Animal Care & Ethics Committees

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 and liver disease (Oglesbee and Lord, 2021; 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

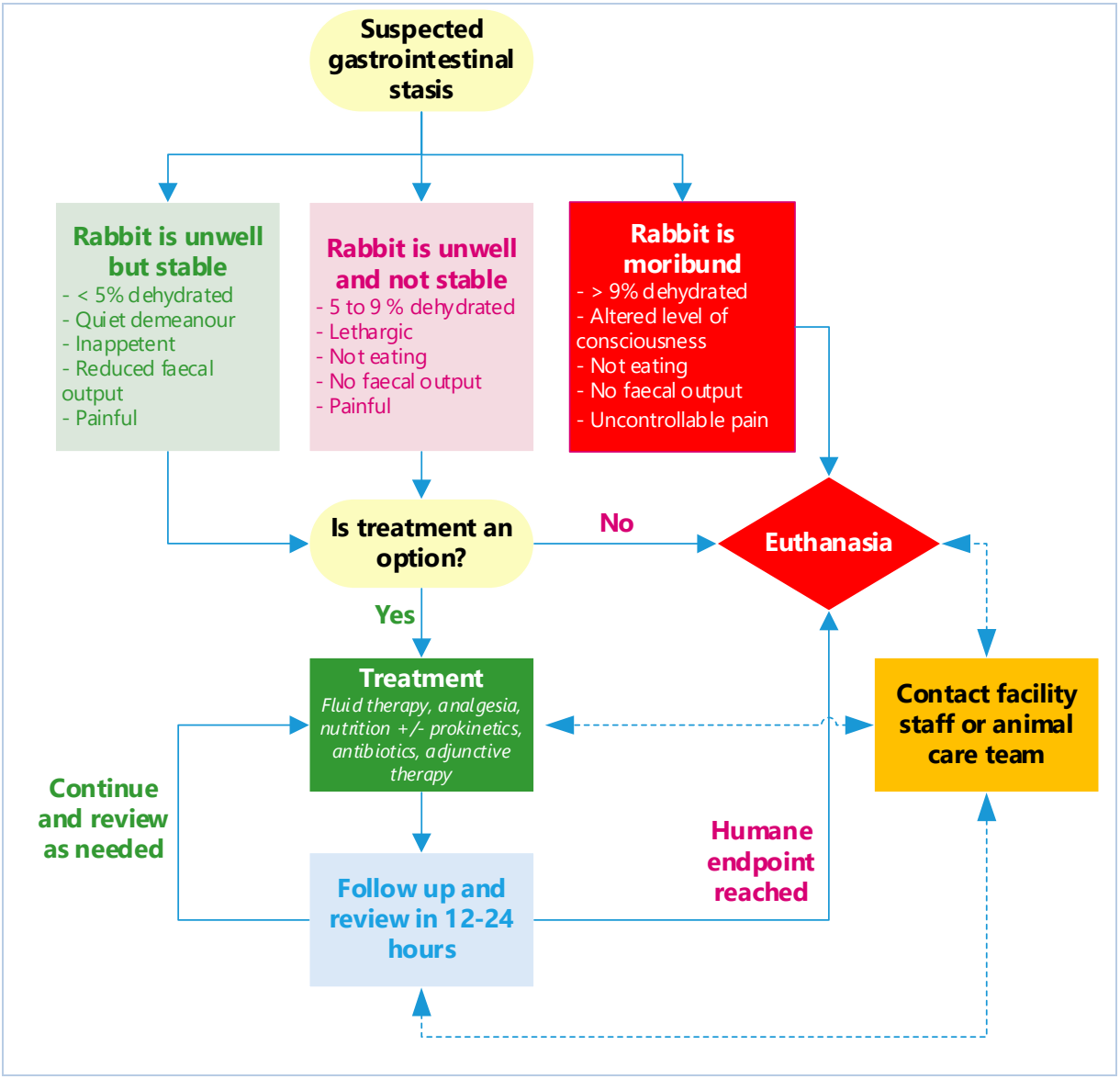

FIGURE 1 - Decision tree for management of GI stasis

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 Lord, 2021).

