroxide can be administered via oral syringe until emesis occurs.
- It should administer cautiously, especially in cats, because aspiration of H. Peroxide foam causes severe aspiration pneumonia.
- When small amounts are administered, 3% hydrogen peroxide is relatively nontoxic. Stronger concs. are more toxic.

Syrup of Ipecac:

- The active ingredient is emetine, a toxic alkaloid, produce vomiting by acting as a stomach irritant.
- Act locally by irritating gastric mucosa & centrally by stimulating CTZ.

Used to induce vomiting in dogs & cats after ingestions of toxic compound.
Antiemetic drugs [Treatment of vomiting]

- Nausea & vomiting, as defense systems of GI tract, Cats are well known for their tendency to vomit, particularly to dislodge hairballs from the throat or upper GI tract.
- Chronic vomiting in cats indicate underlying thyroid, liver, or kidney dysfunctions.
- Dogs also vomit (frequently after eating grass).
- Protracted Continual vomiting is physically exhausting cause dehydration, acid-base and electrolyte disturbances, and aspiration pneumonia.
- Antiemetic drugs used to stop vomiting.
- Antiemetic drugs are used to control excessive vomiting once an etiologic diagnosis made, to prevent motion sickness and psychogenic vomiting, and to control emesis from radiation & chemotherapy.
# Antiemetic drugs in dogs and cats

<table>
<thead>
<tr>
<th>Drug</th>
<th>Route(s)</th>
<th>Dose(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acepromazine</td>
<td>IV, IM, SC</td>
<td>1–3 mg/kg, PO</td>
</tr>
<tr>
<td>Chlorpromazine</td>
<td>IV, IM, SC</td>
<td>tid-qid</td>
</tr>
<tr>
<td>Prochlorperazine</td>
<td>IM, tid-qid; 1 mg/kg, PO, bid</td>
<td></td>
</tr>
<tr>
<td>Aminopentamide</td>
<td>PO, SC, or IM</td>
<td>bid-tid</td>
</tr>
<tr>
<td>Diphenhydramine</td>
<td>2–4 mg/kg, PO</td>
<td>tid</td>
</tr>
<tr>
<td>Cyclizine, Meclizine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Butorphanol (Dog)</td>
<td>IM, once to twice daily</td>
<td></td>
</tr>
<tr>
<td>Metoclopramide</td>
<td>IM, SC, or PO</td>
<td>tid; or as IV infusion</td>
</tr>
</tbody>
</table>

Marked drugs are available for use in dogs.
Anti-emetics are classified into:

I. Central anti-emetics: drugs act by depression the vomiting center or by blocking the dopaminergic receptors in CTZ.

- a. Phenothiazine tranquilizers are $\alpha_2$-adrenergic antagonists & antagonize CNS stimulatory effects of dopamine & decrease vomiting from motion sickness in cats.
- Also have antihistaminic and weak anticholinergic action.
- Potential adverse effects include hypotension due to $\alpha$-adrenergic blockade, & excessive sedation.

- b. Anticholinergic drugs block cholinergic afferent pathways from GI tract & vestibular system to vomiting center.
- Aminopentamide is approved for use in dogs & cats as an injectable formulation and oral tablets.
- **Aminopentamide** is more efficacious in treatment of motion sickness in cats than in dogs, because muscarinic M1 receptors are found in the vestibular apparatus of cats.
- Aminopentamide has low efficacy for other causes of vomiting.
- **Isopropamide** have some anti-emetic effect, and used in dogs to control motion sickness.
- **Isopropamide** is a long-acting anticholinergic drug, used in the treatment of peptic ulcers & other GI disorders involving hyperacidity (GI acidosis) and hypermotility.

- c. **Antihistamines**: as diphenhydramine, cyclizine, meclizine
- used for treatment and prevention of motion sickness & as antiemetic in small animals. diphenhydramine cause sedation
- Block both cholinergic & histaminic N. transmission responsible for transmission of vestibular stimulus to vomiting center of dog
d. Metoclopramide

- The most useful drug for both dogs and cats and is available for both oral and parenteral administrations.

