



PET TALK

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American College of Veterinary Pharmacists

CONSTIPATION: THE MOVING TRUTH ABOUT A TOUGH TOPIC IN PETS!

Why discuss constipation?

The reason we are discussing constipation in this Pet Talk newsletter is because it is an issue many owners aren't aware of in their pets. Occasional irregularity in both humans and animals does happen. However, when it happens often or for extended periods of time, this is very worrisome as it affects your pets overall health and quality of life.

How prevalent is this condition?

Chronic constipation is a highly debilitating condition that not only affects human patients but our four legged friends as well! Though this condition is equally widespread amongst the numerous veterinary species, there are a few specific groups who are more at risk. For example, prevalence of constipation is higher in the following dog breeds: English Bulldogs, Boston Terriers, and German Shepherds. Cats who are most affected include Siamese, Domestic Shorthair, and Manx as well as those cats who are middle-aged and male. Horses, rabbits, guinea pigs, and chinchillas may also experience various forms of constipation due to their unique digestive systems.



What causes constipation?

As with most diseases in the veterinary world, the exact cause or causes of constipation are varied depending on the species being discussed, where in their gastrointestinal tract the problem is occurring, and any accompanying conditions they may also have that are contributing to constipation.

Dogs: In man's best friend, constipation has many origins. A dog's digestive tract is complex and various factors can impede this multifaceted process. Such examples include ingesting foreign objects (i.e., socks, garden hoses, shoes), anal sac inflammation, long term opioid use (i.e., tramadol), chemotherapeutic medications (i.e., vincristine), obesity, old age, immobility, and dehydration. However, other more severe underlying physiologic etiologies such as neuromuscular disease, diabetic gastroparesis, or a neoplastic gastrointestinal obstruction may also be attributable to your dog's gastrointestinal stasis.

Cats: Cats can also develop constipation from several causes as their process of defecation is fairly similar to that observed in dogs. It can be due to a hairball impaction, dehydration, obesity, old age, diabetes, immobility, pain from trauma to the low back, bladder infection, or an anal sac infection. In cases that are more chronic, underlying disease such as colitis or Irritable Bowel Syndrome (IBS) may be the culprit. On the other hand, the cause may be idiopathic which is frustrating since this form is most difficult to treat.

Horses: Despite their large size,

horses have incredibly delicate digestive systems.

During times of illness or stress horses may stop eating, drinking, and can develop colic which even in the mildest form, results in pain and abnormal motility. Colic has many origins but the forms most likely to cause constipation are impaction colics due to fecal material, parasites, or sand. Other causes for gut immobility include impaction from food, poor food quality, an inability to access free forage, dehydration, severe hind limb pain or injury, or long term use of anticholinergic medications such as atropine.



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Rabbits: Rabbits have digestive systems that resemble horses, rather than dogs or cats. Perhaps it is for this reason that they too are very prone to GI stasis. A diet low in fiber ultimately increases their gastric pH which destroys natural helpful bacteria that live there.

A diet high in carbohydrates and an excessive amount of protein can also cause a disruption of this healthy gut bacteria or microflora. Obesity, inactivity, spinal trauma, hairballs, dehydration, excess fruit or nuts in their diet, in combination with all of the aforementioned reasons, will surely result in a final outcome of poor gastric motility

Rodents: Guinea pigs and chinchillas have a high metabolic rate, a monogastric stomach, and an impressive cecum that takes up approximately ½ of their body cavity. In the cecum, much like in horses and rabbits, there is fermentation by key microflora. If their diets aren't maintained appropriately with high fiber and low carbohydrates (similar to rabbit), a disruption of their natural bacteria occurs resulting in GI distress. Other reasons for constipation include dehydration, old age, spinal pain, obesity, excess fatty diet, a lack of exercise, and dental disease than can severely impair eating and drinking.

How will I know if my pet is constipated?

The classical clinical sign of constipation is straining to defecate without production of feces, droppings, or manure. Affected animals can be of either sex, although in cats there is a male predilection, and of any age though often younger or older animals are most affected. Besides straining, there may also be signs of general discomfort, irritability, a decrease in appetite, and a frequent need to want to defecate with posturing and lifted tail. Variations of these physical demonstrations will be species specific. These problems, if not resolved, can become life threatening.

Chronic constipation causes severe pain, toxin accumulation, damage to intestinal tissue, and if not medically managed aggressively, may lead to surgery.



What are signs of constipation?

1. Increased straining
2. Failure to defecate
3. Fecal matter, if passed, is reduced in quantity and is usually dry and hard
4. Presence of blood in stool
5. Feces that are particularly foul smelling
6. May continuously get in and out of litter box without passing fecal material
7. Circling or pacing the stall with intermittent straining
8. Decreased activity and lethargy likely due to pain
9. Painful and/or bloated abdomen
10. Decreased interest in food
11. Irritability

If you notice any of these changes in your pet, please contact your veterinarian as soon as possible



What will my vet do for my pet's constipation?

