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THE UNIVERSITY OF NEWCASTLE

ANIMAL CARE AND ETHICS COMMITTEE

POLICY DOCUMENT

Preferred drugs and regimes for animal anaesthesia and analgesia

As detailed in the NSW Animal Research Act and Regulations, and the "Australian Code of Practice for the Care and Use of Animals for Scientific Purposes", the use of anaesthetic, analgesic and tranquillising agents must be suitable for the species, appropriate for the purpose of the study, and consistent with current veterinary and medical practice. Surgical procedures must be performed under appropriate local or general anaesthesia. Analgesia must be provided for animals undergoing recovery surgery. The pre-anaesthetic preparation of the animal, monitoring of the administration and depth of the anaesthesia, post-anaesthetic monitoring and importantly, the relief of pain and distress must receive careful attention.

This document describes a range of analgesic agents and anaesthetic techniques recommended for many species of laboratory animals. It is intended to provide broad guidelines only, rather than exhaustive information on the range of agents and regimes available.

Since new anaesthetic agents are continually being developed, researchers should consult with the University Veterinarians regarding regimes that are not discussed in this document (Dr Robyn Gentle, 02-49216222; Dr Mary Bate, 02-49217086).

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PART 1. DEFINITIONS

Anaesthesia: loss of sensation as the result of drug-induced depression of nervous tissue, either locally or centrally.

Analgesia: the temporary abolition or diminution of pain perception.

Local anaesthesia/analgesia: loss of sensation in a prescribed body area (usually infers blockade of a specific nerve or infiltration of a small area with local anaesthetic, eg. intercostal nerve block).

Regional anaesthesia/analgesia: loss of sensation in a larger, though limited body area (usually infers blockade of a large nerve or group of nerves with local anaesthetic, eg. epidural anaesthesia).

General anaesthesia: loss of consciousness, analgesia, suppression of reflex activity and muscle relaxation.

Tranquillisation: state of reduced anxiety and relaxation, but still aware of surroundings.

Sedation: state of CNS depression and drowsiness; including reduced awareness of surroundings.

Narcosis: drug induced state of deep sleep, from which the patient may or may not be arousable.

Light anaesthesia: the state of immobility and unconsciousness, with retention of responsiveness to even minor surgical procedures.

Surgical Anaesthesia: stage/plane of general anaesthesia that provides unconsciousness, muscle relaxation, and analgesia sufficient to allow painless surgery.

Balanced Anaesthesia: the use of multiple drugs with complementary actions to induce and maintain anaesthesia; each drug used usually provides one component of anaesthesia, and can often be used at reduced doses to minimise adverse side effects.

Balanced analgesia: the use of a combination of drugs with different modes of action to produce sequential blocks in the nociceptive pathways, and achieve beneficial additive or synergistic analgesic effects.

Dissociative Anaesthesia: the state of anaesthesia produced by drugs (e.g. ketamine) that disassociate the thalamocortical and limbic systems, resulting in a cataleptoid state, usually with muscle rigidity.

Neuroleptanalgesia: a state of quiescence, altered awareness and analgesia, produced by the administration of a combination of a neuroleptic (tranquilliser/sedative) agent and a narcotic (opioid) analgesic (eg. acepromazine + morphine).

PART 2. ABBREVIATIONS

CNS	Central Nervous System
IM	intramuscular
IP	intraperitoneal
IV	intravenous
NSAID	Non-steroidal Anti-Inflammatory Drug
PO	per os, or by mouth
SC	subcutaneous
WFI	Water For Injection

PART 3. GENERAL

Analgesic agents decrease or prevent the perception of pain. Anaesthesia involves analgesia with suppression of reflex activity, loss of muscle tone, and central nervous system (CNS) depression to variable degrees. Analgesia, and unconsciousness must always be achieved during anaesthesia unless local anaesthesia is required. The requirement for depression of reflex activity, muscle tone and the central nervous system will vary with the procedure to be performed. The anaesthetic agent chosen must be safe

and humane for the animal, safe for humans, and cause minimal interference to the experiment.