- **MOA:** Metoclopramide exert antiemetic effects via 3 mechanisms.
  1. At low doses, it inhibit dopaminergic transmission in the CNS.
  2. At high doses, it inhibits serotonin receptors in the CRTZ.
  3. Peripherally, Met increase gastric & upper duodenal emptying.

- Metoclopramide is a useful antiemetic for dogs. Because CRTZ D2 dopamine receptors are important in mediating emesis in cats.

- Metoclopramide is less effective in cats than in dogs. used to control emesis induced by chemotherapy, nausea and vomiting associated with delayed gastric emptying, reflux gastritis, and viral enteritis.

- At high doses or with rapid IV administration, metoclo cause CNS excitement by dopamine antagonism (similar to phenothiazines).

- This is counteracted with antihistamine as diphenhydramine
e. **Butorphanol**

- Effective antiemetic for dogs receiving cisplatin chemotherapy.
- Butorphanol cause only mild sedation.
- Butorphanol exert its antiemetic effect directly on vomiting center.

f. **Serotonin antagonists**: as Ondansetron, & Dolasetron.

- Specific inhibitors of serotonin subtype 3 receptors in the CRTZ.
- The most effective antiemetics used in people undergoing radiation & chemotherapy, and also used in cats & dogs receiving chemotherapy.
- They are not effective for emesis caused by motion sickness.
Stomach ulcers are a common problem in small animals, in association with physiologic stress (endogenous cortisol), or as a side effect of drugs that can cause ulcers.

The common antacids neutralize stomach acid to form water and a neutral salt. Antacids frequently interfere with the GI absorption of drugs that are administered at the same time.

Because they are difficult to administer & require frequent dosing in dogs and cats. they are not as popular as newer therapies.

Antiulceratives include: histamine H$_2$-receptor antagonists, muscarinic receptor antagonists, and gastrin receptor antagonists, agonists (prostaglandin E analogues).

Dr. Nehal Afifi
# Antiulcerative Drugs

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antacids</strong></td>
<td><em>(dog &amp; cats)</em>: 2–10 mL, PO, every 2–4 hr</td>
</tr>
<tr>
<td><strong>Sucralfate</strong></td>
<td><strong>Cats:</strong> 250 mg, bid-tid</td>
</tr>
<tr>
<td></td>
<td><strong>Dogs:</strong> 500 mg to 1 g, tid-qid</td>
</tr>
<tr>
<td></td>
<td><strong>Foals:</strong> 1–2 g, qid</td>
</tr>
<tr>
<td><strong>Cimetidine</strong></td>
<td><strong>Dogs:</strong> 5–10 mg/kg, PO, qid</td>
</tr>
<tr>
<td><strong>Ranitidine</strong></td>
<td><strong>Horses:</strong> 4 mg/kg, IV, bid; 18 mg/kg, PO, bid</td>
</tr>
<tr>
<td><strong>Famotidine</strong></td>
<td><strong>Dogs:</strong> 0.5–1 mg/kg/day, PO</td>
</tr>
<tr>
<td></td>
<td><strong>Horses:</strong> 4 mg/kg/day, PO</td>
</tr>
<tr>
<td><strong>Omeprazole</strong></td>
<td><strong>Dogs:</strong> 2–5 mcg/kg, PO, tid-qid.</td>
</tr>
<tr>
<td><strong>Misoprostol</strong></td>
<td><strong>Dogs:</strong> 0.5–1 mg/kg/day, PO</td>
</tr>
</tbody>
</table>
Antacids

- The bases of aluminum, magnesium, or calcium (Aluminum hydroxide, Magnesium oxide or hydroxide, & Calcium carbonate).
- Antacids neutralize stomach acid to form water & a neutral salt.
- Antacids are not absorbed systemically.
- Antacids decrease pepsin activity, binding to bile acids in stomach & stimulating local prostaglandin (PGE₁) production.
- Antacids interfere with GI absorption of concurrently administered drugs (digoxin, tetracyclines, fluoroquinolones).
- Antacids are not as popular as newer therapies (difficult to administer in dog& cat and require frequent dosing).
**Sucralfate**

- Antiulcerative drug has a cytoprotective effect on GI mucosa.
- **MOA:** disassociates in acid pH of stomach to sucrose octasulfate + aluminum hydroxide.
- Sucrose octasulfate polymerizes to a viscous, sticky subs that create a protective effect by binding to ulcerated mucosa.
- In addition, sucralfate increases the mucosal synthesis of prostaglandins, which have a cytoprotective role.
- Sucralf is not absorbed, so cause virtually no adverse effects.
- Sucrel is frequently administered to horses and all small animals as an ulcer preventive.

