Research Ethics & Compliance Support

Guidelines for the Management of Gastrointestinal Stasis in Rabbits

Purpose: This guideline has been developed to ensure the wellbeing of rabbits exhibiting signs of gastrointestinal stasis. The main goal is to provide information on how to recognise, manage and treat cases of gastrointestinal stasis in rabbits. Additionally, this guideline aims to establish a humane endpoint where euthanasia is indicated in order to alleviate suffering when necessary and to reduce premature euthanasia of animals.

Background

Gastrointestinal (GI) stasis, also known as gut stasis or ileus, is a common life-threatening condition in rabbits within both clinical and laboratory settings. There are a large number of causes, such as impaction, obstruction, gas accumulation, primary gastroenteritis, adhesions, pancreatitis and liver disease (Lichtenberger and Lennox, 2010). Stress, poor diet, pain and dehydration are contributing factors and if left unmanaged can worsen the animal's condition (Huynh et al., 2016; Lichtenberger and Lennox, 2010). In most cases, the underlying cause of gastrointestinal stasis is unknown (Lichtenberger and Lennox, 2010), however it is important to know that it can occur acutely during recovery from surgery and anaesthesia (Jang et al., 2017). Once diagnosed, aggressive treatment is necessary to achieve the best outcome for the animal. Animals in critical condition or those not responsive to treatment will require euthanasia to alleviate further suffering as death is not an acceptable experimental endpoint.

Assessment

Rabbits with GI stasis may display the following clinical signs (Ager, 2017):

- Anorexia (not eating)
- Reduced or absent faecal output
- Small hard faecal pellets
- Lethargy
- Tachycardia (abnormally fast heart rate)
- Tachypnoea (abnormally fast respiratory rate)
- Pain - Hunched posture, bruxism (teeth grinding)
- Depression
- Reduced or absent gut sounds
- Dehydration
- Bloating
- Hypothermia (decreased body temperature)

The presence of several of these signs can be indicative of GI stasis and immediate treatment is recommended.

