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The use of sevoflurane in a 2:1 mixture of nitrous oxide and oxygen for rapid mask induction of anaesthesia in the cat

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An inhalational technique for rapid induction of anaesthesia in unsedated cats using sevoflurane and nitrous oxide is described. Using a pliable, tight-fitting, face mask, sevoflurane (7.5–8%) was delivered from an out-of-circuit precision vaporiser connected to a coaxial non-rebreathing system using a fresh gas flow of 1 l oxygen and 2 l nitrous oxide per min. Cats were restrained with gentle but firm pressure applied by scruffing the dorsal cervical skin until the righting reflex was lost and the patient could be positioned in lateral recumbency. Typically, cats could be positioned on their side in a light plane of anaesthesia within 1 min of applying the mask, at which time the sevoflurane concentration was reduced to 5% or less. A similar protocol, using a lower initial concentration of sevoflurane, is recommended for old or debilitated patients. Maintenance of light sevoflurane (2–4%) anaesthesia by mask permitted minor interventions to be performed readily, including blood collection, intravenous chemotherapy, abdominal palpation, radiography and ultrasonography. More painful procedures, such as bone marrow aspiration, required a deeper plane of anaesthesia. Cats were sufficiently deep to be intubated, if this was required, about 3 min after commencing the induction. Recovery from sevoflurane/nitrous oxide anaesthesia was smooth and rapid, with most cats being able to right within 5 min of discontinuing the agents. This protocol for rapid inhalational induction and recovery is particularly suited to feline practice, where rendering an uncooperative patient unconscious greatly facilitates the completion of many minor diagnostic and therapeutic procedures, especially when these must be performed on successive days or when peripheral vascular access is limited. For longer procedures, isoflurane may be substituted for sevoflurane for maintenance of anaesthesia in order to minimise cost.

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General anaesthesia has an important role in feline practice because cats are inclined to be more fractious and less stoic than dogs. Thus, a number of diagnostic and therapeutic procedures that can be performed in dogs using firm physical restraint are less readily undertaken in the conscious cat, particularly in certain individuals. Therefore, it is often necessary to chemically restrain or to anaesthetise feline patients to perform these tasks.

Procedures requiring patient immobilisation include examination of a painful extremity, thorough abdominal palpation, inspection of the oral cavity, wound dressing, placement of urinary or intravenous catheters (particularly into the jugular vein), cystocentesis, radiography, ultrasonography, fine needle aspiration, bone marrow biopsy, administration of chemotherapy agents and radiotherapy. Drug combinations based on either a cyclohexamine (ketamine, tiletamine) combined with a second agent (benzodiazepine or phenothiazine derivative) used to effect muscle relaxation (Chambers & Dobson 1989), or an α_2-adrenoreceptor agonist (xylazine, medetomidine) sometimes combined with an opioid or ketamine (Cullen 1996), have gained widespread acceptance for this purpose.

All these drug combinations have potential undesirable side effects, including protracted or 'stormy' recoveries, vomiting, cardiovascular

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and respiratory depression and hyperglycaemia (Cullen 1996, Johnson 1999). Also, these agents are generally administered by injection, which may in itself cause a fractious patient to decompensate. The level of sedation produced by these drugs is dose dependent, and effective concentrations frequently produce a state approaching anaesthesia. Patients debilitated by old age or disease, especially those with renal or hepatic insufficiency, may experience a delayed recovery. Thus, many practitioners feel more comfortable anaesthetising feline patients for diagnostic and therapeutic procedures using propofol (Beaver & Raptopoulos 1990), alphaxolone or inhalational agents (isoflurane or halothane). Administration of these drugs on successive days may be problematic, however, as their repeated use can cause cumulative morbidity, for example by reducing appetite and food intake. Furthermore, propofol cannot be used safely in cats on successive days because of oxidative damage to feline haemoglobin, development of Heinz body anaemia and other adverse sequellae (Andress et al 1995). Clearly there is a need for a technique which rapidly and reversibly renders cats amenable to minor interventions, thereby facilitating sequential diagnostic and therapeutic procedures over a protracted period. The present report concerns the use of the new inhalation agent sevoflurane for this purpose.