**H₂-Receptor Antagonists**

- **Cimetidine, Ranitidine, Famotidine** are the commonly used H₂-receptor antagonists.
- Ranitidine is 3–13 times as potent as Cimetidine in inhibiting gastric acid secretion. Famotidine is 20–150 times as potent as cimetidine.
- Cimetidine strengthen the gastric mucosal defenses against ulceration and enhances cytoprotection.

- Cimetidine reduce metabolism of other drugs (warfarin, phenytoin, lidocaine, metronidazole, theophylline) by inhibiting hepatic microsomal enzyme systems.

- Ranitidine inhibit hepatic metabolism of some drugs only (10%)

- Famotidine have no effect on metabolism of other drugs.

- Cimetidine suppresses gastric acid secretion in dogs for 3–5 hr.

- Ranitidine has a longer elimination half-life, it suppresses acid for up to 8 hr and so it administered less frequently.

- Oral bioavailability in horses for these drugs is only 10%–30%, so large oral doses must be administered.
**Misoprostol**

- Misoprostol is a synthetic prostaglandin E₁ analogue.
- Used in dogs to reduce the risk of GI ulcers induced by chronic NSAID therapy.
- **MOA:** It suppresses gastric acid secretion by inhibiting the activation of histamine-sensitive adenylate cyclase. It has a cytoprotective effect from stimulation of bicarbonate and mucus secretion, increased mucosal blood flow, decreased vascular permeability, and increased cellular proliferation and migration.
- Misoprostol is clinically effective in preventing GI bleeding and ulceration from NSAID therapy.
- **Adverse effects:** mainly limited to diarrhea and flatulence. Magnesium-containing antacids may aggravate the diarrhea. Misoprostol is contraindicated in pregnant dogs, because it can induce abortion.
Proton Pump Inhibitors (PPI)

- The most widely used PPI is Omeprazole.
- In dogs and horses, a single dose of omeprazole inhibits acid secretion for 3–4 days.
- Proton pump inhibitors (PPIs) irreversibly block the H⁺/K⁺-ATPase proton pump of the gastric parietal cell.
- They are given in an inactive form, which is neutrally charged (lipophilic) and readily crosses cell membranes into intracellular compartments (like the parietal cell canaliculus) that have acidic Ph. The inactive drug changes into its active form, and irreversibly binds to and deactivates the proton pump.
- A specific equine product has developed, because oral bioavailability of human omeprazole formulation is poor in horses.
- Although ulcers in horses will heal while on omeprazole therapy, they tend to recur once therapy is discontinued.
- Human formulations are used in dogs and cats.
[Treatment of Diarrhea]

Drugs Used in Diarrhea

- Therapy for diarrhea includes fluids, electrolyte replacement, maintenance of acid/base balance, and control of discomfort. Additional therapy may include intestinal protectants, motility modifiers, antimicrobials, anti-inflammatory drugs, & antitoxins.

1. Mucosal Protectants & Adsorbents

- **Kaolin-pectin** are popular for symptomatic therapy of diarrhea.
- Kaolin is a form of aluminum silicate, and pectin is a carbohydrate extracted from the rind of citrus fruits.
- kaolin-pectin acts as a demulcent & adsorbent in treatment of diarrhea by the binding of bacterial toxins (endotoxins and enterotoxins) in the GI tract. Kaolin-pectin products adsorb or bind other drugs administered PO & reduce bioavailability.
### Antidiarrheal Drugs