Many anaesthetic agents are not registered for use in small laboratory animals. This means that extensive evaluation is necessary, not only of the physiological effects and efficacy of the agent as an anaesthetic or analgesic, but also of their histological effects on various tissues especially those at the injection site, and their effects on research parameters.

When selecting an anaesthetic regime, the following factors must be considered:

- scientific parameters and goals
- species to be used
- plane or depth of anaesthesia/analgesia required
- whether the procedure is recovery or non-recovery
- duration of anaesthesia
- drugs to be used, and their physiological interaction and effect that may influence experimental results
- humaneness of the technique (eg. ease of induction, smoothness of recovery)
- side-effects of the drugs on the animal (eg. diarrhoea, vomiting)
- method(s) of administration and dose rates
- experience of investigators with technique
- anaesthetic monitoring techniques
- monitoring during the recovery period
- safety of investigators
- available equipment

Only after all of these factors have been considered can an effective anaesthetic regime be devised.

PART 4. SPECIFIC ISSUES

Variations in response

There are significant variations in response to anaesthetic and analgesic agents according to the species, strain and sex of the animal. There may also be considerable individual variations between animals of the same strain and sex.

It is unwise to extrapolate from one species to another. In addition, direct extrapolation from human to animals is as faulty as is the reverse.

Interactions with research protocol

When selecting an anaesthetic or analgesic agent or regimen, it is important to consider potential interactions with the research protocol. To minimise these interactions, the major pharmacological and physiological effects of the various agents should be reviewed. It is important to appreciate that a superficial consideration of the compound's effects may be insufficient. In addition, one should not to assume that such an assessment has been carried out by research workers whose publications include details of the anaesthetic regimen used. Finally, it is important to place such interactions in the context of the overall response to anaesthesia. There is little point in carefully selecting an anaesthetic, then allowing the animal to become hypothermic, hypoxic and hypercapnic because of poor anaesthetic management. The procedure itself (eg. cannulation, surgery) may also produce prolonged effects that interact with the research protocol.

It is not within the scope of this document to provide information on these aspects of anaesthesia and analgesia. Researchers should consult widely concerning these issues so that anaesthetic and analgesic regimens may be selected that are both humane and provide the minimum of interference with the overall aims of the research project.

Use of "stock solutions"

Dilution of drugs may be necessary prior to their use in small laboratory animals. Such dilutions may also involve mixture of common anaesthetic or drug combinations. However, the long-term storage and subsequent use of any "stock solution" following its dilution for use in a batch of animals is not recommended. Concerns regarding this practice include the lack of data or studies with respect to:

(i) The stability of the components of the drugs when they are mixed and stored.
(ii) The length of time that a stock solution can be safely stored.
(iii) The effect of dilution on the bacteriostatic action of the preservative in the parent solutions.
(iv) Specific recommendations on the manner in which stock solutions should be stored.

The animal research legislation requires the use of anaesthetic, analgesic and tranquillising agents to be consistent with current veterinary and medical practice. The storage and use of stock solutions does not accord with best veterinary or medical practice.

All dilutions of anaesthetic and analgesic drugs used in laboratory animals must be prepared fresh prior to use. Provided the solution is discarded immediately following the procedure, preparation of dilutions of anaesthetic or analgesic drugs for individual batches of animals is acceptable.

Care must be taken that only compatible drugs are mixed in the same solution.

Dilution of drugs

For most drugs, dilution with sterile “water for injection” (WFI) rather than saline is recommended in order to prevent precipitation. However, investigators should check the directions accompanying the drug.

