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Current anaesthetic considerations and techniques in rabbits

Part II: Induction, maintenance and the post-anaesthetic period

Yvonne van Zeeland[1] *and Nico Schoemaker*[1]

SUMMARY

Rabbit anaesthesia is perceived by many as a difficult, high-risk procedure. Many veterinarians therefore do not feel comfortable when having to sedate or anaesthetize a rabbit. Fortunately, the arrival of newer, safer anaesthetic agents, development of specialized anaesthetic equipment, and increased knowledge about veterinary anaesthesia has greatly reduced the risks of anaesthesia-related morbidity and mortality. In particular the use of endotracheal tubes or supraglottic airway devices, administration of intra-operative fluids and provision of adequate thermal support, combined with adequate and continued monitoring of the patient are important to prevent potentially fatal conditions such as hypoxia, hypovolaemia and/or hypo- or hyperthermia. Vigilant monitoring of the patient should, however, not only be limited to the anaesthetic procedure, but also extend to the pre- and post-anaesthetic period, in which a thorough evaluation of the patient may help to detect pre-existing conditions or post-anaesthetic complications that need to be dealt with in order to maximize chances of success. Various injectable and inhalant anaesthetics, premedicants and analgesics may be combined to achieve a balanced anaesthesia which minimizes the chances of adverse events. The second part of this review discusses the various aspects that need to be taken into consideration during induction, maintenance and the post-anaesthetic period.

Keywords: Rabbit; *Oryctolagus cuniculi*; Anaesthesia; Intubation; Anaesthetic monitoring; Anaesthetic emergency

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Introduction

As discussed in part I of this review, anaesthesia comprises of 4 distinct yet equally important phases, including the pre-anaesthetic evaluation and premedication phase, induction, maintenance and recovery. In part I, we focused on the pre-anaesthetic considerations that need to be taken into account when anaesthetizing a rabbit, including the most commonly used analgesics and anaesthetic drugs that may be used when composing an anaesthetic protocol that is tuned to the individual patient. This second part will discuss the various aspects that need to be taken into account during induction, maintenance and recovery, including the provision of appropriate supportive care and peri- as well as post-anaesthetic monitoring of the rabbit patient.

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Induction of general anaesthesia

Anaesthetic agents may be delivered topically (see part I 'local anaesthetics'), parenterally (see part I 'injectable anaesthetics') and/or via inhalation (see part I 'inhalant anaesthetics'). An anaesthetic protocol usually comprises of a combination of injectable and/or inhalant anaesthetics and/or premedicants (see part I 'sedation and premedication', 'injectable anaesthetics' and 'inhalant anaesthetics') and/or one or multiple analgesics (see part I 'analgesia'). To determine the optimum anaesthetic protocol, various factors need to be considered, including the clinical condition and stability of the patient, the practitioner's knowledge and experience with the various anaesthetic agents used including their side-effects, and options for monitoring and supporting the patient during the procedure [1]. Commonly used protocols include premedication with butorphanol and midazolam, followed by induction and maintenance with isoflurane or sevoflurane; induction with ketamine and medetomidine (+/– butorphanol) followed by inhalant anaesthesia [2,3]; and fentanyl/fluanisone combined with midazolam or diazepam followed by inhalant anaesthesia [4].

Total injectable anaesthesia is usually reserved for short diagnostic or surgical procedures, mainly because the rabbit's high metabolism results in short-lived effects, necessitating higher doses and/or frequent redosing thereby posing a higher risk for side-effects and/or prolonged recovery. This is less problematic when using inhalant anaesthetics, which can easily be titrated to effect and adjusted to the length of the procedure. Thus, most anaesthetic regimens in rabbits comprise of inhalant anaesthetics as their primary component. The induction is typically accomplished using a face mask (Fig. 1).

In order to reduce resistance and avoid breath holding in response to the smell of anaesthetic vapours, premedicants can be administered [1,5]. Gradual introduction of the anaesthetic vapours ('low to high induction') may also help to avoid these reactions [5].

After induction, the oral cavity should always be checked for the presence of food remnants, and cleaned with cotton swabs (Fig. 2), if necessary. Furthermore, sterile, ophthalmic ointment may be applied to the cornea to prevent desiccation and/or irritation. It is also recommended to provide oxygen to the animal during the induction and maintenance phase. Preferably, the animal is intubated using an endotracheal tube or supraglottic airway device to allow effective delivery of oxygen to the lower airways and manually- or mechanically

Figure 1. A regular anaesthesia cone can be used as a face mask. To reduce leakage of anaesthetic gases, the cone can be covered with latex of a glove to decrease the opening.

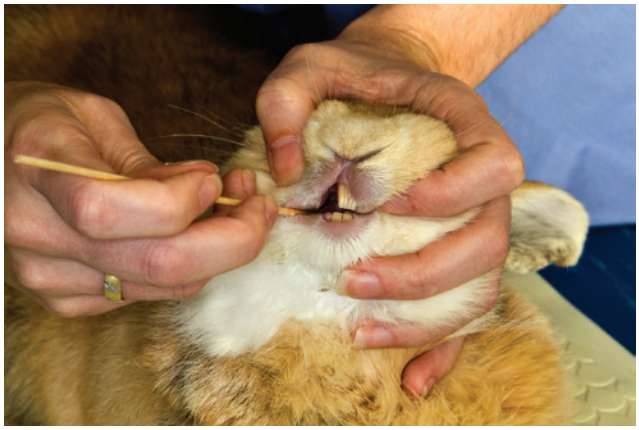

Figure 1. A regular anaesthesia cone can be used as a face mask. To reduce leakage of anaesthetic gases, the cone can be covered with latex of a glove to decrease the opening.

assisted breathing, in case the rabbit stops breathing spontaneously (see intubation and oxygen delivery). In addition, the animal should be positioned carefully in such a way that the airway remains unobstructed at all times, and weight of the viscera is taken away from the diaphragm to allow easy breathing [5].

Intubation and oxygen delivery

Delivery of oxygen during the anaesthetic procedure is beneficial to any patient, independent of the anaesthetic protocol that is used. Oxygen may be delivered by facemask, through an endotracheal or nasal tube or supraglottic airway device. To be able to intubate a rabbit and place an endotracheal tube or supraglottic airway device, the rabbit should be sufficiently sedated. This can be accomplished using injectable anaesthetics that are administered either intravenously (e.g. propofol, alphaxalone) or intramuscularly (e.g. a combination

of ketamine and medetomidine and/or butorphanol), or following face mask induction with inhalant anaesthetics. The latter technique is not recommended as rabbits will start waking up as soon as the mask is removed and intubation may take some time. When using induction agents such as propofol or alphaxalone, care should furthermore be taken to avoid overdosing as this may lead to respiratory depression, apnoea and hypoxia if a patent airway cannot be accomplished quickly. In addition, the absence of breath sounds and condensation resulting from the respiratory depression may complicate blind intubation, as these parameters are often used as guidelines to evaluate if the tube is placed correctly.