<table>
<thead>
<tr>
<th>Drug</th>
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<tbody>
<tr>
<td>Kaolin-pectin</td>
</tr>
<tr>
<td>Activated charcoal</td>
</tr>
<tr>
<td>Bismuth subsalicylate</td>
</tr>
<tr>
<td>Aminopentamide</td>
</tr>
<tr>
<td>Isopropamide</td>
</tr>
<tr>
<td>Loperamide, Paregoric</td>
</tr>
<tr>
<td>Propantheline</td>
</tr>
</tbody>
</table>
**Activated charcoal**

- Activated charcoal is very effective for adsorbing bacterial enterotoxins and endotoxins that cause some types of diarrhea.
- It also adsorbs many drugs & toxins and prevents GI absorption, so it is a common nonspecific treatment for intoxications.
- Activated charcoal is not absorbed, so overdose is not a problem.
- **Bismuth subsalicylate** is considered to be the symptomatic treatment of choice for acute diarrhea.
- Its efficacy (enterotoxigenic *E. coli* or “traveller's diarrhea”).
- Bismuth adsorbs bacterial enterotoxins & endotoxins and has a GI protective effect.
- The salicylate component has antiprostaglandin activity. Practically all of the salicylate is absorbed systemically when administered to dogs and cats.
- **Salicylate toxicosis is possible, especially in cats**
- animals dislike the taste of bis s, and it will turn the feces black.
- This interfere with evaluating the feces for hemorrhage.
II. Motility-modifying Drugs

Anticholinergic drugs

- Anticholinergic drugs are common ingredients in antidiarrheal preparations, because they decrease intestinal motility & secretions.
- They relax spasms of smooth muscles & decrease the urgency associated with some forms of diarrhea in cats and dogs, the amount of fluid secreted into the intestine, and abdominal cramping associated with an overactive intestine.
- Use of anticholinergic drugs is limited in vet.med. because few types of diarrhea in animals classified as overactive.
- Atropine is the best known anticholinergic drug, but because it has many other systemic effects, not used for antidiarrheal effect.
- Quaternary amines as Aminopentamide, Isopropamide, Propantheline are preferred [not cross blood-brain barrier].
- Anticholinergics also have profound systemic pharmacologic effects. If administer in sufficient doses adverse effects include severe ileus, urine retention, tachycardia, and CNS excitement.
Hyoscine butylbromide is antispasmodic & anticholinergic drug that relaxes the smooth muscle of GI tract.

- approved for treatment of uncomplicated, spasmodic colic in horses [relief of pain within 5–10 minutes, with a duration of action of 3–4 hr].
- Hyoscine administered concurrently with NSAIDs and sedatives.

- Opiates have both antisecretory & antimotility effects by action on the µ (mu) and δ (delta) receptors of the GI tract.

- They are frequently used for treatment of diarrhea in dogs, but their use in cats is controversial [may cause excitement ]

- Paregoric is a tincture of opium product & a controlled substanc (5 mL of paregoric corresponds to ~2 mg of morphine).

- Diphenoxylate, loperamide are two synthetic opiates that have specific action on GI tract without causing other systemic effects.

- They have been used in small animals & large animal neonates.

- Diphenoxylate is a controlled substance in a formulation that contains atropine to discourage abuse; at therapeuti dose, No effect from atropin

- Opiates can have potent effects on GI tract & should be used cautiously.
III. Antimicrobial Therapy

- Non absorbed antimicrobials are frequently combined with motility modifiers, adsorbents, and intestinal protectants in some preparations.
- Antimicrobials frequently are a treatment for diarrhea in animals, but conditions that have a known etiology specific antimicrobial is indicated.
- *Campylobacter* enteritis, from infection with *Campylobacter jejuni*, is seen in cats and dogs and can be zoonotic.
- Suggested antimicrobial therapy includes erythromycin, enrofloxacin, clindamycin, tylosin, tetracycline, or chloramphenicol.
- Intestinal bacterial overgrowth is usually due to *E. coli* or *Clostridium* spp, so therapy is initiated with an oral drug effective in GI lumen with anaerobic activity (eg, metronidazole, amoxicillin, ampicillin, tylosin, or clindamycin).
- Equine monocytic ehrlichiosis (Horse Fever) is caused by rickettsial organism *Neorickettsia (Ehrlichia) risticii* but clinically resembles salmonellosis. Treatment of choice is IV oxytetracycline.
- Oral doxycycline can be used in mildly affected horses.
Enteritis from a variety of pathogens is common in young animals. When integrity of intestinal mucosa is lost, septicemia or endotoxemia occur. Severe bloody diarrhea, fever, scleral injection, dehydration, and alteration in leukogram (early leukopenia, followed by leukocytosis).