Sevoflurane is a fluorinated hydrocarbon chemically similar to isoflurane. Although first synthesised in the 1970s, it was not used widely in human anaesthetic practice until 20 years later (Patel & Goa 1996). Sevoflurane is very similar to isoflurane in terms of its chemical structure and effects on the cardiovascular and respiratory systems. However, it differs in three important respects: it has lower solubility in blood than isoflurane (or halothane; blood gas partition coefficients 0.68, 1.4 and 2.5, respectively); is non-irritating to the respiratory passages; and has a pleasant smell (Clarke 1999). These features greatly facilitate rapid mask inductions in human patients, which typically occur without breath holding, coughing or sneezing (Patel & Goa 1996). This contrasts with isoflurane, which causes increased secretions, coughing and breath holding as a result of its pungency and irritant effects. Sevoflurane has become the agent of choice for inhalational induction of adult and paediatric human patients, and is widely used in human anaesthetic practice generally, especially for day-stay procedures where a speedy recovery is important (Patel & Goa 1996). A single-breath inhalation induction technique has been developed to produce sevoflurane anaesthesia rapidly in cooperative human subjects (Patel & Goa 1996, Hall et al 1997).

The use of sevoflurane in canine (Mutoh et al 1995, 1997) and feline anaesthesia has been described, however, its place in small animal anaesthesia has not yet been defined. In particular, a protocol for rapid inhalational induction in cats which exploits its unique pharmacological profile has not been described. The minimum alveolar concentration (MAC) of sevoflurane in the cat has been found to be 2.6% (Doi et al 1988), and its cardiopulmonary effects are very similar to those of isoflurane, with a dose-dependent fall in systemic vascular resistance and arterial blood pressure, but preservation of a near normal cardiac output at clinical planes of anaesthesia (Hikasa et al 1996a b, Hikasa et al 1997a b, Hiyashi et al 1998). Sevoflurane causes minimal sensitisation of the heart to the arrhythmogenic effects of catecholamines (Hayashi et al 1988, Hikasa et al 1996a), a desirable property for an agent used to produce anaesthesia in fractious feline patients. Like isoflurane, sevoflurane produces dose-dependent respiratory depression associated with a reduced respiratory rate (Hikasa et al 1996a b) and it appears effective in reversing bronchospasm (Mitsuhata et al 1994).

Sevoflurane is currently very expensive. Therefore, a technique was developed to exploit its attributes, but minimise the amount of the agent used, thereby making sevoflurane anaesthesia cost-effective in a general practice setting.

Technique

Sevoflurane (Sevorane; Abbott Australasia) is ideally administered from an agent-specific precision vaporiser, which is available with either cage or Selectatec mounts. Our preference is for machines with the Selectatec mounting system, as they permit movement of the sevoflurane vaporiser to different anaesthetic machines throughout the hospital. Generally, a machine (CIG anaesthetic apparatus) with a manifold incorporating two Selectatec mounts is utilised, as this permits sevoflurane (Penlon Elite; Sigma Chemical) and isoflurane (Isotec 3; Omeda, BOC Healthcare, Streeton, UK) vaporisers to be used sequentially (Fig 1).

Ideally, cats should be fasted for at least 6 and preferably 12 h before anaesthetic induction to ensure they have an empty stomach (Sparkes et al 1997) and thereby minimise the risk

Fig 1. Anaesthetic machine with sevoflurane and isoflurane precision vaporisers mounted using the Selectatec system.

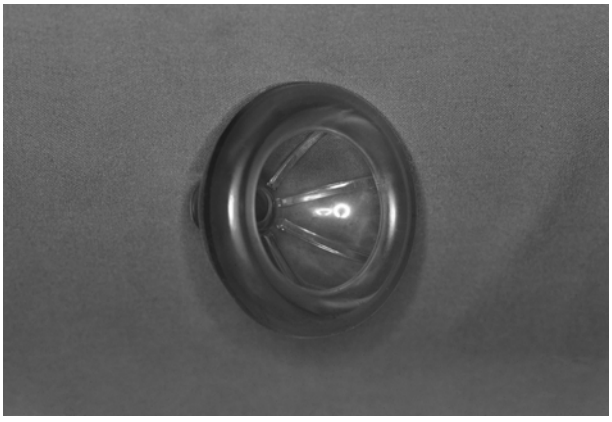

Fig 2. Conforming, pliable, silicone face mask favoured for use with domestic crossbred cats.

Fig 3. Conical, black rubber face mask favoured for use in Siamese cats.