Face mask

Many veterinarians do not routinely intubate rabbits. Instead, injectable anaesthetics and/or a face mask are used for induction and/or maintenance of inhalant anaesthesia and/or oxygen delivery. Over the years, various types of facemaskshave become commercially available. Preferably a tight-fitting facemask is used and placed over the mouth and nose (Fig. 1). For dental procedures, the facemask may also be placed solely over the nose. As rabbits are obligate nasal breathers, this will generally be sufficient to maintain anaesthesia when the rabbit is also premedicated. Care should, however, be taken to prevent the head being tilted into a vertical position, as this may result in the dislodgement of the epiglottis from the soft palate whereby the rabbit will start to breathe through the mouth and wake up.

Although tight-fitting facemasks allow some assisted breathing, this is generally insufficient to ensure a free airway and effective oxygen delivery to the lungs in case of respiratory arrest and/or airway obstruction. The facemask furthermore does not protect against aspiration of (regurgitated) food remnants that are present in the oral cavity or oesophagus, thereby posing a significant risk for morbidity and/or mortality. Moreover, the facemask can also have potential detrimental effects to the staff's health as a result of leakage of volatile anaesthetic gases (see Table 1 for a list of pros and cons of face mask anaesthesia).

Endotracheal intubation

For maintenance of anaesthesia and assisted ventilation, endotracheal intubation is ideal. Although the technique is feasible in (larger-sized) rabbits, it is considered more difficult than intubating a dog or cat due to several anatomical features that hinder direct visibility of the larynx including a) the inability to open the mouth wide; b) the relative narrowness of the oral cavity and isthmus faucium; c) the relative large base of the tongue; d) the relative small size of the larynx; and e) the permanent positioning of the epiglottis on top of the soft palate. Endotracheal intubation may be accomplished either using a blind technique or by direct visualization of the larynx using a laryngoscope or endoscope. For both techniques, the rabbit is preferably placed in sternal recumbency, with the neck hyperextended in a vertical position, whereby the larynx and trachea are aligned with the oropharynx to facilitate intubation (Fig. 3) [6,7]. Local anaesthetics (e.g. xylocaine spray) may be applied prior to intubation to desensitize the larynx and prevent laryngospasm [7]. Care should furthermore be taken to ensure that the rabbit is adequately anaesthetized to prevent laryngospasm or

Figure 3. To allow tracheal intubation the nose of the rabbit needs to be directed dorsally to align the oropharynx with the larynx and trachea.

Table 1. Pros and cons of the use of a face mask to maintain anaesthesia

Advantages	Disadvantages
• Easy to use • No airway irritation • Dental inspection is possible with the mask placed over the nose and incisors	• Leakage of anaesthetic gases (hazard for personnel) • Increase of dead space • Assisted breathing is (almost) impossible • No protection against aspiration • No protection against obstruction of the airways

Table 2. Pros and cons of endotracheal intubation to maintain anaesthesia in rabbits[8,10]

Advantages	Disadvantages
• Procedure can be performed relatively quickly with experience • No risk of aspiration of food • Ventilation is possible during breath holding • Free airway is guaranteed • Permits continuous administration of oxygen • Better control over depth of anaesthesia • Assisted breathing (incl. IPPV) is possible • Reduction of dead space • Virtually no leakage of anaesthetic gases • Suitable for surgery to the head (although dental inspection may be more difficult to perform)	• Technique requires experience • Deeper level of anaesthesia is often required • Risk of laryngeal spasm in insufficiently sedated animals • Increased risk of tracheal and/or laryngeal trauma (incl. oedema, haemorrhage, stenosis and/or strictures) • Risk of obstruction due to increased mucus production • Risk of introducing foreign bodies (especially with blind intubation) • Possibility of incorrect intubation (into oesophagus, bronchi) • Post-anaesthetic reaction to tube placement (including coughing, gagging, reduced appetite)

damage to the larynx and pharynx which may subsequently result in haemorrhage, oedema and (post-anaesthetic) stenosis and strictures (Table 2).

Blind intubation, which requires some practice and experience, is generally accomplished by positioning the rabbit in the aforementioned position and advancing the tube through the diastema over the tongue into the oropharynx. At this point, it is possible to see cyclic condensation and clearing in the endotracheal tube and/or hear breath sounds, which become louder when the tube is passed into the region of the larynx. If it passes beyond the larynx into the oesophagus, breath sounds and condensation cease to appear. Once it has been ascertained that the position of the tip of the tube is in front of the larynx (i.e. maximum breathing sounds are heard), the tube can gently and slowly be advanced into the larynx. Gentle rotation (without force!) may help to guide the tip between the arytenoids. Passing of the tube into the larynx and trachea may elicit a slight wheeze or cough. Condensation, breath sounds or capnography can subsequently be used to check correct positioning prior to securing the tube in place with adhesive tape or gauze ties. In general, a 2.5 to 4.0 ID (inner diameter) uncuffed endotracheal tube can be used to intubate rabbits [5]. In case the first attempt is unsuccessful, the use of a smaller tube can be considered.

For laryngoscope- or endoscope-assisted intubation, the procedure is more or less similar [1,5,7]. An assistant may help to position the head and hold the mouth open using gauze strips, or, alternatively, a mouth gag may be used for this purpose. A laryngoscope or otoscope may subsequently be used to visualize the glottis and facilitate intubation[1,5,7]. Alternatively, the endotracheal tube may be placed over the end of a rigid endoscope. The soft palate may need to be pushed away with the tip of the endotracheal tube or endoscope before being able to visualize the entrance to the larynx and the tube can be passed carefully into the trachea (Fig.4 and 5) [11,12].