Reversible anaesthesia

Many anaesthetic regimes are associated with prolonged recovery periods. This is especially true for rodent anaesthesia where many anaesthetic regimes administered via the intraperitoneal or subcutaneous route share a common feature of producing 30-60 minutes anaesthesia, followed by recovery times of two to four hours. During the recovery period, the animals remain susceptible to hypothermia and have some degree of respiratory and cardiovascular depression. **These effects can be largely overcome by use of reversible anaesthetic regimens.** Antagonists for opioids (eg. morphine) such as naloxone have been available for many years, and the alternative of using partial agonists or mixed agonist/antagonists (eg. buprenorphine and butorphanol) has also been well established. The alpha-2 adrenoreceptor antagonist, atipamezole, provides rapid and complete reversal of alpha-2 adrenergic agonists such as medetomidine and xylazine. Atipamezole has been developed specifically to reverse the effects of medetomidine. Although reversal of xylazine with atipamezole is possible, it is preferable to use medetomidine if reversal is contemplated. (Yohimbine is a relatively non-selective antagonist of xylazine and medetomidine and is not recommended.) An antagonist for benzodiazepines, flumazenil, has been available for some time, but there have been few reports of its use in laboratory species.

Isoflurane versus halothane

Some inhalation anaesthetic agents are potentially dangerous to personnel. To minimise occupational health and safety concerns, the use of isoflurane is recommended in preference to halothane because, in humans, only 0.17% of the inspired isoflurane is metabolised by the liver and kidneys. In contrast, 20-25% of inspired halothane in humans is metabolised by the liver and kidneys.

Isoflurane may be more expensive per bottle compared to halothane. However, the cost of isoflurane has decreased significantly in the last few years. When costs are compared on the basis on the volume required to anaesthetise an animal, the cost of halothane and isoflurane are similar.

Neonatal anaesthesia

Anaesthesia of neonatal animals is challenging because they have a reduced capacity to detoxify a wide range of drugs and hence their response to anaesthetics can differ considerably from adult animals. Prolonged recovery may lead to depletion of hepatic glycogen stores and result in hypoglycaemia. Other problems are increased susceptibility to hypothermia, increased possibility of poor pulmonary and circulatory function, and rejection of the young by the mother following the procedure (particularly in rodents). For these reasons, it is preferable to use inhalation anaesthesia (eg. halothane, isoflurane) so that recovery is rapid and normal feeding is resumed as soon as possible. Neonatal animals usually require a higher concentration of anaesthetic (eg. neonatal rats require 2-3% halothane for maintenance compared to approximately 2% for adult rats).

<u>Hypothermia for anaesthesia neonatal rodents</u>

Hypothermia has been recommended for anaesthesia of neonatal rats and mice up to 10-14 days of age. It

seems likely that during hypothermia, the degree of suppression of the peripheral and central nervous system is sufficient to prevent the animal experiencing pain. Disadvantages include increased risk of ventricular fibrillation, tissue hypoxia and metabolic acidosis after rewarming.

Rapid chilling can be achieved by placement of the pups into a prepared container, with the container then placed on crushed or dry ice, in ice water, or in a freezer compartment of a refrigerator. Placement of pups directly onto a cold source may result in tissue necrosis and is not recommended. The resultant torpor may last up to 10 minutes. Recovery from anaesthesia can be rapid. However, do not use aggressive re-warming techniques (eg. heating pads or lamps) to avoid tissue damage. An incubator at 33^0C for 20-30 minutes is appropriate.

PART 5. ANAESTHETIC MANAGEMENT TECHNIQUES

Pre-Anaesthesia

(i) Acclimatise the animal to handling to reduce the affects of stress and the possibility of injury to animal and personnel during induction.

(ii) Check that the animal is healthy, and free from hepatic, renal or respiratory disorders.

(iii) Record body weight and food and water intake. This will assist in the post-operative monitoring.

(iv) Withhold food (12-16 hours) and water (3-4 hours) for those species that may vomit during induction of anaesthesia (cat, dog, ferret, non-human primate). Pigs rarely vomit on induction although withholding food for 12 hours is common.

Pre-anaesthetic fasting of small rodents and rabbits is generally unnecessary since vomiting during induction does not occur in these species. In addition, fasting of small animals may result in a depletion of glycogen reserves, and the development of hypoglycaemia. Rabbits and rodents are coprophagic. Hence if an empty stomach is required for the research protocol, measures to prevent ingestion of faeces are necessary. Guinea pigs store food in their cheek pouches and may aspirate this material during induction.