Decision Tree

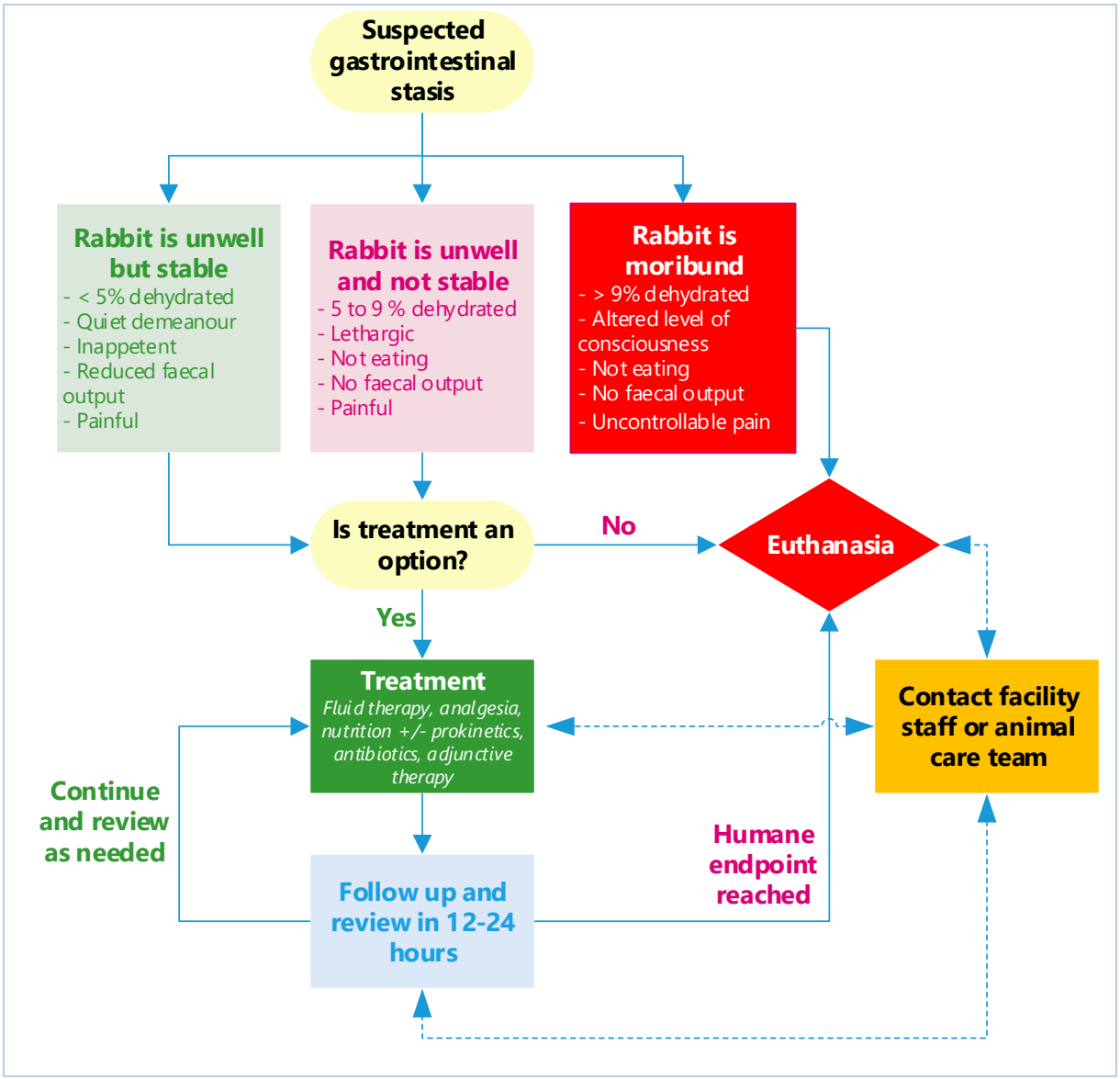

FIGURE 1 - Decision tree for management of GI stasis

Treatment

Treatment of GI stasis primarily involves fluid therapy, to ensure normovolaemia with adequate hydration of the animal and its gastrointestinal contents, pain relief and continual nutrition (Oglesbee and Jenkins, 2012).

1. **Fluid therapy**

- Fluid therapy is a form of drug administration and as such, should be given the same considerations as undesirable effects can occur from haphazard use. Excessive fluid administration can lead to fluid overload, pulmonary oedema and left sided congestive heart failure. In contrast, inadequate fluid administration or inappropriate fluid choice can lead to a poorer prognosis as the animal's fluid deficit is not being replaced, worsening ongoing dehydration and/or hypovolaemia.
- It is important to note that current best practice in rabbits is intravenous (IV) fluid therapy. This can be administered using an electronic fluid pump or by gravity. If administering fluids by gravity, please consider using a burette or smaller fluid bags (e.g. 250 mL, 500 mL) to prevent fluid overload. Directions on how to use these devices extend beyond the scope of this guideline. Please consult the veterinary and medical literature on best practice in their use.
- With regards to fluid choice, isotonic crystalloids (e.g. Hartmann's, Lactated Ringer's, 0.9% NaCl) are appropriate for meeting replacement and maintenance requirements. If hypotonic solutions, hypertonic solutions or colloids need to be used, please consult the Animal Care Team as these should be given on a case-by-case basis. The recommended maintenance fluid rate for rabbits is 4 mL/kg/hr, which can be approximated to 100 mL/kg/day (Varga, 2014; Grint, 2013).

- **Making a fluid plan**

I. Determine the degree of dehydration experienced by the rabbit:

TABLE 1 – Determining the degree of dehydration (Odunayo, 2018; Grint, 2013)

Percentage dehydrated (%):	Physical examination findings:
< 5%	No overt signs of dehydration but there is a history of fluid loss (e.g. not eating or drinking, diarrhoea)
5 – 7%	Skin tenting and dry mucous membranes
7 - 9%	Skin tenting, dry mucous membranes, sunken eyes
9 – 12%	Skin tenting, dry mucous membranes, sunken eyes, evidence of hypovolaemia, altered level of consciousness
12 – 15%	Skin tenting, dry mucous membranes, sunken eyes, evidence of hypovolaemia, moribund, death is imminent

II. Calculate the fluid deficit and daily maintenance:

$$Fluid\ deficit = \ body\ weight\ (kg) \times percentage\ dehydrated\ (\%)\ \times 1000\ mL$$

$$Daily\ maintenance\ for\ rabbits = 100\ ml/kg/day$$

III. Replace the animal's fluid deficit and meet its daily fluid maintenance requirements. Examples of individualised fluid plans can be found at the end of this section (Table 2).