A small gauge urinary catheter (2-5 Fr), threaded through the tube prior to inserting it into the larynx, or specially designed introducers may also be used as a guiding tool to facilitate intubation [13,14]. The main advantages of

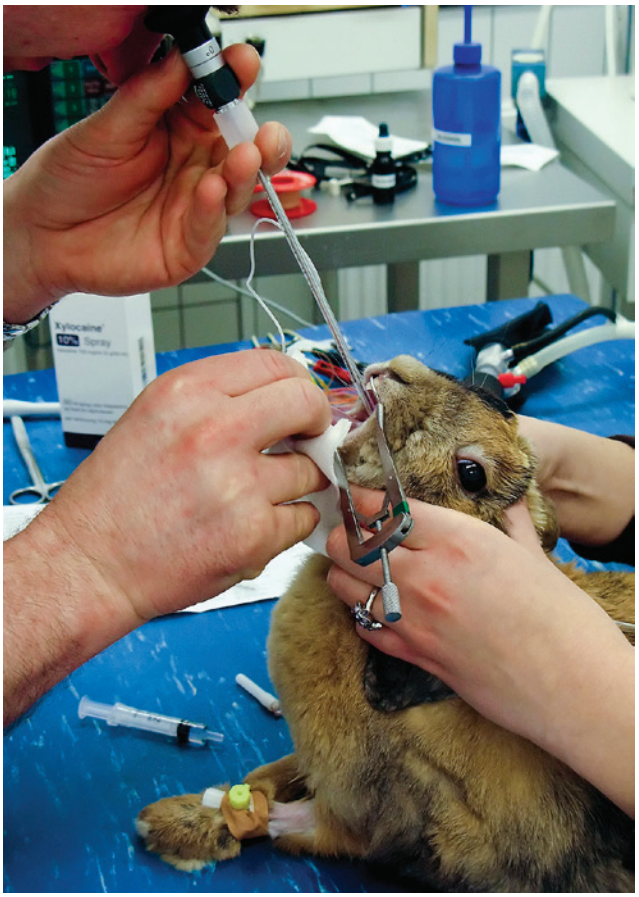

Figure 4. By inserting an endoscope in the endotracheal tube and directing the endoscope into the trachea, visual placement of the tube into the trachea is easily accomplished.

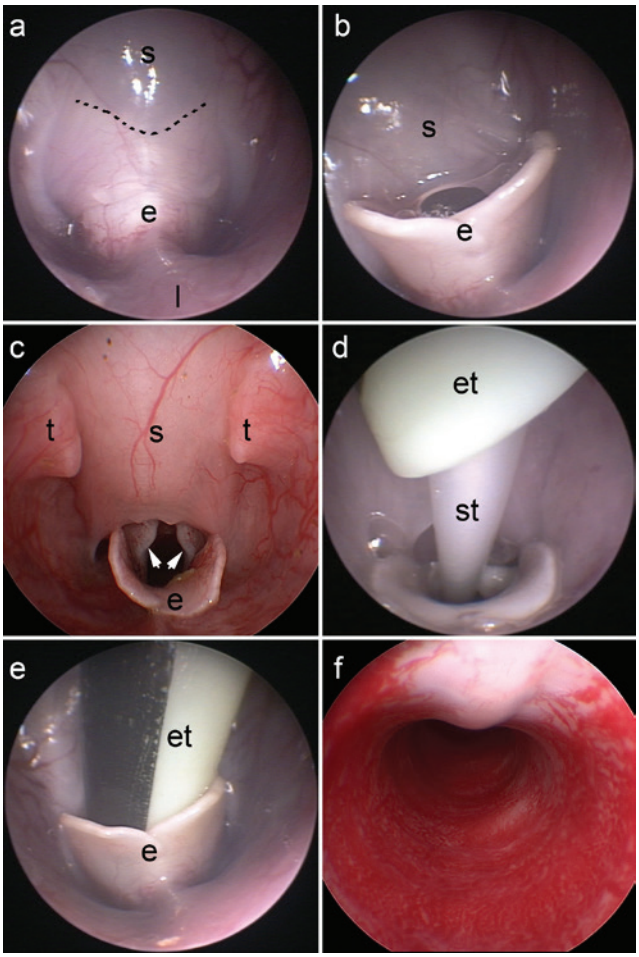

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Figure 5. Rabbit laryngotracheoscopy and intubation.
a. *View of the normal larynx in the nasal breathing rabbit. Note that the epiglottis (e) at the base of the tongue (l) is buttoned over the caudal edge of the soft palate (s). The cranial edge of the epiglottis can be seen through the semitransparent caudal soft palate (dotted line).*
b. *By placing gentle dorsal pressure on the anaesthetised rabbit it is easy to disengage the cranial edge of the epiglottis (e) from the soft palate (s). If the rabbit is semi-consciousthen swallowing quickly re-engages the epiglottis and soft palate.*
c. *View of the larynx in an anaesthetized rabbit, after dorsal displacement on the caudal soft palate has disengaged the epiglottis. The freed epiglottis (e), arytenoid cartilages (arrows), caudal soft palate (s) and tonsils (t) are visible.*
d. *Intubation in a rabbit using side by side endoscopic guidance. An endotracheal tube (et) and stylet (st) have been introduced into the caudal buccal cavity. The stylet is first directed through the glottis under endoscopic (or laryngoscopic) view to act as a guide for the endotracheal tube.*
e. *Intubation in a rabbit using side by side endoscopic guidance. The endotracheal tube (et) is then advanced along the stylet, over the epiglottis (e) and into the trachea.*
f. *Intubation in a rabbit using over the endoscope technique. The endotracheal tube is slid up the endoscope, before the endoscope is passed through the glottis and into the anterior trachea. Once a clear view of the trachea has been obtained, as shown, then the endotracheal tube is advanced off the endoscope and into the trachea, as the endoscope is withdrawn.*

visualization compared to blind intubation are the decreased risk of trauma and the ability to estimate more accurately which size tube to use, thereby enabling use of larger-sized tubes and considerably reducing the resistance during respiration.

Alternative to endotracheal intubation, nasal intubation may be attempted, in which the tube is passed into the ventral nasal meatus. Small soft nasogastric tubes or 1.0-1.5 mm endotracheal tubes are considered suitable for this purpose [5]. In order to enable successful delivery of the anaesthetics, high flow rates are required. This technique may be particularly useful in small rabbits which are difficult to intubate endotracheally. It is also possible to advance an endotracheal tube through the nasal passages and pharynx into the trachea, but this poses a risk of introducing pathogens (e.g. *Pasteurella multocida*) from the nasal cavity into the deeper airways [15].

Supraglottic airway devices

Supraglottic airway devices, also referred to as laryngeal masks, are the latest devices used for the delivery of volatile anaesthetics. Rather than being passed though the glottis, a supraglottic airway device resides on top of the larynx, thereby posing less risk of damage or irritation to the larynx or trachea while having similar advantages as endotracheal intubation (Fig. 6; Table 2). In addition, placement of the supraglottic device is quick and easily accomplished, and does not require a lot of skill or experience. In human medicine, supraglottic airway devices have been employed for some time, and shown to provide a good alternative for endotracheal intubation [15, 16].