Fig 4. Technique of restraining the cat by 'scruffing' a fold of the dorsal cervical skin, while slightly suspending the cats forequarters above the anaesthetic table.

of gastro-oesophageal reflux or aspiration. Anaesthesia is induced using a tight-fitting face mask connected to a non-rebreathing system. The expiratory limb of the Bain circuit or T-piece is connected to an active scavenging device using venturi suction to minimise contamination of the workplace with anaesthetic gases. Cats are not premedicated routinely, although some extremely fractious cats may require a light dose of sedative to allow handling. Best results are obtained with one person handling the cat and mask, with a second on hand to alter vaporiser settings, and assist as required.

The cat is firmly restrained by 'scruffing' its dorsal cervical skin, and a face mask gently apposed to its' face (Robinson 1975). A rounded, pliable, silicone mask (Fig 2) is favoured for most domestic crossbred cats, however, a conical black rubber mask usually produces a better fit in Siamese cats (Fig 3). The cat is maintained in a standing position during the induction. It is usually necessary to hold the scruff more firmly as the cat passes through the excitement stage and in some individuals it is beneficial to lift the forequarters slightly off the table top during this period.

Gas flows are started immediately after applying the mask to the cat's face. High flows are used (1 l of oxygen per min and 2 l of nitrous oxide per min) with the sevoflurane vaporiser set on 7.5–8% (approximately 3 MAC). A total gas flow of 3 l per min ensures the dead space of the mask is adequately flushed with fresh gas to prevent rebreathing of expired gases. The vast majority of cats accept the mask with minimal or no protest, and continue to breathe rhythmically and with a normal tidal volume during the induction (Fig 4). The occasional cat attempts to dislodge the mask from its face using its forelegs. In these cases, the mask in repositioned with firmer pressure, and with the operator's hands

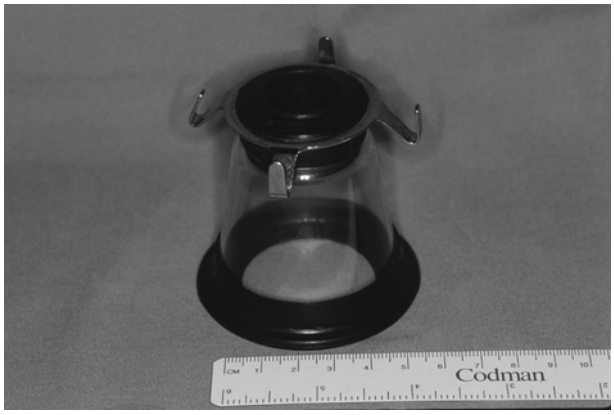

Fig 5. Self-securing transparent face mask, incorporating a black rubber diaphragm, favoured by some operators for maintenance of inhalational anaesthesia.

further along the Bain circuit tubing (out of scratching range). Restraining the cat in this fashion is only required for the 30–60 s it takes to effect a light plane of anaesthesia; muscle tone is then reduced sufficiently to position the cat in lateral recumbency. The sevoflurane concentration is then reduced to 5% (or less), and the head is extended to maintain an unobstructed airway, with the mask still applied firmly to the cat's face. At this stage, some operators prefer to exchange the conforming silicone mask for one incorporating a transparent plastic cone (through which the colour of gums and tongue can be observed readily) and a self-retaining rubber diaphragm, which minimises leakage of anaesthetic gases, but without the requirement for an assistant to manually secure the mask in place (Fig 5).

One to 2 min after applying the face mask it is generally possible to perform a variety of non-noxious procedures such as venipuncture, intravenous chemotherapy, abdominal palpation, blood collection, etc. It is also possible to desensitise the cat's larynx with topical lignocaine, and pass an endotracheal tube. For most short procedures, however, the authors' preference is to continue anaesthesia by mask. For more painful procedures, it is necessary to deepen the plane of anaesthesia for a few extra minutes before, for example, obtaining a bone marrow specimen. For procedures taking less than 5 min, sevoflurane/nitrous oxide anaesthesia is used exclusively for maintenance at concentrations of 3–4% sevoflurane (approximately 1.0–1.5 MAC), depending on the individual patient. At the completion of the procedure nitrous oxide and sevoflurane are discontinued and the oxygen flow is increased to 3 l per min. Typically cats regain consciousness, and the righting reflex, within a few minutes. Prior to recovery, sterile ophthalmic ointment is applied to the eyes, and gauze swabs are used to remove any saliva that may have accumulated in the dependant part of the cat's mouth and the adjacent portion of the mask. Cats are usually able to be positioned unassisted in sternal recumbency in a cage within 5 min of discontinuing sevoflurane, and are routinely left under a radiant heat source while recovering fully.