If septicemia is suspected, systemic antimicrobials are warranted along with NSAIDs.

Neonates with diarrhea deteriorate rapidly. Thus, broad-spectrum antimicrobial therapy should be initiated.

Suggested antimicrobials (depending on species) include:

- Fluoroquinolones,
- A penicillin or cephalosporin plus an aminoglycoside (gentamicin, amikacin),
- Ampicillin or Amoxicillin,
- Tetracyclines,
- Potentiated sulfonamides,
- Chloramphenicol, or florfenicol.

In septic animals, GI absorption is to be altered, so Parenteral administ. preferred
IV. Nonsteroidal Anti-inflammatory Drugs (NSAIDs)

- Nonsteroidal anti-inflammatory drugs reduce the amount of prostaglandin produced in the body.
- Prostaglandin is a hormone involved in the process of muscle contraction.
- Prostaglandins are important intracellular messengers for stimulating hypersecretion by the intestinal mucosa, possibly by stimulating an increase in cAMP.
- Antiprostaglandin drugs may directly inhibit fluid and electrolyte hypersecretion by the intestinal cells.
- The antiprostaglandin activity of NSAIDs may be beneficial with some types of diarrhea and may be important in treatment of septicemia or endotoxemia.
- However, NSAIDs should be given cautiously because they can cause adverse gastrointestinal, liver, and kidney effects.
• Fluid therapy:
  • To correct the acid base balance and dehydration.
  • Intravenous fluid therapy using saline solutions is only necessary in severely affected, comatose animals.
  • In most animals, oral fluid therapy is both effective and practical.
  • Glucose & amino acids continue to be actively absorbed from gut in the diarrheic animal & accompanied by the absorption of sodium and water. Thus, there is a net increase in absorption (oral rehydration).
  • A typical fluid therapy contain glucose, glycine, sodium, potassium and citrate or acetate.
  • Commercial formulations contain sodium chloride are available.
Cathartic and Laxative Drugs

- Cathartics increase the motility of the intestine.
- Administered to increase the passage of GI contents associated with intestinal impaction,
- To cleanse the bowel before radiography or endoscopy,
- To eliminate toxins from the GI tract,
- To soften feces after intestinal or anal surgery.
- Cathartics work by stimulating or irritating the nerves of intestinal lining, others draw fluid into intestines & increase the feces bulk.
- Laxatives & fecal softeners work by increasing the water content of feces or the amount of non-digestible material in intestines.
- **1. Bisacodyl:**
  - A direct irritant purgative increase peristalsis by direct stimulation of intestinal smooth muscle & increase fluid and ion accumulation.
<table>
<thead>
<tr>
<th>Drug</th>
<th>Animals &amp; Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Castor oil</strong></td>
<td>Dogs: 5–25 mL, PO Foals: 25–50 mL, PO</td>
</tr>
<tr>
<td><strong>Bisacodyl</strong></td>
<td>Dogs: 5–20 mg, PO, once to twice daily Cats: 2.5–5 mg, PO, once to twice daily</td>
</tr>
<tr>
<td><strong>Lactulose</strong></td>
<td>Dogs: 5–15 mL, PO, tid Cats: 2–3 mL, PO, tid</td>
</tr>
<tr>
<td><strong>Magnesium sulfate</strong></td>
<td>Dogs: 5–25 g, PO Cats: 2–5 g, PO Horses: 30–100 g, PO</td>
</tr>
<tr>
<td><strong>Linseed oil</strong></td>
<td>Horse</td>
</tr>
<tr>
<td><strong>Docusate sodium</strong></td>
<td>Dogs and cats: 2 mg/kg/day, PO Horses: 10–20 mg/kg in 2 L water</td>
</tr>
<tr>
<td><strong>Magnesium hydroxide</strong></td>
<td></td>
</tr>
<tr>
<td>(milk of magnesia)</td>
<td></td>
</tr>
</tbody>
</table>
• **Caster oil:**
• It hydrolyzed in intestine by bile into *resinolic acid* and *glycerol.*
• Resinolic acid will combine with sodium of bile forming sodium resinolate which exerts a mild irritant effect.
• The effect is seen within 4-8 hours.
• A part of caster oil acts as a lubricant before hydrolysis.
• Castor oil is most suitable for dogs and cats and is better given in the form of emulsion.