In companion animal medicine, these devices have also

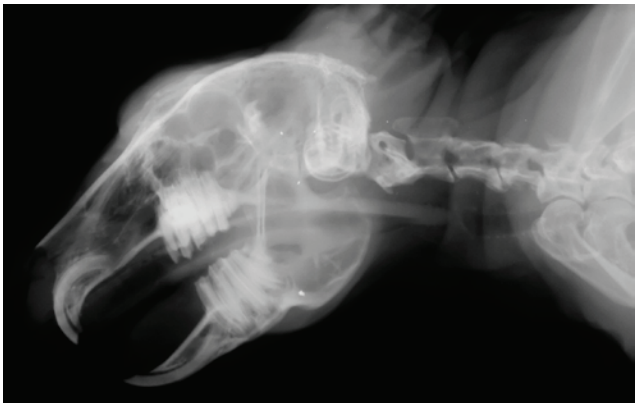

Figure 6. A radiograph of the head of a rabbit with a supraglottic airway device in place. The opening of the device is placed over the glottis.

been used. In rabbits, however, their use was limited primarily to laboratory animals and research settings [16-19]. Recently however, a new device (V-gel®, DocsInnovent Ltd, London, UK) was developed and tailored specifically to the rabbit's unique oropharyngeal anatomy [20]. The device, which is available in 6 sizes (Fig. 7; Table 3), has recently been tested in a clinical setting and found useful in most situations (including emergencies) except in patients requiring dental care. In >95% of cases, patent airways could be established rapidly on the first attempt and maintained successfully for the duration of the procedure in both spontaneously breathing animals and those with assisted ventilation [21]. Minor complications, including transient linguocyanosis (blue discolouration of the tongue due to restricted venous blood flow), gastric bloat and insertion difficulties due to improper anaesthetic depth or dental abnormalities, however, were encountered in a minority of cases [21].

Similar to endotracheal intubation it is important to ensure the patient is properly anaesthetized prior to inserting the supraglottic airway device, though lower amounts of anaesthesia seem to be required to allow proper placement without resistance [17]. A useful, commonly used, anaesthetic protocol by the authors to induce this level of anaesthesia includes the use of ketamine (5-10 mg/kg IM), medetomidine (200-250 µg/kg IM) and butorphanol (1 mg/kg IM). Once these anaesthetics have taken effect, the rabbit's mouth is opened, the tongue pulled out and the V-gel® inserted into the oropharynx with a slight twisting motion. The use of a water-based lubricant is recommended to allow for smooth placement. After ensuring proper positioning of the device (e.g. using capnography), the V-gel® is subsequently secured into place using a strap or tie (Fig. 8).

Table 3. Size of the available rabbit V-gels. For each size, the weights of the rabbit for which this device is considered suitable, is mentioned.

Size	Body weight of the rabbit (kg)
R1	0.5 - 1.5
R2	1.0 - 2.0
R3	1.8 - 3.5
R4	2.5 - 4.0
R5	3.5 - 5.0
R6	> 4.5

Figure 7. The largest size (R6) supraglottic airway device currently commercially available for rabbits. This device is suitable for rabbits weighing more than 4.5 kg. The smallest device is suitable for rabbits 0.5 kg and up.

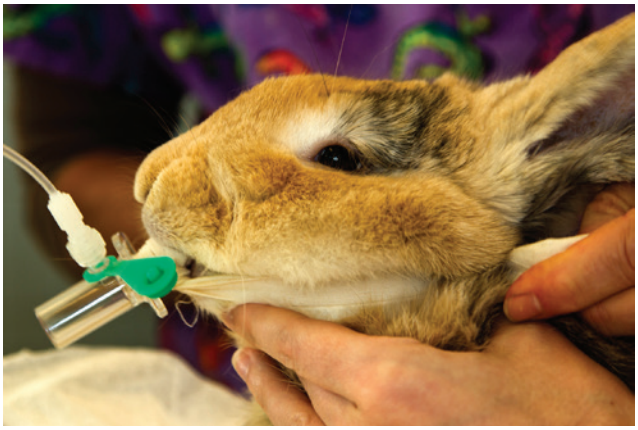

Figure 8. After ensuring correct positioning of the supraglottic airway device, it is secured into place using cotton straps.

Maintenance of general anaesthesia

Once the rabbit is intubated, it can be connected to either a rebreathing circuit (if the animal weighs >2.5 kg) or a non-rebreathing circuit (for animals <2.5 kg) to allow administration of oxygen and inhalant anaesthetics. Traditionally, non-rebreathing circuits such as the Ayre's T-piece or Bain circuit are the most commonly used for rabbits and smaller exotic patients as they result in relatively low dead space volumes and low resistance. It is generally recommended to use a fresh gas flow of 2-3 times the respiratory minute volume (i.e., approximately 450 ml/kg) [23], resulting in a gas flow of 1-3 L/min for most rabbits [24]. Once connected to the anaesthetic machine, the animal may either be allowed to breathe spontaneously, or to be mechanically- or manually ventilated. Assisted ventilation is particularly important when the animal does not breathe spontaneously, or during procedures in which the thoracic cavity is opened (e.g. explorative

thoracotomy) or paralytic drugs (e.g. atracurium) are used. When using intermittent positive pressure ventilation (IPPV), the ventilator is usually set to a tidal volume of 10-15 ml/kg, with a respiration rate of 20-40 breaths per minute and pressures of approximately 15-20 mm Hg [8,25,26].

Intra-operative fluid therapy

Normal water consumption in rabbits is generally considered to be 100-150 mL/kg per day, which is higher than that in dogs or cats [27]. Thus, a reduced water intake in sick rabbits may rapidly result in dehydration and/or shock. Preferably, the fluid deficit is corrected prior to the anaesthetic procedure, but even in properly hydrated rabbits, fluid therapy during anaesthesia remains important as many anaesthetics result in decreased cardiac output and hypotension. In addition, fluid requirements are increased because of increased fluid loss due to breathing dry, cold air (if inhalant anaesthetics are used), haemorrhage and/or exposure of viscera to the room air. IV access may furthermore be advantageous as it allows quick and easy administration of emergency drugs and/or additional anaesthetics and/or may help to regulate body temperature, if necessary.