For procedures lasting longer than 5 min, such as abdominal ultrasonography, blood donation, or administration of a subcutaneous amphotericin B infusion, sevoflurane is used to induce anaesthesia, however, in the interests of economy anaesthesia is maintained subsequently using isoflurane. As sevoflurane is a more insoluble agent, the patient may become excessively light if it is discontinued abruptly, before isoflurane has reached effective alveolar concentrations. Therefore, we administer sevoflurane and isoflurane simultaneously during a transition period. This is achieved as follows: once the cat is in lateral recumbency, the sevoflurane concentration is reduced from 8 to 5%, and the isoflurane concentration set at 3%. Over the ensuing 5 min the sevoflurane concentration is gradually reduced to zero, while maintaining the isoflurane vaporiser on 3%.[1] The isoflurane concentration is subsequently reduced further, typically to between 1.5 and 2%, depending on the level of stimulation encountered. At the completion of the procedure, nitrous oxide and isoflurane are discontinued, 100% oxygen is administered and the cat recovers. Typically, recovery from isoflurane anaesthesia is indistinguishable from recovery from sevoflurane, even following prolonged procedures. During such long procedures it is prudent to lubricate the eyes and remove saliva from the corner of the cat's mouth and the mask periodically, or to intubate the patient. As with other halogenated anaesthetics, sevoflurane produces peripheral vasodilatation, resulting in heat loss from the body core to the extremities and environment (Machon et al 1999). For this reason, cats anaesthetised using this technique should be placed on a thermostatically controlled

[1]This is not possible with contemporary anaesthetic work stations because modern vaporisers connected in series have interlock devices that allow only one vaporiser to be turned on at a time. However, the older-style Isotec 3 vaporiser does not have such an interlocking device, so it is possible to deliver both sevoflurane and isoflurane simultaneously. Contamination of the downstream isoflurane vaporiser with sevoflurane no doubt occurs, but adverse effects referable to this have not been observed.

Table 1. Qualitative scoring system used to assess the induction and recovery from sevoflurane/nitrous oxide anaesthesia

Category	Criteria
(a) Induction	
Excellent	Nil or negligible excitement; minimum pressure on the scruff required for restraint; no struggling; smooth transition to a surgical plane of anaesthesia
Good	Minimal excitement (some paddling or vocalisation) *or* one episode of minor resistance requiring firmer physical restraint ('scruffing') *or* coughing or sneezing (less than 5 s duration)
Satisfactory	More than two episodes of struggling *or* a prolonged episode of resistance lasting in excess of 20 s *or* coughing or sneezing (greater than 5 s duration)
Poor	Constant struggling throughout the period of induction with continued resistance to restraint *or* any significant adverse event (vomiting, protracted coughing or sneezing) *or* struggling sufficiently severe that the induction had to be abandoned
(b) Recovery	
Excellent	No excitement; quiet and smooth progression through the stages of anaesthetic recovery
Good	One minor episode of excitement (less than 30 s duration) *or* coughing or sneezing (less than 5 s duration)
Satisfactory	An episode of excitement (lasting more than 30 s) requiring manual restraint *or* one significant adverse event (dyspnoea, vomiting, protracted sneezing lasting longer than 5 s)
Poor	Violent ballistic recovery *or* two significant adverse events

heating device, and subjected to an appropriately positioned radiant heat source.

Results

Sevoflurane in nitrous oxide and oxygen has been used to induce anaesthesia in excess of 150 cats since March 1999. In 36 anaesthetics administered to 28 cats by the senior author (ST) using an initial sevoflurane concentration of 7.5%, the loss of the righting reflex took a median of 53 s (range 25–81 s), while recovery (defined as the ability to lift the head) took a median of 240 s (range 60–500 s). In the 11 cats that were subsequently intubated, the median time to intubation was 185 s (range 124–247 s). The quality of induction of anaesthesia (Table 1) was considered excellent in 29 cats, good in six cats and satisfactory (some struggling) in one cat. It was not necessary to abandon the induction due to violent struggling, vomiting or other adverse sequelae in any cat. It should be emphasised that several cats anaesthetised in this fashion were considered too fractious for even a routine physical examination to be performed prior to induction. During stable sevoflurane/nitrous oxide anaesthesia the median heart rate was 168 (range 116–250 beats per min), the median respiratory rate was 28 (range 16–56 breaths per min) and the median systolic blood pressure measured indirectly using a Parkes Doppler device was 131 (range 70–149 mmHg). The quality of recovery (see Table 1) was considered excellent in 26 cats, good in five cats, satisfactory in one cat and not recorded in four. Recovery from sevoflurane/nitrous oxide anaesthesia was characteristically rapid, smooth and complete. Nausea and vomiting were not observed during the recovery period, but shivering was noted occasionally.