Large or medium-sized birds (eg. ducks, chickens, pigeons) may be starved for 6-12 hours to reduce the risk of regurgitation of the contents of the crop. Smaller birds should not be fasted for longer than 2 hours, to avoid the risk of inducing hypoglycaemia.

Opinion varies as to whether ruminants should be starved before induction of general anaesthesia. Fasting and water deprivation may have little effect on the volume of digesta present in the rumen, and whether or not regurgitation of rumenal contents occurs. However, fasting may reduce the incidence of rumenal tympany (“bloat”) by decreasing the volume of fermentable ingesta. This appears to be a greater problem in animals that are grazing. Even with these precautions, some ruminants will develop rumenal tympany while others will regurgitate.

(v) Any premedication is usually given 30-40 minutes before anaesthetic agents.

(a) Analgesics given pre-operatively will inhibit nociceptive input to the central nervous system, thus providing a degree of prevention as opposed to treatment of pain. These agents can be combined with a sedative (eg. acepromazine - buprenorphine).

(b) Sedatives (eg. acetylpromazine, diazepam) may reduce the anxiety of the animal and assist it its restraint.

(c) Anticholinergic agents (atropine or glycopyrrolate) will reduce the side effects of many anaesthetic agents eg. the stimulation of respiratory secretions and the parasympathetic stimulation of the cardio-pulmonary system. **Do not use** anticholinergic agents to treat bradycardia, either simultaneously with medetomidine or following medetomidine, as the combination could lead to adverse cardiovascular effects.

(d) Following the use of a sedative, tranquilliser or analgesic, the dose of some anaesthetic agents may need to be reduced.

Stages of Anaesthesia

It is important to realise that the time taken for an animal to pas through each stage of anaesthesia outlined below will vary with the anaesthetic agent used, and the response of the individual animal.

The signs of the stages of anaesthesia are based on:

1. Observation of the patient
2. Changes in blood pressure and pulse
3. Eye patterns and reflexes
4. Respiratory pattern
5. Chest and abdominal muscles
6. Warmth of the skin
7. Capillary refill time and mucous membrane colour.

The sequential effects of an increasing arterial concentration of an anaesthetic agent can be summarised as follows:

1. Analgesia and amnesia
2. Loss of consciousness and motor co-ordination
3. Reduction of protective reflexes
4. Blockage of afferent stimuli
5. Muscular relaxation
6. Respiratory and cardiovascular depression
7. Depression of cardiovascular and respiratory reflexes
8. Apnoea - respiratory arrest
9. Cardiac arrest

Stage 1. Voluntary excitement. Stage of analgesia without loss of consciousness; some disorientation. Characterised by voluntary motor excitement, struggling and ataxia. This stage lasts from beginning of anaesthesia to loss of consciousness.

1. heart rate (HR) increases
2. respiration rapid and deep
3. excessive salivation
4. urine and faeces voided
5. pupils normal or dilated.

Stage 2. Involuntary excitement. Stage of narcosis. Characterised by a period of involuntary excitement or delirium with the animal beginning to lose consciousness and voluntary control. Late in this stage, analgesia is present and, in humans, awareness and recall are absent.

1. cortical depression and loss of consciousness
2. release of higher centres control (exaggerated reflex struggling)
3. pupils dilate
4. brisk nystagmus may be present
5. swallowing, retching, vomiting may occur
6. irregular respiration with breath-holding.

Stage 3. Surgical Anaesthesia. Characterised by loss of consciousness, pain sensation and powers of coordinated movement. Arbitrarily divided into 4 planes which reflect the progressive dose-dependent depression of the CNS from the cortex to the midbrain to the spinal cord.

Plane 1: Analgesia and muscle relaxation are only sufficient for minor non-invasive procedures.

1. regular respiration - denotes onset of Stage 3
2. pupils constricted
3. may be nystagmus and change in position of eye
4. lid and palpebral reflexes present
5. pharyngeal and laryngeal reflexes persist
6. salivation persists
7. muscle tone persists

Plane 2: Difficult to generalise with different agents. Analgesia and muscle relaxation are sufficient for most surgical procedures.