If possible, fluids are administered via the intravenous route, using small (22-26 G) over-the needle catheters that can be placed in the marginal ear vein (Fig. 9), the cephalic or lateral saphenous vein [28,29]. Alternatively, fluid can be administered via the intraosseous (in the proximal humerus, femur or tibia) or subcutaneous route. When providing fluids via the intravenous or intraosseous route, care should be taken not to overhydrate the rabbit, as this may lead to severe lung oedema, dyspnoea and potentially death. In general, volumes of 10 ml/kg/h are well tolerated throughout the anaesthetic procedure. Alternatively, subcutaneous fluids may be administered in the loose skin on the dorsum in volumes of 100-150 ml/kg, divided over 2-3 treatments per day. Both crystalloids and colloids may be used for intra-operative fluid therapy. Colloids (e.g. hetastarch, dextran) are particularly useful in case rapid increase in osmotic pressure and blood volume is required and may be administered as boluses of 5 mL/kg over 5-10 min, repeated every 15 minutes, if necessary [28,29]. Alternatively, isotonic crystalloids (e.g. physiologic saline, Ringers) may be administered rapidly in doses of 10-15 mL/kg [28,29]. In case of severe blood loss, blood or haemoglobinbased oxygen carriers (e.g. Oxyglobin®, OPK Biotech LLC, Cambridge, Massachussetts, USA) may also be used.

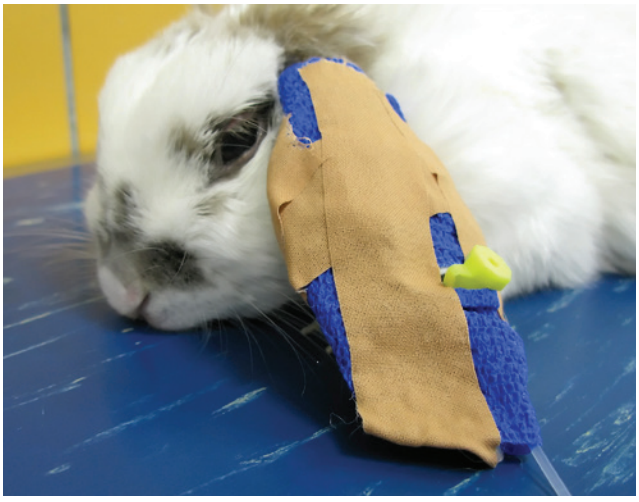

Figure 9. An IV catheter is placed in the marginal ear vein of this rabbit. IV access not only allows for continuous fluid therapy during anaesthesia, but also guarantees a direct vascular access allowing for a more rapid application of drugs during an emergency crisis.

Thermal support

Anaesthesia usually results in loss of body temperature, particularly in animals with a high body surface area to size ratio [30]. Heat may be lost via the skin, respiratory tract (due to inhalation of cold gases) and/or surgical field (due to exposure of viscera to room air). In addition, anaesthetics suppress normal thermoregulatory mechanisms and behaviours, thereby predisposing to hypothermia and hypothermia-associated complications such as respiratory and cardiovascular suppression, prolonged recovery times and even death [31]. Hyperthermia is less common, but may also occur in densely furred rabbits if excessive heat is applied. Therefore, close monitoring of body temperature is warranted (see 'anaesthetic monitoring').

To thermoregulate the patient, a variety of passive insulators (e.g. blankets, aluminium foil, plastic or paper drapes) and active heating devices (e.g. forced-air or conductive warming systems, or radiant heating devices) can be used. In addition, minimizing the amount of presurgical antiseptic solution used to prepare the patient (with a preference to use povidone-iodine over alcohol), administration of warm fluids, heating and humidifying inspired anaesthetic gases, use of low flow techniques and/or minimizing the duration of anaesthesia may further help to prevent a drop in body temperature [30,31]. When using active heating devices (in particular electrical pads), care should be taken to avoid thermal burns.

In case of hyperthermia, treatment may be initiated by administering cold IV fluids and/or applying cold water or alcohol to the footpads or exposed skin.

Anaesthetic monitoring

Continued monitoring of the patient during anaesthesia is vital for its survival. The task of monitoring anaesthesia should preferably be assigned to a trained and experienced technician that is closely monitoring the depth of anaesthesia, cardiopulmonary parameters and body temperature. In addition, anaesthetic monitoring equipment may be used to monitor vital parameters, although it should be emphasized that no equipment can replace an observant assistant that is able to evaluate the observations in light of presurgical baselines and intraoperative events and can decide to take action whenever he or she suspects that intervention is required.

Clinical observations and monitoring of the patient

Depth of anaesthesia is generally monitored by assessment of the various reflexes. These include the righting, palpebral, corneal, toe pinch - leg withdrawal, and pinna reflex [8], of which the pinna and toe pinch - leg withdrawal reflex (particularly when tested in the hind legs) are considered to be the most reliable [32-34]. Whereas the toe pinch – hind leg withdrawal reflex will result in a slow withdrawal in rabbits that are under a light plane of anaesthesia, it will not elicit a reaction in rabbits that are under a surgical plane of anaesthesia. The front leg withdrawal reflex will stay present for a much longer period. The corneal reflex, in contrast, will usually be preserved until dangerously deep levels of anaesthesia are achieved. In rabbits which have received medetomidine, however, the corneal reflex may be (temporary) absent as a result of the administration of the drug itself, thereby classifying it as a less reliable parameter to evaluate the anaesthetic depth [35].

In addition to the aforementioned reflexes, other parameters may be used as indicators for determining the anaesthetic depth, including (loss of) muscle and jaw tone; presence or absence of vocalizations and/or gross purposeful movements; and changes in the rate, depth and pattern of respiration or heart frequency [5,8]. Eye reflexes, position and movement are generally considered unreliable because they vary based on the type of anaesthesia that is used [23].

The rate, depth and pattern of respiration can usually be assessed by direct observation of the thoracic wall or rebreathing bag. Assessment of respiratory effort may, however, be complicated when breathing is shallow. In addition, drapes may obscure the view of the patient, although the use of clear plastic drapes greatly help to overcome this issue [6]. Changes in respiratory rate (reference: 30-60 breaths per min in an awake rabbit) may indicate excessive or too light anaesthesia and/or hypercapnia, whereas changes in the quality of respirations (e.g. increased effort made by the animal or decrease in rebreathing bag movements) may signal an obstructed airway [8,34].

Information on the adequacy of ventilation may also be derived from direct observation of colour of the nose and mucous membranes (lips, gingiva, tongue), which may be facilitated by using clear facemasks and/or pulling the tongue out of the mouth. Cyanosis of the mucous membranes may indicate presence of hypoxia as a result of apnoea, hypopnoea or upper airway obstruction (e.g. caused by secretions or kinking of the tube due to altered neck position), although the administration of medetomidine may also result in a blue to purple discolouration [33]. In addition, the capillary refill time (CRT) and colour of the mucous membranes provide information on peripheral circulation, with pale discolouration and/or CRT of >2 sec indicating compromised circulation, e.g. due to hypovolaemia or decreased cardiac contractility.