One of the authors (RM) has utilised a technique using 8% sevoflurane (rather than 7.5%), but without detailed record keeping, in excess of 200 feline anaesthetics to facilitate many different procedures, including routine general anaesthesia for teeth scaling, castration and lancing cat fight abscesses. The technique has proved versatile and has improved the speed and efficiency

with which diagnostic and therapeutic procedures can be completed through the course of a busy day in a general veterinary hospital. Several cats received several successive anaesthetics using this technique, for example, to deliver subcutaneous amphotericin B infusions (which are given on a twice weekly basis for 10 weeks to treat cryptococcosis; Malik et al 1995), intravenous chemotherapy for lymphosarcoma (which is given every two weeks for 16 weeks, then monthly; Gabor et al 1996) or blood donation for transfusion therapy. Cats have tolerated successive anaesthetics without any untoward sequelae, and without becoming excessively wary of the mask. The use of sevoflurane/nitrous oxide anaesthesia to facilitate these procedures has been perceived universally as a substantial improvement over techniques used in the past. The technique has proved particularly applicable to adult cats of an agreeable temperament, although numerous cats considered too fractious to attempt venipuncture without sedation were successfully anaesthetised using this new technique. Indeed, it has become our method of choice for restraining cats for short painful procedures and for managing intractable cats, supplanting our previous approach, which consisted of subcutaneously administered midazolam (0.3–0.5 mg/kg)/ketamine (4–6 mg/kg) for sedation, often supplemented with inhalation agents by mask.

It should be mentioned that on many occasions this crash induction technique has been used in aggressive cats that were shown subsequently to have significant systemic disease. On four occasions patients became excessively deep, necessitating temporary discontinuation of inhalational agents, administration of 100% oxygen and in two occasions intermittent positive pressure ventilation via the tight fitting face mask for 30–60 s. This has not been a continuing problem, as our evolving experience when confronted with cats likely to be systemically ill is to utilise lower concentrations of sevoflurane throughout both the induction and maintenance phases of anaesthesia.

Discussion

The present report describes a practical method for using sevoflurane/nitrous oxide to induce rapidly light surgical anaesthesia suitable for restraint of cats for short diagnostic and therapeutic interventions, or to facilitate endotracheal intubation with subsequent maintenance of anaesthesia using isoflurane. The induction of anaesthesia was generally fast, smooth and pleasant for the patient, as was the recovery.

Although sevoflurane/nitrous oxide anaesthesia is more costly and requires greater observation of the patient compared to ketamine or medetomidine-based sedation, it offers the following advantages:

(a) It is not necessary to give an intramuscular, subcutaneous or intravenous injections to cats which are already fractious and about to lose their composure. Thus, cats on the border of becoming intractable are not 'pushed over the edge' by the prick of a needle or the sting of low pH solutions;

(b) Procedures can be completed more rapidly, as the onset of immobilisation with sevoflurane is faster than with intramuscular or subcutaneous ketamine;

(c) The depth of anaesthesia can be tailored to the physical status of the individual patient, and the particular procedure being undertaken. It is possible, for example, to deepen the plane of anaesthesia transiently, immediately before performing a painful or critical procedure;

(d) The transition to intubation and full general anaesthesia using isoflurane is made readily if circumstances dictate, and with a more normal respiratory pattern than is encountered following the administration of ketamine;

(e) As neither sevoflurane nor nitrous oxide has a requirement for hepatic or renal biotransformation for recovery from anaesthesia, they can be administered to patients with liver or kidney disease without concern that the duration of anaesthesia will be unduly prolonged;

(f) Recovery from anaesthesia is not only faster but of a vastly superior quality to recovery following a cyclohexamine based anaesthetic. Indeed, it is typically impossible to tell that the cat had been anaesthetised 30 min after completion of the procedure. The smooth and pleasant recoveries are in striking contrast to the protracted and sometimes stormy recoveries encountered following midazolam/ketamine;

(h) There is no need to subject peripheral veins to repeated venipuncture, therefore maintaining them in a state conducive to catheterisation should the need arise;

(i) Heart rate, blood pressure, respiratory rate and alveolar ventilation are very similar to that encountered during isoflurane anaesthesia, or indeed the conscious state (Patel & Goa 1996, Hikasa et al 1997a);

(j) Although the agent is expensive per se, there are hidden cost benefits related to its use such as less time expended in monitoring during the recovery period and more efficient utilisation of personnel and time. At a dial setting of 8% and with a fresh gas flow of 3 l/min, 1.3 ml/min of sevoflurane is consumed theoretically. The wholesale price of 5 min of sevoflurane anaesthesia is thus approximately $9, as 250 ml of this agent currently costs $330 (Australian).