1. usually eyeball becomes centrally located and motionless; with halothane eyeball remains eccentric
2. decrease in depth and increase in rate of respiration. Surgical stimulation will create a respiratory response
3. maintenance of heart rate and blood pressure (varies with species and agent)
4. oral and pharyngeal reflexes may still be present in the cat
5. lachrymation and salivation diminished
6. muscle tone lessens

Ketamine, nitrous oxide, enflurane, chlorose and trichloroethylene are examples of agents that are incapable of inducing "Stage 3, Plane 2" anaesthesia. Accordingly, they should not be used alone for painful procedures.

Plane 3: As this plane is achieved, all reflexes are abolished and paralysis of intercostal muscles begins.

1. respiratory effort changes as intercostal muscle paralysis develops; respiration becomes mainly abdominal
2. eyeball centrally fixed
3. lacrimation, salivation, oropharyngeal reflexes abolished
4. vagal reflexes due to traction on abdominal or thoracic viscera retained
5. muscle relaxation marked

Plane 4: A dangerous level of anaesthesia, characterised by complete paralysis of intercostal muscles, papillary dilatation, and severe cardio-pulmonary depression.

1. intercostal and abdominal muscles completely paralysed
2. lid and corneal reflexes absent
3. pupils dilated and photomotor reflexes abolished
4. heart rate decreased; cardiovascular compensatory reflexes seriously diminished.

Stage 4. Bulbar paralysis. All reflex activity is lost. Characterised by jerky irregular respiration and respiratory arrest. Cardiac arrest follows closely after respiratory arrest. At this point, immediate vigorous corrective therapy is required to successfully resuscitate the patient.

Anaesthesia

(i) Decide on anaesthetic technique based on species, experimental protocol, and whether the procedure is survival or non-survival. Anaesthetics should be administered with appropriate equipment, in a room away from other animals.

(ii) When administering gaseous anaesthesia, use the appropriate machine and vaporiser so that the dose (percent) of administered anaesthetic can be controlled. Use of an anaesthetic "jar", where the animal is placed into a chamber containing a pad of gauze or cotton wool soaked in liquid anaesthetic, is not recommended. With this technique, the concentration of anaesthetic achieved within the container is unpredictable and is invariably dangerously high if potent, easily vaporised anaesthetics such as halothane or isoflurane are used. In addition, direct contact with liquid anaesthetic is extremely unpleasant for the animal as it is irritant to mucous membranes. It is also difficult to prevent contamination of the environment with anaesthetic vapour and thus presents a potential occupational health and safety hazard.

(iii) When administering gaseous anaesthesia to small animals (<10kg), an Ayres T-piece or a Bain coaxial circuit is recommended to provide a low resistance, low dead space circuit.

(iv) Following induction, place the animal in a position with its head and neck extended to help ensure that its airway remains clear and unobstructed.

(v) Intubation of the trachea will ensure an adequate airway. This can be achieved in most species. The use of lignocaine spray on the larynx prior to intubation has been used to prevent laryngospasm that occurs in some species (eg. cat, diving birds).

(vi) If inhalation agents are not used, provision of oxygen by face mask is advisable to prevent the development of hypoxia.

(vii) Monitor effects of the anaesthetic.

(a) As a minimum, monitor the depth of anaesthesia via assessment of the presence or absence of reflexes. For example, surgical anaesthesia is achieved when the following reflexes are lost:
- righting reflex ie. animal will not attempt to right itself if placed on its back.
- palpebral reflex in response to stroking eyelids.
- withdrawal reflex ie. flexion of leg when interdigital skin is pinched.
- tail pinch reflex ie. movement following a firm pinch of the tail (rats and mice).
- ear pinch reflex ie. head shaking in response to pinching the pinna (guinea pigs, rabbits and cats).
- anal sphincter tone, and the muscle tone of the jaw.