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 RECS 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 are used when giving SC to minimise discomfort. Recommended volumes are variable but approximately 30 to 50 mL per site can be used (Grint, 2013). A total volume of 100 to 120 mL/kg/day of subcutaneous fluids divided into 2-3 treatments daily can be easily tolerated by most rabbits (Oglesbee and Lord, 2021). 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 q12-24hr) or carprofen (1-5 mg/kg q12-24hr SC, PO) (Oglesbee and Lord, 2021; Hedley, 2020; Nield and Govendir, 2019; Allweiler, 2016; Varga, 2014; Cooper et al., 2009; Turner et al., 2009).

- Opioids for pain management of GI stasis, particularly buprenorphine, have been considered controversial as they can reduce GI transit, faecal output and food/water intake (Hsi et al., 2022; Feldman et al., 2021). Despite this, opioids are an appropriate consideration when NSAIDs do not provide enough analgesia. Multimodal analgesia is recommended when moderate to severe pain is anticipated. As such, withholding analgesia in painful animals is not a valid form of treating GI stasis. Pain and subsequent stress will inhibit gut motility and worsen prognosis (Varga, 2014; Lichtenberger and Lennox, 2010). Moreover, safe use of buprenorphine can be achieved with careful monitoring (Feldman et al., 2021). It is always important to review the ongoing analgesia plan and consider making adjustments as necessary based on the animal's status.

- The anti-emetic drug, maropitant, has been suggested as a potential analgesic due to its ability to block substance P from binding to NK-1 receptors. Despite this, a 2023 veterinary paper found that there was no improvement in post-surgical pain scores with the addition of maropitant to a buprenorphine and meloxicam analgesic regimen (Roeder et al., 2023). As such, careful consideration must be made on a case-by-case basis when deciding to use maropitant for pain management. The drug's effect on gastrointestinal motility can be found on page 7 under "1. Prokinetics".

3. Nutrition

- Ingestion of high fibre foodstuff is critical for establishing GI motility in rabbits (Oglesbee and Lord, 2021; Varga, 2014). 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 Lord, 2021; 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 only administer them until there are signs of improving condition (please see Monitoring section).

    - A 2019 pharmacokinetic study found that maropitant may have positive effects on rabbit gastrointestinal motility. Doses of 1 mg/kg administered SC or IV to New Zealand White rabbits reached therapeutic plasma concentrations similar to dogs and were associated with increased faecal output (Ozawa et al., 2019).

TABLE 3 – Prokinetic drugs for use in rabbits

Drug	Dose	Reference
Ranitidine*	4-6 mg/kg q8-24hr SC or PO	(Hedley, 2020)
Metoclopramide*	0.5 - 1.0 mg/kg q6-12hr SC or PO	(Hedley, 2020)
Cisapride**	0.1 – 1.0 mg/kg q8-12hr PO	(Hedley, 2020)

***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.*

****Cisapride is difficult to obtain in Australia and may result in cardiac arrhythmia when used.*

2. **Antibiotics**
    - Antibiotics can be administered if there is evidence of severe dysbiosis, which can clinically manifest as diarrhoea (Oglesbee and Lord, 2021). 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 Lord, 2021). Furthermore, enrofloxacin 15-20 mg/kg PO q12hr and trimethoprim-sulfamethoxazole 30 mg/kg PO q12hr can be used if *E. coli* is suspected (Oglesbee and Lord, 2021).

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 Lord, 2021).
- 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 Lord, 2021). 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 (RGS) can be used to generate a cumulative score out of 10 by which pain can be measured (Keating et al., 2012). Another scoring system that was recently developed is the CANCRS (Centro Animali Non Convenzionali Rabbit Scale) that incorporates the aforementioned Rabbit Grimace Scale with clinical parameters such as heart rate and respiratory rate to generate a score out of 24 (Banchi et al., 2022). High scores indicate the presence of pain that needs treating. It is recommended to use pain scoring 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 RGS or CANCRS
- 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.

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