We have found a few adverse effects associated with inhalational inductions using sevoflurane in nitrous oxide and oxygen:

(i) The technique is generally less successful for brachycephalic cats, especially in those individuals with stenotic nares. Firstly, it is more difficult to coapt the mask to the cat's face. Secondly, the partial upper airway obstruction impedes uptake of the anaesthetic agents and thereby prolongs the induction. The technique is similarly not suitable for cats with other causes of upper airway obstruction, and an intravenous agent that provides rapid control of the airway (such as ketamine or propofol) is preferred;

(ii) Inhalational anaesthesia is not inherently safe and a rapid induction protocol with sevoflurane in nitrous oxide is probably not dissimilar to intravenous propofol or thiopentone in terms of its cardiovascular and respiratory effects, apart from the 'retrievability' of the gaseous agents. Induction using 7.5–8% sevoflurane/nitrous oxide in cats with debilitating systemic disease is probably unsafe, as patients may become excessively deep. In these cats, using the same technique but with a lower initial concentration of sevoflurane (4–6%) is undoubtedly safer;

(iii) Minor contamination of the environment with sevoflurane and nitrous oxide is unavoidable using this technique, although the extent of the problem can be minimised by use of tight fitting face masks, appropriate scavenging of the anaesthetic system using a venturi suction device and having the vaporiser turned off whenever the mask in not apposed to the cat's face. Environmental contamination, however, is substantially less than that which occurs using an induction chamber. Induction room contamination may be reduced further by use of novel face mask designs, such as the recently developed 'Double Mask' manufactured by Swedish Medicvent AB company. In this system, a gas extraction sleeve is positioned around the mask, so that the scavenger in the coupler housing removes in excess of 90% of those gases escaping from between the mask and the patient;

(iv) Recovery from sevoflurane/nitrous anaesthesia is so rapid that it is prudent to administer an opioid (eg methadone, butorphanol or buprenorphine) some time before discontinuing the anaesthetic when painful procedures have been performed, to provide a smooth transition to analgesia in the recovery period (Patel & Goa 1996, Clarke 1999).

Following the guidelines provided, the use of sevoflurane should prove cost effective in feline practice, as the expensive agent is only administered briefly, typically for less than 5 min. Our experience has been that clients readily accept the additional cost of sevoflurane anaesthesia once the benefits of the procedure are explained. Where a longer period of immobilisation is required, maintenance of anaesthesia using isoflurane in nitrous oxide and oxygen is far more economical. Restriction of sevoflurane to the induction of anaesthesia exploits its major advantages which make the onset of anaesthesia rapid and smooth. The use of new low resistance, lightweight, non-rebreathing systems such as the Miller Maxima (Life-Air Ltd, Pietermaritzburg, South Africa) and 'Uniflow' (Intersurgical, UK) may make the use of sevoflurane more affordable for both induction and maintenance of anaesthesia, as they require much lower fresh gas flows than either the Bain or modified Ayre's T-piece (Holden 2000).

Sevoflurane can be utilised similarly without the concurrent administration of nitrous oxide. In preliminary experiments in ferrets and kittens we have found minimal difference in the duration or quality of anaesthetic inductions when using sevoflurane with and without nitrous oxide (Tzannes 1999). We choose to use nitrous oxide to speed the induction of sevoflurane anaesthesia further through the second gas effect, to reduce the amount of halogenated anaesthetic used for maintenance (as nitrous oxide reduces the MAC for sevoflurane) and to provide additional analgesia during interventions that are transiently painful. In practices where nitrous oxide is unavailable, sevoflurane can be used in 2–3 l per min of 100% oxygen in an identical fashion to the method we describe here.

In practices that wish to use sevoflurane but cannot afford the cost of a new sevoflurane vaporiser, enflurane vaporisers (which can be obtained inexpensively second-hand) can be used to deliver sevoflurane with reasonable accuracy at concentrations of up to 5% or 7%, depending on the vaporiser (Greene & Cregan 1997).

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