IV. Reassess animal status and review fluid plan within 12-24 hours. Determine whether any changes are required based on the animal's health status. Continue to meet fluid replacement and maintenance requirements until fluid therapy is no longer indicated. This is typically when the animal is eating and drinking with no clinical signs.

- Administration of fluid therapy via the intravenous (IV) route is the most effective method. However, if IV access is not possible, subcutaneous (SC) administration can be alternatively used. Please use multiple injection sites and ensure that smaller volumes (30 to 50 mL per rabbit) are used when giving SC to minimise discomfort. Recommended volumes are variable but approximately 30 to 50 mL per rabbit can be used (Grint, 2013). It is important to note that SC administration is not as effective as IV as it takes several hours for the fluid to be absorbed systemically. Moreover, there is additional handling, stress and discomfort from the numerous injections required.
- The intraperitoneal (IP) route is not recommended due to the risk of gut perforation (Ager, 2017).
- Warmed fluids are not recommended as there is insufficient evidence in the literature for any conferred benefit in fluid therapy (Jourdan et al., 2017; Soto et al., 2014; Lee at al., 2014; Chiang et al., 2011). Moreover, improvisational warming of fluids for fluid therapy can have unpredictable effects, in some cases leading to thermal burns (Bharti et al., 2017; Sieunarine and White, 1996; Dunlop et al., 1989).

TABLE 2 – Examples of individualised fluid plans

Example of fluid plan using IV administration:	**Example of fluid plan using SC administration:**
A 3 kg male New Zealand White rabbit has been reported to not be eating or drinking after recovery from surgery. No fluids were administered during surgery and anaesthesia. His mucous membranes appear normal and he has no detectable skin tent. **1.) Rehydration** The rabbit is approximately 3% dehydrated so the fluid deficit is *Body weight (kg) x percentage dehydrated (%) x 1000 mL* *= 3 kg x 0.03 X 1000 mL* *= **90 mL*** **2.) Maintenance** The daily maintenance fluid requirement is *100 mL/kg/day* *= 100 mL x 3 kg* *= **300 mL per day*** **3.) Determining fluid rate** Total volume to administer in the next 24 hours is **390 mL** Administer 50% (195 mL) over the **first 6 hours** at **33 mL/hr** Administer the remaining 50% (195 mL) over the **remaining 18 hours** at **11 mL/hr**	*A 2.5 kg female Japanese White rabbit has been reported to not have eaten in the past 12 hours. No recent procedures have been performed on her. She has a detectable skin tent with dry mucous membranes.* **1.) Rehydration** The rabbit is approximately 5% dehydrated so the fluid deficit is *Body weight (kg) x percentage dehydrated (%) x 1000 mL* *= 2.5 kg x 0.05 x 1000 mL* *= **125 mL*** Administer **125 mL SC split over THREE different injection sites** (50 mL, 50 mL and 25 mL) **2.) Maintenance** The daily maintenance fluid requirement is *100 mL/kg/day* *= 100 mL x 2.5 kg* *= **250 mL per day*** Administer **FIVE 50 mL SC injections** over the next 24 hours

2. **Analgesia**

- Rabbits can experience severe gut pain during GI stasis. Many will not regain their appetite and eat until this pain is ameliorated. If a rabbit is painful, buprenorphine (0.01 – 0.05 mg/kg SC IV q6-12hr) can be administered with an NSAID such as meloxicam (0.2 – 1.5 mg/kg SC PO q24hr) or carprofen (2-4 mg/kg q24hr SC, PO) (Varga, 2014; Oglesbee and Jenkins, 2012). The aforementioned doses have been derived from reviewing the currently available literature (Nield and Govendir, 2019; Allweiler, 2016; Meredith, 2015; Cooper et al., 2009; Turner et al., 2009).
- Withholding analgesia in fear of reducing gut motility (i.e. opioids such as buprenorphine) is not a valid form of treating gut stasis as there are also non-opioid analgesics that can be used. Pain and subsequent stress will inhibit gut motility and worsen prognosis (Varga, 2014; Lichtenberger and Lennox, 2010). If the animal has had prior surgery, it is important to review the current analgesia plan and consider increasing analgesic doses and/or the additional use of adjunct analgesics.