When you bring your animal in for an appointment, your vet will likely take a complete history of your pet which includes what has been going on and for how long. You want to be as detailed with them as possible so they can give you the best diagnosis and treatment. It is very important to discuss with your veterinarian any changes in your pet's diet or daily bathroom habits. Then

they will likely perform a thorough physical exam to include rectal and abdominal palpation to feel for any problems inside and an oral exam to make sure dental issues aren't interfering with food or water intake. They may also have you take your pet outside on a leash or harness in a grassy area to carefully observe your pet's behavior. With your consent, blood tests will be run in order to identify and/or rule out other disease processes such as diabetes or an underlying infection. X-rays and ultrasounds allow both you and the practitioner, to see what's going on inside without actually being physically invasive.

How is constipation treated?

There are several options available for veterinarians to treat constipation in your pet. Most of these treatments are focused on the underlying disease such as giving fluids for dehydration or surgically removing an obstruction. Along with plenty of water, increasing the amount of fiber in your animal's diet and decreasing the amount of carbohydrates is very important to their GI health. The choice of medication therapy will be determined by your veterinarian based on the species of your pet and the exact type of gastric distress they are experiencing. Pain control will also be considered as chronic constipation is painful and it is hard for your patient to relax their abdomen to encourage normal bowel movements if they are tense with pain. Surgical therapy, if warranted, can be helpful (i.e. impacted hairball) but has significant risks, is costly, and often times the underlying cause must still be identified and corrected.

Mineral Oil

This substance is a lubricant laxative to help ease the passage of fecal matter and increase the water content of stool. For short term use this is an appropriate option but for chronic constipation, as soon as laxative use ceases, constipation often returns. Side effects are oily feces and abdominal cramping. Even though this product is available over-the-counter NEVER give this to your pet due to the deadly risk of lung aspiration! Please only let your vet administer this product.

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Lactulose

This is a disaccharide sugar containing both fructose and galactose. It creates a laxative effect by osmosis in the colon as it is a non-absorbed sugar that retains water in the intestine after oral administration. Side effects from excessive use may cause fluid and electrolyte loss. Use with caution in diabetic animals since it carries a risk for increasing their blood sugar levels. In rabbits and rodents this medication isn't recommended as the side effect of severe diarrhea can be detrimental to their overall health.

Gallimycin (erythromycin)

This macrolide antibiotic can be given to "restart" the stomach during acute episodes of gastric stasis in which oral intake is not tolerated. Erythromycin induces gastric contractions via stimulation of motilin receptors which increase smooth muscle activity to help unload solid and non-digestible materials out of the stomach. Side effects include diarrhea (especially in horses), hyperthermia in foals, and vomiting. This medication may NOT be given orally to rabbits, guinea pigs, or other rodents.

Zithromax (azithromycin)

This is another macrolide antibiotic that has been used as an alternative to the aforementioned erythromycin. This medication doesn't appear to have the drug-drug interactions seen with erythromycin and is also associated with less side effects. However, there are limited studies for its use in the treatment of delayed gastric emptying. There is also concern for its higher cost and using it for gastric emptying instead of for antimicrobial treatment of an actual infection that may eventually create the potential for antibiotic resistance. Side effects include vomiting and diarrhea though it is better tolerated than erythromycin.

Zantac (ranitidine) & Axid(nizatidine)

Both of these medications are histamine receptor antagonists aka "H2 blockers." However, they are unique from others in their class in that they have the ability to improve gastrointestinal stasis via their prokinetic proper-

ties that improve gastric emptying. Side effects are generally mild and noted at higher doses, but may include dizziness, nausea, diarrhea, and muscle pain.

Propulsid (cisapride)

This medication is a non-selective benzamide 5-HT4 receptor agonist and a 5-HT3 receptor antagonist. This drug is recognized for its ability to promote gastrointestinal motility. It is most often associated with its success in cats with IBS. However, due to an association with cardiac arrhythmias and death in humans, it is currently not on the market and the only makers in India have recently moved to cease production. Side effects in veterinary patients appear minimal but may include vomiting, diarrhea, and abdominal discomfort.

Gastride (mosapride)

Mosapride citrate is a selective benzamide peristaltic stimulating agent that works as a selective 5-HT4 receptor agonist to create prokinetic gastrointestinal movements to alleviate GI symptoms associated with gastritis. Unlike cisapride that works throughout the entire gut, mosapride only works on the stomach and small intestines (i.e. upper GI tract). The only side effect noted in these dosing trials was one case of mild depression. This product is not currently available in the U.S.

Resolor (prucalopride)

This medication is a serotonin agonist with selective affinity for 5-HT4 receptors. In human clinical trials, prucalopride provided daily accelerated whole gut, gastric, small bowel and colonic transit times in constipated patients. Side effects in these studies collectively expressed such adverse events as headache, nausea, abdominal pain or cramps and diarrhea. Prucalopride is available in Europe and Canada, but not in the United States.