(b) Other monitoring criteria may include those related to the respiratory and cardiovascular systems:

Respiratory system
- Clinical observations - Monitor depth and rate of respiration (increase in depth and decrease in rate signify anaesthesia).
- Respiratory monitor (eg. Ap-Alert). Some instruments may not be sufficiently sensitive to detect apnoea in small species such as the rat or mouse.
- Pulse oximetry – to measure the percentage saturation of arterial blood (cardiorespiratory function).
- End-tidal CO_2
- Blood gas analysis.

Note: Respiratory obstructions may be caused by secretions, foreign objects, tongue, or abnormal neck positions. Respiration can be compromised by compression of the thorax by the weight of an arm or equipment.

Cardiovascular system
- Clinical observations – colour of mucous membranes, capillary refill time, heart sounds and heart rate (stethoscope of oesophageal stethoscope), peripheral pulse quality.
- Electrocardiography.
- Blood pressure – systemic arterial pressure, central venous pressure.

(c) Body temperature may be monitored, depending on the size of the animal and the equipment available. Maintain as close to normal levels as possible, especially in small species. Smaller animals have a high surface area/weight ratio and will lose heat rapidly under surgical anaesthesia. Therefore the use of a heating pad or warm hot water bottle is recommended.

(viii) Maintain body fluids. Intravenous or subcutaneous infusion of suitable fluids (eg. lactated ringers, normal saline) is especially important with lengthy anaesthetics or highly invasive surgery.

(ix) When using gaseous anaesthetics, and in particular nitrous oxide, the animal should be given a minimum of 5 minutes of oxygen (no anaesthetic agent) at the end of the procedure to ensure adequate oxygenation of tissues.

(x) The use of anaesthetic monitoring checklist is recommended. A sample checklist is provided in Appendix 1.

Indications of anaesthetic overdose

(i) Respiration is slow and irregular, becomes diaphragmatic, or may cease.
(ii) Mucous membrane and skin colours may be pale to cyanotic.
(iii) Pulse is weak to imperceptible.
(iv) Blood pressure is reduced to shock level.
(v) Cardiac dysrhythmias may occur.
(vi) Capillary refill time progressively slows to 3 or more seconds.
(vii) Cardiovascular, CNS, musculoskeletal, gastrointestinal, and ocular reflexes are greatly diminished or cease.

Post-Anaesthesia

Animal must be observed during recovery from anaesthesia to ensure:

- a patent airway.
- that the animal's body temperature is maintained.
- that it does not injure itself.
- that any post-operative pain is adequately controlled.

If an endotracheal tube is in place, it must not be removed until the swallowing reflex has returned. Non-ruminant species should be placed on their sides with head and neck extended. Ruminants should be propped up on their sternums to minimise the risk of over-distension of the rumen with gas (rumenal tympany or bloat) and of inhalation of regurgitated rumen contents.

The animal's homeothermic responses will remain depressed until it has recovered from anaesthesia. Thus, the ambient temperature of the recovery area should be warm (30-35^{o}C for small rodents, 25-30^{o}C for cats and dogs). Supplemental heat may be provided (eg. warming lamp, heat pad, incubator). However, care should be taken not to overheat the animal. Monitor both the body temperature of the animal and the temperature of its immediate environment.

Small rodents should be housed alone during recovery to prevent attack from cage mates. If surgery has been performed, cage bedding should be such as to prevent wound contamination.

If animals have undergone an invasive procedure, careful monitoring during the post-operative period is essential to assess whether analgesia has been effective, and whether additional analgesia is required. The dose or frequency of administration should be modified according to the needs of the individual animal.

Fluids assist in the recovery of the animal. Normal saline (0.9% NaCl) can be given intravenously (slowly), subcutaneously or intraperitoneally at a dose of up to 3-4% of the animal's body weight.

Routes of Administration

(i) Inhalation. Induction of anaesthesia can be achieved using an induction chamber or a facemask.