3. **Nutrition**

- Ingestion of high fibre foodstuff is critical for establishing GI motility in rabbits (Varga, 2014; Oglesbee and Jenkins, 2012). Offer ad lib access to plentiful clean water, fresh hay and vegetables to encourage self-feeding.
- For inappetent rabbits, a slurry made from Oxbow Critical Care and water can be used for syringe feeding. Rabbits tolerate syringe feeding well and will readily eat unless extremely sick (Lichtenberger and Lennox, 2010). It is recommended to syringe feed 4 to 5 times per day (Huynh et al., 2016). With regards to mixing and feed portions, refer to the detailed manufacturer's instructions on the packaging.
- When syringe feeding, gently introduce the tip of the syringe into the gap between their premolar and incisor teeth and slowly inject the food mixture into their mouth. Be careful not to rapidly inject the food as the rabbits can accidentally inhale and aspirate the food. Rabbits that develop aspiration pneumonia will need to be euthanased on welfare grounds.

Additional therapy can be administered on a case-by-case basis:

1. **Prokinetics**

- Use of prokinetic drugs in the treatment of GI stasis is controversial as there is limited evidence in the literature for its efficacy but many practitioners state that there may be some benefit based on anecdotal experience (Schuhmann and Cope, 2014; Oglesbee and Jenkins, 2012; Lichtenberger and Lennox, 2010; Langer and Bramlett, 1997; Paul-Murphy, 2007). It is important to note that prokinetics are contraindicated in cases where a GI obstruction or perforation is suspected (Varga, 2014). If administering prokinetics for treatment of GI stasis, it is recommended to administer them until there are signs of improving condition (please see Monitoring section).

TABLE 3 – Prokinetic drugs for use in rabbits

Drug	Dose	Reference
Ranitidine*	5 mg/kg q12hr SC PO	(Meredith, 2015)
Metoclopramide*	0.5 - 1.0 mg/kg q12hr SC PO	(Meredith, 2015)
Cisapride	0.5 – 1.0 mg/kg q8-12hr PO	(Meredith, 2015)

****Injectable metoclopramide and ranitidine can be administered as a constant rate infusion (CRI) by adding it to IV fluids for slow administration during fluid therapy. This will also minimise the number of SC injections needed to be given.*

2. Antibiotics

- Antibiotics can be administered if there is evidence of dysbiosis, which can clinically manifest as diarrhoea (Oglesbee and Jenkins, 2012). Gastroenteritis of bacterial, viral or parasitic origin is noted to be uncommon (Lichtenberger and Lennox, 2010). If Clostridium *spp.* are suspected, metronidazole can be used at 20 mg/kg PO q12hr (Oglesbee and Jenkins, 2012). Furthermore, enrofloxacin 15-20 mg/kg PO q12hr and trimethoprim-sulfamethoxazole 30 mg/kg PO q12hr can be used against other pathogenic bacterial species (Oglesbee and Jenkins, 2012).

3. Adjunctive therapy

- Reduce stress levels by housing the rabbit in a calm and quiet environment with dim lighting.
- Keep the animal warm by providing supplementary heat such as a heat lamp or heat mat. Ensure that the ambient room temperature is at a comfortable level. The optimum environmental temperature range for rabbits is noted to be between 15 -20°C (Varga, 2014).
- Gentle abdominal massage can be provided if the rabbit is calm and receptive to handling (Ager, 2017). Do not persist if this is too stressful for the rabbit.
- Although being recommended once in the past for the treatment of rabbit GI stasis (Fisher, 2010), there is little benefit in the use of simethicone in animals (Watson, 2014; Oglesbee and Jenkins, 2012).
- Protein-digesting enzymes such as bromelain and papain, derived from pineapple and papaya, can be irritants to the gut mucosa and potentially increase the risk of gastric ulcers in inappetent rabbits (Oglesbee and Jenkins, 2012). As such, careful consideration should be given before their use.