• **Docusate sodium & docusate calcium (colace®) salts:**
• They are fecal softeners that decrease surface tension and allow water and fat to penetrate the formed feces, thus softening the stool of the small animals.

• **Lactulose:**
• A simple bulk disaccharide *(galactose/fructose)* hyper osmotic *cath*
• Not hydrolyzed by gut enzymes but metabolized in the colon.
• Increase osmotic pressure causing a laxative effect & used in cats.
- **Magnesium sulphate** (Epsom salts): 
  - A Saline bulk hypertonic solution.
  - **MOA:** The purgative effect is due to their ability to raise the osmotic pressure in intestine as they are highly ionized & slowly absorbed so withdraw water from tissues into intestinal lumen. This increases the bulkiness of intestinal content which reflexly stimulate intestinal motility.
  - Saline purgative should not be used in dehydrated animals.
  - They are most suitable for ruminants.
  - In dogs and cats, they cause gastric irritation and vomiting.
  - Purgation occurs after 3-12 hours in simple-stomached animals.

- **Magnesium hydroxide** (milk of magnesia): 
  - Reduce stomach acid, and increases water in the intestines to induce defecation.
  - Magnesium hydroxide is used as a laxative to relieve occasional constipation (irregularity) and as an antacid to relieve indigestion, and sour stomach.
Treatment of Chronic Colitis (Monogastric)

- The specific cause of chronic colitis in animals is unknown; therefore, it is difficult to prescribe a specific treatment.
- Colitis is often classified as plasmacytic/lymphocytic, eosinophilic, or granulomatous.
- The goal of colitis therapy is to restore normal intestinal motility and to relieve inflammation, spasm, or ulceration.
- **Sulfasalazine**
  - Composed of sulfapyridine & 5-aminosalicylic acid (mesalamine) joined by an azo bond.
  - The bond is broken by bacteria in colon to release the two drugs.
  - Sulfonamide component is absorbed into the circulation,
  - Salicylic acid component is active locally in the GI tract.
  - Clinical efficacy due to the anti-inflammatory effect of salicylate comp.
## Drugs Used in Treatment of Chronic Colitis

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sulfasalazine</td>
<td>10–30 mg/kg, PO, bid-tid</td>
</tr>
<tr>
<td>Tylosin</td>
<td>40–80 mg/kg/day</td>
</tr>
<tr>
<td>Metronidazole</td>
<td>10–30 mg/kg, PO, once to three times daily</td>
</tr>
<tr>
<td>Prednisone</td>
<td>2–4 mg/kg, PO, every other day</td>
</tr>
<tr>
<td>Budesonide</td>
<td>3 mg/m²/day, PO</td>
</tr>
<tr>
<td>Raw linseed oil</td>
<td>1 oz/day in the feed</td>
</tr>
<tr>
<td>Azathioprine</td>
<td>50 mg/m², PO, daily for 2 wk</td>
</tr>
</tbody>
</table>
- **Sulfasalazine** is commonly used in small animals in therapy of ulcerative or idiopathic colitis or plasmacytic-lymphocytic colitis once dietary causes have been excluded.
- Sulfonamide component cause **keratoconjunctivitis sicca in dogs**,
- Salicylate component may cause toxicity in cats.
- Dosage recommendations for sulfasalazine vary widely, & the dosage is gradually reduced after an initial response.
- New products have developed to overcome the difficulty of the 5-aminosalicylic acid reaching the colon and systemic adverse effects.
- **Mesalamine** is a pH-sensitive, coated 5-aminosalicylic acid.
- The polymer coating prevent release of active drug until it reach the colon.
- Mesalamine is also available as an enema. Rectal administration allows delivery of active drug to the colon.
- Useful in dogs with chemotherapy-induced hemorrhagic colitis
- It also be useful in dogs with perianal fistulas.
- **Olsalazine** consists of two molecules of 5-aminosalicylic acid joined together by an azo bond.
- **Tylosin**
  - A Macrolide antimicrobial used successfully in animals with colitis.
  - It is commonly administered on a chronic basis as an alternative to sulfasalazine therapy.
  - **MOA:** is unknown, but it is suspected that its activity against mycoplasmas, spirochetes, and Chlamydia is important.