During the initial phase of mask induction, the animal should be allowed to become accustomed to breathing air through the facemask. 100% oxygen is introduced. Then the vaporiser concentration is gradually increased up to approximately 4% until the animal is anaesthetised. Once this is achieved, anaesthesia is maintained using 0.75 - 2.0% (halothane) or 1 - 2.5% (isoflurane) concentration of the gas. Intubation is recommended for prolonged procedures.

Induction chambers are usually made of an aquarium type of plastic or glass box of various sizes. Up to 5% of the gaseous anaesthetic agent, with high flow rates of oxygen (5+ litres per minute), is used until the animal loses its righting reflex. The chamber is then either filled with 100% oxygen, or the anaesthetic gas is evacuated from the chamber, or the lid of the chamber is opened under a fume hood. The animal is then taken out of the chamber, and placed on a facemask or intubated. Anaesthetic administration is continued at the maintenance level.

Regardless of the method used, scavenging of excess anaesthetic gas must be performed, in a manner to prevent exposure of personnel to waste gases.

Advantages:
(a) Relatively simple to administer.
(b) Accurate control over depth of anaesthesia.
(c) Rapid induction.
(d) Rapid recovery.
(e) Augmentation of the oxygen content of the blood with provided of high levels of oxygen during induction and maintenance.

Disadvantages:
(a) Specialised equipment is usually needed.
(b) Constant monitoring of the animal is necessary.
(c) Good ventilation and scavenging equipment is required at all times as some agents may be potentially dangerous to personnel.

(ii) Intravenous. Induction of anaesthesia is usually rapid. In most circumstances, half the calculated dose of anaesthetic is given rapidly (typically over a 5-10 second period), then additional anaesthetic is given to produce the desired effect. With large animals, the jugular and cephalic veins have proven to be the most accessible vessels. In rodents, the tail vein is used with a 27 - 28 gauge needle, while in guinea pigs and rabbits, the marginal ear vein is the usual site (25 gauge needle). Following intravenous induction, anaesthesia may be maintained using gaseous agents, or continuous intravenous infusion.

Advantages:

(a) Rapid action of the anaesthetising agent.
(b) Drug can be administered to effect to provide the desired depth of anaesthesia. Thus, the dose of the administered drug can be tailored to the individual animal.

Disadvantages:

(a) Requires some expertise on the part of the operator.
(b) Good restraint of the animal is essential.

(iii) Intraperitoneal. The onset of action is slower compared to intravenous administration, and the animal will pass through a phase in which it becomes progressively ataxic ("wobbly"), may exhibit some excitation and hyperactivity, then lose its ability to right itself, and eventually lose consciousness. Anaesthesia then becomes progressively deeper until the pedal withdrawal reflex is lost. For rats, mice, guinea pigs and rabbits, use a 25-27g needle inserted 3mm lateral to the umbilicus on the right hand side of the animal. Larger gauge needles are useful for larger species (22-23g for dogs, cats). Always draw back on the plunger prior to injection to ensure that the needle has not penetrated an abdominal organ.

Advantages:

(a) Relatively simple to administer.

Disadvantages:

(a) A "set dose" of the drug(s) is administered to the animal. Because it is impossible to adjust the dose according to the individual animal's response, inadvertent over-dosing and under-dosing will frequently occur.
(b) Once the dose is administered, it cannot be removed. Thus overdose is difficult to manage.
(c) Relatively large doses of anaesthetic must be given to produce the required effect. Absorption is slow relative to intravenous administration. Residual drug effects can persist for prolonged periods, and so full recovery can be very prolonged.
(d) Injection of an irritant compound can cause unnecessary pain or discomfort to the animal. Repeated doses may result in abdominal adhesions.

(iv) Subcutaneous. The onset of action is slower compared to intravenous and intraperitoneal administration, and the animal will pass through a phase in which it becomes progressively ataxic ("wobbly"), may exhibit some excitation and hyperactivity, then lose its ability to right itself, and eventually lose consciousness. Anaesthesia then becomes progressively deeper until the pedal withdrawal reflex is lost. Dorsolateral areas of neck and shoulder are the most useful sites. This route is useful for local anaesthesia.