Other cardiovascular parameters that may be monitored routinely include the heart rate, and pulse rate and quality. The heart rate may be monitored intermittently by auscultation with a stethoscope and/or palpation of the ictus cordis at the level on either side of the thoracic cavity [36]. Pulse rate and quality can be evaluated by palpating the central auricular or femoral artery. Typical heart rates in conscious rabbits lie between 240-280 beats per min (range 125-325 bpm, dependent on size and stress levels), but these may drop to 120-160 bpm after administration of e.g. medetomidine [37].

Body temperatures are generally measured using a rectal thermometer or rectal probe. The latter may also be inserted into the oesophagus, which appears to result in less variation [5]. To avoid hyper- or hypothermia, body temperature should be checked regularly throughout the anaesthetic procedure and post-anaesthetic period, with appropriate measures taken accordingly to maintain body temperature as close to normal levels (i.e., 37-39 °C) as possible.

Anaesthetic monitoring equipment

A variety of different anaesthetic monitoring techniques is available to monitor the cardiovascular, respiratory and thermal parameters of a patient during surgery (Fig 10). Each of these techniques will be discussed below.

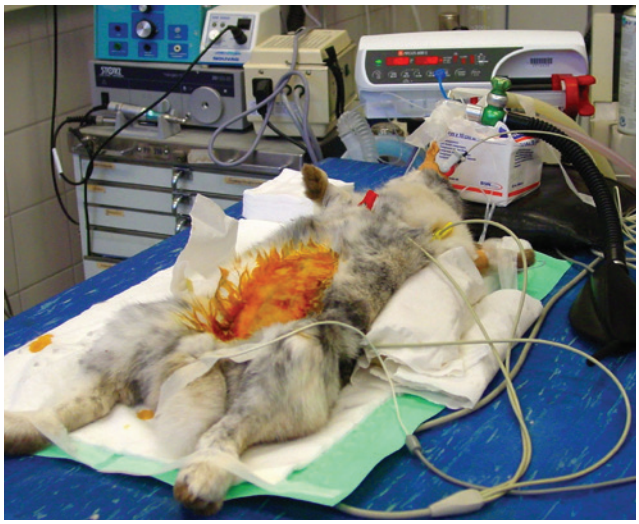

Figure 10. Rabbit prepared for abdominal surgery. After induction of anaesthesia, the rabbit was intubated with a 3.5 mm endotracheal tube using endoscope-guided assistance. In addition, a 26G IV catheter was placed in the cephalic vein to enable fluid administration throughout the procedure. The rabbit was furthermore placed on a heat mattress, with temperature checked continuously throughout surgery using a rectal probe. Monitoring further included evaluation of end-tidal C02 levels and respiration rate using capnography, evaluation of heart rate and rhythm using an ECG (connected to the extremities using alligator clips) and evaluation of 02 saturation using a pulse-oximeter placed on the tongue.

Capnography

Capnography is used to measure the carbon dioxide concentrations in expired air as a function of time. Endtidal carbon dioxide tension ($ETCO_2$) is generally used to provide a non-invasive estimate of the arterial partial pressure of carbon dioxide ($PaCO_2$) [38]. Side stream samples generally add less resistance to the anaesthetic circuit than in-line sampling, but also provide less accurate results in small-sized patients due to their relative low respiratory minute volume.

Electrocardiography (ECG)

Electrocardiography has been used in rabbits to monitor heart rate and rhythm. In contrast to dogs and cats, leads are usually attached just lateral to the elbows and laterally between the stifle and hock as the presence of fur on the ventral surface of the feet results in poor conduction [39]. Crocodile clips, hypodermic needles or pads may be applied to the skin to obtain a signal (Fig. 11). Electrode gel or alcohol may be used to improve contact. For anaesthetic monitoring, the ECG is most commonly viewed in lead II [32]. Due to the high heart rate of rabbits, however, not all monitors are able to obtain reliable heart frequencies. In addition, it should be emphasized that ECGs only

Figure 11. ECG electrodes can be connected to the body by means of alligator clips, blunted alligator clips, subdermal needles, needle electrodes and ECG-stickers [Previously published in Schoemaker & Zandvliet (2005) Electrocardiograms in Selected Species. Sem Avian Exot Pet Med 14, [26-33]]

demonstrate electrical activity and do not indicate adequate myocardial function and contractility.

Doppler flow detection

A Doppler ultrasonic flow probe is commonly used as a monitoring tool in small exotic patients [32]. By placing the probe directly over a peripheral artery (i.e., central auricular, carotid or femoral artery) or the heart, it detects a change in frequency of sound reflected back by the blood flow, which is converted into an audible sound and allows continuous monitoring of the pulse (or heart) rate and rhythm [32]. In addition, the Doppler probe may be used in combination with an occlusive cuff placed just distal to the elbow (over the dorso-medially running brachial artery) or proximal to the knee (over the dorso-medially running femoral artery) in order to obtain an indirect arterial blood pressure. To obtain the best results, the cuff should preferably be placed on the forelimb and have a width to limb circumference ratio of approximately 40% [40]. Although values obtained using this technique should not be considered as absolute, repeated measurements may be compared to track trends in blood pressure over time [32].

Arterial blood pressure measurement

In addition to non-invasive, indirect blood pressure measurement, blood pressure may also be measured directly in rabbits through arterial cannulation of the central auricular artery [40]. In general, systolic arterial pressures of 90 mm Hg or mean arterial pressures of 60 mm Hg are recommended as a minimum [32]. Blood pressure in the central auricular artery is furthermore found to be approximately 10 mm Hg lower than in the carotid artery [41].

Although the central ear artery is easily accessible, the cannulation technique is not commonly used in practice, as the equipment needed to perform such measurements is relatively expensive. In addition, the cannulation may damage the artery, resulting in necrosis and sloughing of the ear tip.

Arterial blood gas analysis

Arterial blood gas analysis may be performed to assess the patient's oxygenation and acid-base status. Although both venous and arterial samples may be collected, arterial samples are generally considered to give the most reliable results [42]. Collection sites for arterial blood samples in rabbits include the femoral, metatarsal and auricular artery (Fig 12).