- **Metronidazole**
  - has fair efficacy against *Giardia*, and it is also efficacious in some cases of diarrhea in which giardiasis was not definitively diagnosed.
  - It is suspected that this efficacy is related to the activity of metronidazole against anaerobic bacteria.
  - Metronidazole also has an immunosuppressive effect on the GI mucosa by decreasing the cell-mediated response.
  - Adverse neurologic effects have been reported in dogs and cats treated with metronidazole.
  - Diazepam appears effective for treatment of neurotoxicity.
• **Glucocorticoids**
  
  Efficacy of glucocorticoids for treating colitis is related to their **anti-inflammatory and immunosuppressive capabilities**.

  Some cases of colitis due to **auto antibodies & T lymphocytes** directed against colonic epithelial cells. So glucocorticoids suppress immune reaction and are used in eosinophilic or plasmacytic-lymphocytic colitis.

  Glucocorticoid used in dogs, cats, and horses, when all other forms of therapy have failed.

  Immunosuppressive doses of oral **prednisone or dexamethasone** are administered & slowly tapered to every-other-day therapy with the lowest effective dose.

  **Budesonide** is a glucocorticoid used in people to treat inflammatory bowel disease & appears clinically effective in some dogs.

  Budesonide has a high affinity for glucocorticoid receptors, high hepatic clearance, and high local and low systemic activity compared with prednisone or dexamethasone.

  Human formulation of budesonide consist of coated granules with a matrix of ethyl cellulose to target release into lumen of ileum or ascending colon.
• **N-3 fatty acids** (Raw linseed oil)
  • fatty acids suggested for therapy in people with ulcerative colitis
  • Addition of n-3 fatty acids to diet make fewer n-6 fatty acids available for the arachidonic acid cascade.
  • Several formulations are available for small animals,
  • Raw linseed oil added to horses' grain for this effect.
• **Immunosuppressive** drugs as *Azathioprine*
  • Azathioprine metabolized to 6-mercaptopurine, which is **immunosuppressive** by interfering with nucleic acid synthesis and by impairing lymphocyte proliferation.
  • It take several weeks or months of therapy to become effective.
  • Cats particularly should be monitored for adverse effects, including myelosuppression, hepatic, acute pancreatic diseases
• **Chlorambucil** used in place of azathioprine in difficult or refractory cases of feline inflammatory bowel disease.
  • It is too expensive to use in all but very small dogs.
Gastrointestinal Prokinetic Drugs

- Prokinetic drugs increase movements of food through GI tract.
- They are useful in treatment of motility disorders because they help coordinate motility patterns.

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Animals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metoclopramide</td>
<td>Dogs &amp; cats: PO or SC, tid or as IV infusion. Horses: given diluted administered IV over 60 min</td>
</tr>
<tr>
<td>Cisapride</td>
<td>Dogs: 0.1 mg/kg, PO, tid Cats: 2.5 mg/cat, tid for cats &lt;5 kg</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>Dog, 0.5–1 mg/kg, PO, bid-tid</td>
</tr>
<tr>
<td>clarithromycin</td>
<td></td>
</tr>
<tr>
<td>Domperidone</td>
<td>Dog, horse: 0.1–0.5 mg/kg, IM; 0.5–1 mg/kg, PO</td>
</tr>
</tbody>
</table>