Monitoring

1. Physical examination

The following parameters can be monitored to assess whether a rabbit is in improving or declining condition:

TABLE 4 – Determining whether a rabbit is in improving or declining condition (Lichtenberger and Lennox, 2010)

Improving Condition	Declining Condition
• Eating unassisted • Syringe feeding well • Appearance of well-formed stools • Resolution of fluid deficits • Normal posture and grooming • Reduction in gas accumulation via abdominal palpation	• Not eating unassisted • Refusing syringe feeding • Decreasing or absent faecal output • No resolution of fluid deficits • Abnormal and painful posture • Gas accumulation detected via abdominal palpation

2. Pain scoring – Rabbit Grimace Scale

The Rabbit Grimace Scale can be used to generate a cumulative score out of 10 by which pain can be measured (Keating et al., 2012). High scores indicate the presence of pain that needs treating. It is recommended to use the pain score when examining the animal to assess pain levels and whether further analgesia is required.

Humane Endpoint: Criteria for Euthanasia

Euthanasia is recommended when one or more of the following criteria is present:

- Altered level of consciousness
- > 9% dehydration
- Uncontrollable pain – scoring consistently high on the Rabbit Grimace Scale
- Not eating on its own or with syringe feeding
- Absent faecal output
- Not responsive to treatment after 24 to 48 hours

Prevention

The prevention of GI stasis is significantly easier than its treatment. Firstly, it is always important to provide access to high fibre feed (fresh hay and vegetables) and clean water at all times. Both create a gastrointestinal environment conducive to gut motility, which is essential for hindgut fermenters such as rabbits. Secondly, pain and stress reduce gut motility (Varga, 2014; Lichtenberger and Lennox, 2010) and as such, all measures should be taken to minimise both. When undergoing potentially painful procedures, the administration of analgesics need to be considered. Housing and handling should be carried out with careful consideration as to how stress can be minimised as much as possible. Early recognition of clinical signs consistent with gut stasis is critical and immediate management with pain relief, nutrition and fluid therapy alone can make the difference between a good and poor prognosis.

References

1. Ager, L. (2017). Ileus in rabbits – current thinking in treatment, nursing and prevention. *Veterinary Nursing Journal*, 32(7), 201-205. doi:10.1080/17415349.2017.1314781
2. Allweiler, S. I. (2016). "How to Improve Anesthesia and Analgesia in Small Mammals." *Veterinary Clinics of North America: Exotic Animal Practice* **19**(2): 361-377.
3. Bharti, V., et al. (2017). "Intravenous burn following accidental warm saline infusion." *Saudi Journal of Anaesthesia* **11**(4): 498-499.
4. Chiang, V., Hopper, K. and Mellema, M.S. (2011), In vitro evaluation of the efficacy of a veterinary dry heat fluid warmer. *Journal of Veterinary Emergency and Critical Care*, **21**: 639-647. doi:10.1111/j.1476-4431.2011.00684.x
5. Cooper CS, Metcalf-Pate KA, Barat CE et al. Comparison of side effects between buprenorphine and meloxicam used postoperatively in Dutch Belted Rabbits (*Oryctolagus cuniculus*). *Journal of the American Association of Laboratory Animal Science* 2009;**48**:279–285.
6. Dunlop, C.I., Daunt, D.A. and Haskins, S.C. (1989), Thermal Burns in Four Dogs during Anesthesia. *Veterinary Surgery*, **18**: 242-246. doi:10.1111/j.1532-950X.1989.tb01079.x
7. Grint, N. (2013). Anaesthesia. In F. Harcourt-Brown & J. Chitty (Eds). *BSAVA Manual of Rabbit Surgery, Dentistry and Imaging* (pp. 2-25). Gloucester, United Kingdom: British Small Animal Veterinary Association
8. Huynh, M., & Pignon, C. (2013). Gastrointestinal Disease in Exotic Small Mammals. *Journal of Exotic Pet Medicine*, **22**(2), 118-131. doi:https://doi.org/10.1053/j.jepm.2013.05.004
9. Huynh, M., Boyeaux, A., & Pignon, C. (2016). Assessment and Care of the Critically Ill Rabbit. *Veterinary Clinics of North America: Exotic Animal Practice*, **19**(2), 379-409. doi:https://doi.org/10.1016/j.cvex.2016.01.011
10. Jourdan, G., Didier, C., Chotard, E., Jacques, S., & Verwaerde, P. (2017). Heated intravenous fluids alone fail to prevent hypothermia in cats under general anaesthesia. *Journal of Feline Medicine and Surgery*, **19**(12), 1249–1253. https://doi.org/10.1177/1098612X16688990
11. Keating, Stephanie & Thomas, Aurelie & Flecknell, Paul & Leach, Matthew. (2012). Evaluation of EMLA Cream for Preventing Pain during Tattooing of Rabbits: Changes in Physiological, Behavioural and Facial Expression Responses. *PloS one*. 7. e44437. 10.1371/journal.pone.0044437.
12. Langer, J. C. and G. Bramlett (1997). "Effect of prokinetic agents on ileal contractility in a rabbit model of gastroschisis." *Journal of Pediatric Surgery* **32**(4): 605-608.
13. Lee, R. A., Towle Millard, H. A., Weil, A. B., Lantz, G., Constable, P., Lescun, T. B., & Weng, H. Y. (2014). In vitro evaluation of three intravenous fluid line warmers. *Journal of the American Veterinary Medical Association*, **244**(12), 1423-1428. https://doi.org/10.2460/javma.244.12.1423
14. Lichtenberger, M., & Lennox, A. (2010). Updates and Advanced Therapies for Gastrointestinal Stasis in Rabbits. *Veterinary Clinics of North America: Exotic Animal Practice*, **13**(3), 525-541. doi:https://doi.org/10.1016/j.cvex.2010.05.008
15. Meredith, A. (2015). *BSAVA Small Animal Formulary 9th Edition – Part B: Exotic Pets*. Gloucester, United Kingdom: British Small Animal Veterinary Association.
16. Nield, K., & Govendir, M. (2019). Comparison of 0.2 Mg/kg Vs. 1.0 Mg/kg of Oral Meloxicam for Safe and Effective Analgesia in Domestic Rabbits. *Veterinary Evidence*, **4**(2). https://doi.org/10.18849/ve.v4i2.215
17. Odunayo, A. (2018). Fluid Therapy. *Clinician's Brief,* **10**, 71-75.