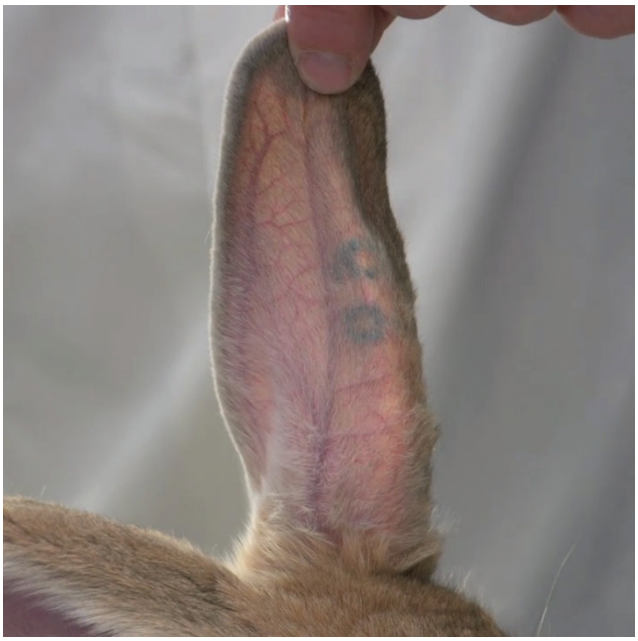

Figure 12. Photograph showing the marginal ear vein (lateral) and medial auricular artery (medial) in the ear of a rabbit. The ear vein is often used for placement of IV catheters or collection of blood samples, whereas the auricular artery is used for collecting samples for blood gas analysis or direct blood pressure measurements.

Pulse oximetry

Pulse oximetry can be used to measure oxygen saturation and appears reliable at saturation levels >85% [43]. In addition to measuring oxygen saturation, pulse oximeters may also be useful to determine the pulse rate and rhythm. The tongue is usually the best site for placement of oximeters, but may not be accessible in all patients. In such cases, the ear, digit or tail may be also be used to try and obtain a satisfactory signal [5,34]. This is, however, not always feasible when the rabbit has been anaesthetized with e.g. α2-agonists such as medetomidine, as these drugs result in vasoconstriction and poor peripheral perfusion [5,6]. In addition, excessive compression of the auricular vasculature by the clamp holding the probe may result in a poor signal [6].

Pulse oximeters require adequate pulsations in order to obtain accurate information. They may therefore be considered unreliable in patients with decreased blood pressure and/or vasoconstriction. In addition, it should be emphasized that pulse oximeters measure a pulse but this does not ensure an adequate blood flow [44].

Thermoregulatory monitoring

Measurement of core body temperature is routinely performed in almost any anaesthetic procedure, and particularly important in smaller-sized animals as they are prone to develop hypothermia. Although a standard or digital thermometer may be used to measure rectal temperature intermittently, the use of rectal or oesophageal probes is preferred as these allow continuous monitoring of the core body temperature [5,6,34].

Anaesthetic emergencies

Several conditions may be encountered in the anaesthetized rabbit that may be considered as an anaesthetic emergency. These conditions include apnoea or severe respiratory depression (<4 breaths per minute), upper airway obstruction, hypovolaemia, hypo- and hyperthermia, bradycardia and cardiac arrest. Using proper anaesthetic management, including careful and continued monitoring of the patient, as well as inhalant anaesthesia which allow better control over anaesthetic depth and duration, the risk that such an emergency situation may occur is decreased, though not completely eliminated. Tables 4 and 5 provide an overview of the various emergencies that may be encountered in rabbit anaesthesia (including their approach) and the different types of drugs that may be used in these emergency situations. Should cardiocerebropulmonary resuscitation be necessary, this follows the same priorities as in other animals: airway (A), breathing (B), circulation (C), and drugs (D). The "window of time" in which resuscitation can be effective, however, is shorter in rabbits compared to dogs and cats because of their relative high metabolic rates [6]. It is therefore generally recommended to calculate the dosages needed and draw up the syringes with the required volumes to enable adequate and timely response in case an emergency should be encountered.

Table 4. Protocol for various emergency situations that may be encountered during anaesthesia

Emergency situation	Actions to be taken
Apnoea or respiratory arrest	• Turn off anaesthetic gas or reverse injectable anaesthetics • Provide 100% oxygen • Gently compress the chest at a rate of once per second to stimulate respiration • Intubate (if not already done) • Provide intermittent positive pressure ventilation (IPPV) • Administer doxapram IM/IV/IO/IT
Upper airway obstruction (e.g. laryngospasm, laryngeal oedema, endotracheal tube blockage)	• Use suction or gauzes to clear the oral cavity of fluids or secretions (if present) • Pull the tongue out of the mouth to prevent the base from blocking the airway • Place an endotracheal tube or supraglottic airway device to create a patent airway, if possible • Ensure correct positioning of the head and neck to prevent kinking of the tube • In case the tube is blocked: remove and replace if necessary • Provide 100% oxygen, reduce anaesthetic gas if recovery is feasible • In case of laryngeal oedema, consider the use of corticosteroids and/or perform an emergency tracheotomy *Note: use of pre-emptive anticholinergics is possible to reduce production of mucous, but considered controversial as it may increase the viscosity of secretions*
Hypovolaemia, shock	• Volume replacement (preferably IV or IO) with warm isotonic fluids (boluses of 10-15 mL/kg), colloids (5-10 mL/kg), or blood
Hypothermia (<37°C)	• Minimize duration of anaesthesia and lower the amount of anaesthetics administered (if possible) • Warm and humidify the inspired air • Provide warm fluids • Provide supplemental heat with active warming devices • Increase room temperature and place rabbit in a pre-heated incubator as soon as possible *Note: hypothermia may be prevented by use of passive insulators, sparing use of antiseptic solutions; minimal shaving and keeping the incision as small as possible*
Hyperthermia (>40.5°C)	• Turn off active heating devices • Administer cold fluids IV • Administer cold water or alcohol to the footpads or exposed skin • Place in a cold environment as soon as possible
Bradycardia, cardiac arrest	• Discontinue or reverse anaesthetics • Provide 100% oxygen, intubate and give IPPV • Administer atropine in case of bradycardia or adrenaline in case of cardiac arrest • Start external cardiac massage over the heart at a rate of approximately 70-90 times per minute • Consider the use of electric shock therapy (defibrillation) in case of ventricular fibrillation (2-10 J/kg)

Post-anaesthetic considerations

As determined in the study by Brodbelt et al., almost twothirds of the anaesthetic-related mortalities occur in the postoperative period [45]. Close monitoring of the patient is therefore recommended, particularly in the first few hours after the anaesthetic period [45]. During this period, heart rate, respiration and temperature should be checked at regular intervals. If hypothermia is encountered, additional thermal support may be provided. Alternatively, the rabbit may be placed in a (pre-)heated incubator until it is fully awake (Fig. 13).