Dr. Nehal Afifi
- **Metoclopramide**
  - A central dopaminergic antagonist & peripheral 5-HT3 receptor antagonist with GI and CNS effects.
  - Metoclopramide increases both acetylcholine release from neurons & cholinergic receptor sensitivity to Ach in the upper GI tract.
  - Stimulate & coordinate esophageal, gastric, pyloric, & duodenal motor activity.
  - Metoclopramide speed gastric emptying of liquids.
  - Effective in treating postoperative ileus in dogs (decrease GI activity & motility).
  - Metoclopramide has little or no effect on colonic motility.
  - Primarily indicated for relief of vomiting associated with chemotherapy in dogs, as an antiemetic for dogs with parvoviral enteritis.
  - Metoclopramide Crosse BL-brain barrier, where dopamine antagonism at CRTZ

- **Cisapride**
  - Chemically related to metoclopramide, but unlike m, not cross BL-brain barrier or have antidopaminergic effects. Therefore, not have antiemetic effect or cause extrapyramidal effects (extreme CNS stimulation).
  - Cisapride is more potent & has broader prokinetic activity than metoclo, increasing motility of colon, esophagus, stomach, and small intestine.
• **Cisapride** is useful in animals with neurologic effects from metoclopramide.
• Very useful in managing **gastric stasis, idiopathic constipation,** & **postoperative ileus in dogs and cats.**
• Cisapride especially useful in managing **chronic constipation in cats with megacolon**; it alleviates or delays the need for subtotal colectomy.
• Cisapride also useful in managing **cats with hairball problems** & in **dogs with idiopathic megaesophagus** that continue to regurgitate frequently.
• **Cisapride** is clearly **superior to other treatments**, nn comparative studies of GI motility in people & animals.

• **Domperidone**
  
  A peripheral dopamine receptor antagonist, regulate the motility of gastric & small-intestinal smooth muscle and has some effect on esophageal motility.
  
  It has antiemetic activity from dopaminergic blockade in the CRTZ. But extrapyramidal reactions are rare.
  
  Because of its favorable safety profile, **domperidone appears to be an attractive alternative to metoclopramide**.

• **Macrolide antibiotics** [**erythromycin** & **clarithromycin**], are motilin receptor agonists. Stimulate cholinergic Rs. to stimulate motility. Erythromycin suspension increases gastric emptying rate in healthy dogs,
Drugs Affecting Digestive Functions

- **Pancrealipase**
  - It contains the pancreatic enzymes lipase, amylase, and protease.
  - It is derived from the pancreatic tissues of swine.
  - These enzymes help digest and absorb fats, proteins, and carbohydrates.
  - Pancrealipase is used to treat dogs and cats with exocrine pancreatic insufficiency.
  - Several formulations are available, including oral capsules, tablets, and delayed-release capsules and tablets.
  - Powdered forms added to food, and the dosage adjusted to maintain normal feces.
  - **Antacids** diminish the efficacy of pancrealipase,
  - **H₂-receptor antagonists** increase the amount of pancrealipase that reaches the duodenum.
- **Ursodiol**, (ursodeoxycholic acid)
- It is a naturally occurring bile acid.
- It suppresses hepatic synthesis & secretion of cholesterol and decreases intestinal absorption of cholesterol.
- Reducing cholesterol saturation allows solubilization of cholesterol-containing gallstones.
- Ursodiol also increase bile flow and reduces the hepatotoxic effect of bile salts by decreasing their detergent action.
- In small animals, ursodiol is useful in treatment of cholesterol-containing gallstones, idiopathic hepatic lipidosis, & chronic active hepatitis.
- The dosage in dogs and cats is 15 mg/kg/day, PO.
- **Milk thistle** (*Silymarin*)
- It is used as a natural remedy for diseases of liver and biliary tract.
- *Silymarin* is the active extract & contain flavonignans that act as antioxidants, scavenging free radicals and inhibiting lipid peroxidation.
- Milk thistle used in human patients with acute or chronic liver disease.
- A veterinary formulation has approved for dogs & cats. in USA