18. Oglesbee, B. L. & Jenkins, J. R. (2012). Gastrointestinal Diseases. In K. E. Quesenberry & J. W. Carpenter (Eds). *Ferrets, Rabbits and Rodents Clinical Medicine and Surgery: 3rd Edition* (pp. 193–204). St Louis, MO: Elsevier Saunders.

19. Oglesbee, B. L. & Jenkins, J. R. (2012). Gastrointestinal Diseases. In K. E. Quesenberry & J. W. Carpenter (Eds). *Ferrets, Rabbits and Rodents Clinical Medicine and Surgery: 3rd Edition* (pp. 193–204). St Louis, MO: Elsevier Saunders.

20. Paul-Murphy, J. R. (2007). Critical Care of the Rabbit. *Veterinary Clinics of North America - Exotic Animal Practice*, **10**(2), 437-461. https://doi.org/10.1016/j.cvex.2007.03.002

21. Schuhmann, B., Cope, I. (2014) Medical treatment of 145 cases of gastric dilatation in rabbits. *Veterinary Record,* **175,** 484.

22. Sieunarine, K., & White, G. H. (1996). Full-thickness burn and venous thrombosis following intravenous infusion of microwave-heated crystalloid fluids. *Burns*, **22**(7), 568-569. https://doi.org/10.1016/0305-4179(96)00020-4

23. Soto, N., Towle Millard, H.A., Lee, R.A. and Weng, H.Y. (2014), In vitro comparison of output fluid temperatures for room temperature and prewarmed fluids. *Journal of Small Animal Practice*, **55**: 415-419. doi:10.1111/jsap.12236

24. Turner P.V., Chen C.H., Taylor M.W. Pharmacokinetics of meloxicam in rabbits after single and repeat oral dosing. *Comparative Medicine* 2006;**56**:63–67.

25. Varga, M. (2014). Digestive Disorders. In M. Varga (Ed). *Textbook of Rabbit Medicine: 2nd Edition* (pp. 303-349). United Kingdom: Elsevier

26. Varga, M. (2014). Therapeutics. In M. Varga (Ed). *Textbook of Rabbit Medicine: 2nd Edition* (pp. 137-177). United Kingdom: Elsevier

27. Watson, M. K. (2014). Therapeutic Review: Simethicone. *Journal of Exotic Pet Medicine* **23**(4): 415-417. https://doi.org/10.1053/j.jepm.2014.08.001