Table 5. Commonly used emergency drugs in rabbits

Drug	Dose	Effects
Adrenaline	0.2 mg/kg IV, IT, IC	Sympathicomimetic, for cardiac arrest (fibrillation or asystole); also start cardiac massage
Atipamezole	2.5-5x medetomidine dose or 10x dexmedetomidine dose	(Complete) reversal of the effects of α2-agonists
Atropine	0.02-0.04 mg/kg IV	Parasympathicolytic, treatment of (vagal-induced) bradycardia
Diazepam	1 mg/kg IM, IV, IP	Benzodiazepine, treatment of seizures
Dexamethasone	2 mg/kg IM, IV	Treatment of shock, laryngeal oedema; may not be effective and can lead to gastric ulceration and immunosuppression
Doxapram	2-5 mg/kg IV, SC	Respiratory stimulant
Flumazenil	150 mg/kg IV	Benzodiazepine antagonist
Furosemide	0.3-5 mg/kg SC, IM, IV, PO	Diuretic, treatment of pulmonary oedema
Glycopyrrolate	0.01-0.02 mg/kg SC	Parasympathicolytic, treatment of bradycardia
Lidocaine	2-4 mg/kg IV, to effect	Treatment of ventricular tachycardia/tachyarrhythmia
Naloxone	0.01-0.1 mg/kg IM, IV	Opiate antagonist, narcotic reversal
Yohimbine	0.2-1 mg/kg IM, IV	Xylazine reversal

IC = intracardiac; IM = intramuscular; IP = intraperitoneal; IV = intravenous; IO = intraosseous; PO = per os; SC = subcutaneous

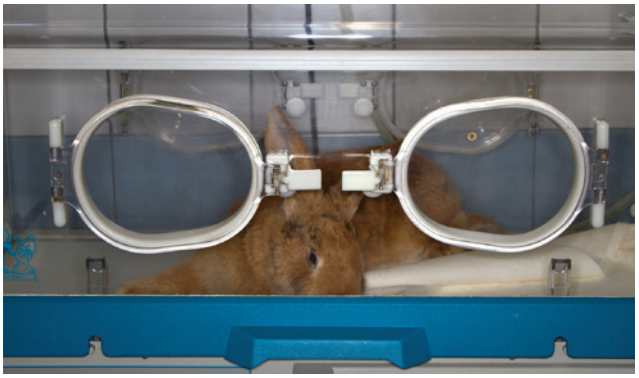

Figure 13. In the post-anaesthetic phase, the rabbit should be allowed to recover in a quiet, stress-free environment. A (pre-heated) incubator may be useful to help achieve normothermia in hypothermic animals. During the postanaesthetic period, the rabbit's vital parameters should be monitored closely.

Preferably, the rabbit is allowed to recover in a quiet, comfortable location where stressors are kept to a minimum (i.e., no barking dogs, or smell of predators). As long as the animal has not regained sternal recumbency and can move around in the enclosure, periodic turning from left to right lateral recumbency is recommended do prevent hypostatic pulmonary congestion [46]. Some authors recommend leaving the IV catheter in place until recovery is complete as this enables rapid administration of fluids, glucose or medication, if necessary [33]. In addition, rabbits may be lightly wrapped in a blanket or towel (burrito style) with the legs flexed against the body to prevent the rabbit from struggling violently and damaging its spine.

As rabbits are prone to develop hypoglycaemia due to their high metabolic rate, they should be granted access to good quality food and water as soon as they are sufficiently awake. Preferably, fibrous foods such as fresh grass, hay and vegetables should be offered as these help to stimulate gut motility and encourage the rabbit to start eating. Anorectic animals may be force-fed with formulas specifically designed for critical care patients (e.g. Critical care for herbivores, Oxbow Animal Health, Murdock, Nebraska, USA; Science recovery, Supreme Pet Foods, Suffolk, UK; Emeraid, Lafeber Company, Cornell, Illinois, USA) to prevent a negative energy balance and hepatic lipidosis. If anorexia is persistent, placement of a nasogastric or oesophagostomy tube may be considered. Anaesthesia, stress related to hospitalization in an unfamiliar environment and pain may all negatively affect the rabbit's gastrointestinal motility. Close monitoring of the rabbit's appetite and faecal production is therefore warranted. Should either be reduced, supportive care should be initiated directly with force-feeding, fluids and prokinetic drugs (e.g. metoclopramide and cisapride) [33]. Ranitidine may be added to reduce acidity of the stomach

content and enhance appetite. In addition, adequate analgesia is vital to ensure that the rabbit will start eating and drinking as soon as possible. As assessment of pain in rabbits may be difficult due to the subtlety and aspecificity of signs indicating pain (e.g. anorexia, unresponsiveness, immobility, tooth grinding and/or sitting in a crouched stance), an anthropomorphic and empirical approach is often used to determine whether and what type of analgesia is needed [47]. When choosing an analgesic regimen, various factors need to be taken into consideration, including mode and duration of action and the risk of adverse side effects to the drug (see part I 'analgesics'). Of the different analgesics available, the opioids butorphanol and buprenorphine, and the NSAIDS meloxicam and carprofen, are the most commonly used. Often, a multimodal approach is employed using both opioids and NSAIDS to ensure adequate analgesia.
Once the rabbit is considered stable enough to be discharged, it is vital to instruct the owners to carefully and closely monitor their rabbit to ascertain that the rabbit is eating and producing faecal pellets. Should the rabbit not have eaten or passed hard faeces within 24-48 hours after anaesthesia, they should be advised to bring the rabbit in for re-examination [5].

Conclusions

Rabbits are frequently sedated or anaesthetized to enable surgery and diagnostic procedures. With the increased knowledge on the pharmacokinetics and pharmacodynamics of anaesthetic agents and the arrival of newer, short-acting but potent drugs, including antagonists to reverse their effects, rabbit anaesthesia has become much more reliable, predictable and therefore safer. In particular balanced anaesthetic protocols, in which well-manageable inhalant anaesthesia is combined with injectable anaesthetics, have become commonplace in rabbit medicine and help minimize risks associated with anaesthesia. Other measures than can be taken to improve anaesthetic safety include 1) administration of oxygen throughout the procedure to prevent hypoxia; 2) assurance of a patent airway through endotracheal intubation or placement of a supraglottic airway device, which also allows assisted ventilation in case of apnoea or respiratory depression; 3) peri-operative administration of fluids to prevent hypovolaemia; 4) careful thermoregulation to prevent hypo- or hyperthermia; 5) improved ability to monitor the anaesthetic depth and vital functions throughout the procedure; and 6) the availability of drugs to counteract the effects of anaesthetics. The increased ability to monitor and manage the patient during the anaesthetic procedure, however, does not automatically guarantee survival of the patient. A thorough pre-anaesthetic evaluation and stabilization of the patient, as well as continued monitoring and support of the rabbit after it is awake, are essential to increase the chances of success and return to normal function. In this context, provision of adequate, multimodal analgesia is of particular importance and may have a significant effect on patient's welfare and outcome of the anaesthesia.

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