Reglan (metoclopramide)

This medication is an antiemetic and prokinetic benzamide that acts as a dopamine antagonist and at higher doses, a serotonin agonist at 5HT4. Metoclopramide ultimately enhances the response to acetylcholine in the upper GI tract tissue which enhances motility and accelerates gastric emptying time. However, since it crosses the central nervous system, there are quite a few side effects. These include restlessness, depression, and extrapyramidal side effects, which limit the use of this drug.

Urecholine(bethanechol)

This medication is considered a cholinergic agonist normally used for urinary retention since it increases bladder muscle tone. However, since it stimulates the parasympathetic nervous system as a whole, bethanechol also stimulates gastric motility, and increases gastric tone. Possible side effects may include low blood pressure, increased heart rate, abdominal cramps, diarrhea, nausea, vomiting, salivation, increased tear production, and throat constriction. Due to these side effects, bethanechol is not recommended for use in rabbits or rodents.

Prostigmin(neostigmine)

This medication is an acetylcholinesterase inhibitor that is usually used as an antidote for anticholinergic intoxication and for treatment of myasthenia gravis and for urinary retention. However, it also has limited evidence for stimulating intestinal motility. It also has a plethora of associated side effects including bradycardia, low blood pressure, convulsions, dizziness, drowsiness, weakness, diarrhea, muscle cramps, nausea, salivation, stomach cramps, vomiting, difficulty breathing, increased throat mucous and increased tear production. Due to the vast array of GI side effects, this medication is not recommended for rabbits or rodents.

Domperidone

This medication is a dopamine antagonist gastrointestinal agent and is not currently approved by the FDA in the USA but is available in Canada and other countries. It works by stimulating the motility of the upper GI tract by inhibiting dopamine receptors, enhance-

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ing the action of acetylcholine in the GI tract, increasing gastric motility, and increasing peristalsis in order to facilitate gastric emptying and speeding up small bowel transit time. Domperidone doesn't cross the blood brain barrier so it doesn't tend to cause the CNS effects noted with metoclopramide. Side effects that may be noted include dry mouth, dizziness, and increased heart rate.

Amitiza (lubiprostone)

This medication is a bicyclic fatty acid that acts locally at the apical portion of the intestine as a chloride channel activator, increasing intestinal fluid secretion and intestinal motility. It is FDA approved for treatment of chronic idiopathic constipation and constipation associated with irritable bowel syndrome in humans. While it is only approved in humans and no studies have currently been conducted in cats, dogs or horses, there was a pilot study that proved its efficacy in reversing opioid induced constipation in guinea pigs. Side effects include headache, nausea, diarrhea, flatulence, abdominal pain, and dizziness. With the lack of available products to treat chronically constipated patients, it is being included for sake of completeness.

Linaclotide

This is currently an investigational drug that acts as a peptide agonist of guanylate cyclase-C receptor. It is minimally absorbed and via this receptor, it stimulates secretion of intestinal fluid and in theory, increases transit time. Two large human trials showed an improvement in bowel movement from baseline and the FDA review and approval should be completed by September 2012. The most common and dose-related adverse event was diarrhea. Since this is a new product, the long-term risks of treating chronic constipation remain unknown.

Botulinum toxin

Botulinum toxin when injected into the pylorus has been proposed to improve gastric emptying and associated symptoms. However, a controlled trial in humans found no significant differ-

ence in gastric emptying or symptoms when compared with placebo at one month. On the other hand, there were no serious side effects. Despite a lack of animal dosing, since it is a newer therapy, it has been included for sake of completeness.

What is the prognosis for constipation?

Once present, motility problems may or may not continue to be a lifetime problem depending on what is the underlying cause. It is very important to increase your pet's hydration whether this is through wet food for dogs and cats, adding a salt supplement to your horse's diet to increase their natural thirst response, or providing a salt wheel for your rabbit and guinea pig for the same reasons. It is also key to increase the fiber in their diets and keep the carbohydrate ratio on the lower side. Hay quality for horses, rabbits, and rodents is very important for their digestive health! No matter what species or size your pet is, good attentive husbandry is critical to overall treatment success.



How can my veterinary pharmacist help?

Treating pets with constipation offers a unique opportunity for veterinary pharmacists to help you and your pet. Many of these products must be compounded because they are simply not commercially available nor in a dosage form acceptable to your pet. Such examples include cisapride capsules, bethanechol for injection, domperidone capsules, and lower volume and flavored H2 blockers for smaller animals. In addition to making compounded medications, your veterinary pharmacist can also provide proper counseling on how to administer these medications

and what side effects to look for. Your veterinary pharmacist will do their best to help you feel comfortable talking about and dealing with your pet's constipation medications. They will also help you become familiar with them in hopes that these medications will alleviate your pet's uncomfortable symptoms. It is important to share any concerns you may have with your pharmacist and note any changes you see in your pet's diet or fecal output so that with your careful observations, your veterinarian's expertise, and your veterinary pharmacist's training in pharmacology, adjustments to your pet's medication regimen can be made for the best possible outcome.

****Further Reading Upon Request***

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