Advantages:

(a) relatively simple to administer

Disadvantages:

(a) A "set dose" of the drug(s) is administered to the animal. Because it is impossible to adjust the dose according to the individual animal's response, inadvertent over-dosing and under-dosing will frequently occur.
(b) Once the dose is administered, it cannot be removed. Thus overdose is difficult to manage.
(c) Relatively large doses of anaesthetic must be given to produce the required effect. Absorption is slow relative to intravenous administration. Residual drug effects can persist for prolonged periods, and so full recovery can be very prolonged.
(d) Injection of an irritant compound can cause unnecessary pain or discomfort to the animal.
(e) Some drugs cannot be administered subcutaneously as they cause tissue damage and skin sloughing (eg. pentobarbitone, thiopentone, ketamine).

(v) Intramuscular. These injections are painful and should be avoided whenever possible. Larger volumes must be administered in multiple sites. The best site is the quadriceps muscle mass (front of femur). Ensure that the needle is not in a blood vessel by withdrawal of the plunger before injecting.

Advantages:

(a) Relatively simple to administer

Disadvantages:

(a) A "set dose" of the drug(s) is administered to the animal. Because it is impossible to adjust the dose according to the individual animal's response, inadvertent over-dosing and under-dosing will frequently occur.
(b) Once the dose is administered, it cannot be removed. Thus overdose is difficult to manage.
(c) Relatively large doses of anaesthetic must be given to produce the required effect. Absorption is slow relative to intravenous administration. Residual drug effects can persist for prolonged periods, and so full recovery can be very prolonged.
(d) Injection of an irritant compound can cause unnecessary pain or discomfort to the animal. There are a number of reports of tissue reactions and myositis with intramuscular administration of some anaesthetic drugs (eg. ketamine, saffan®).
(e) In small animals, the injectate volume is large compared to the volume of muscle mass used for IM administration. This can result in unnecessary pain or discomfort in the animal. For this reason, it is recommended that this route be avoided in small rodents.

Other routes that are used less commonly include oral, epidural, intrathecal, and intra-articular.

PART 6. ANALGESIA AND PAIN MANAGEMENT

General

Pain can result in significant and undesirable physiological, biochemical and behavioural changes in the animal. Providing effective pain relief can have a dramatic effect on the speed with which animals return to normality following surgical procedures. Analgesia also decreases the unwanted experimental variables associated with pain and stress.

Anaesthesia does not always equate with analgesia. General anaesthesia produces loss of consciousness and hence prevents perception of pain while the animal is unconscious. However, noxious stimuli will still be transmitted to and processed by the CNS. Central hypersensitivity can develop in the spinal cord and brain. Thus, while pain perception is absent while the animal is unconscious, post-operative pain perception can be heightened. Some anaesthetic agents do have analgesic effects. However, those that provide poor analgesia (eg. pentobarbitone) must not be used without concurrent use of an algesic agent.

Analgesic agents can be broadly divided into two groups - the opioids or narcotic analgesics, and the non-steroidal anti-inflammatory drugs (NSAIDs). Local anaesthetics can also be used to provide post-operative pain relief by blocking all pain sensation from the affected area. In some species, alpha-2 agonists may be effective (eg. ruminants). A balanced analgesic regime may also include the use of NMDA receptor antagonists (eg. ketamine in sub-anaesthetic doses), sedatives or tranquillisers.

Analgesic agents can be administered via the parenteral routes (intravenous, subcutaneous, intramuscular, intraperitoneal), oral administration, epidural and intrathecal routes, or via transdermal patches (fentanyl, codeine, buprenorphine).

Non-pharmacological methods for controlling post-operative or post-procedure pain include acclimatisation of the animal prior to performance of the procedure. This will act to decrease anxiety and enhance the effect of concurrently administered analgesic agents. Other non-pharmacological methods include good husbandry, nutritional support, and access to con-specifics in social animals.

Strategies to maximise the success of treatment for pain

1. Pre-emptive analgesia

In general, post-operative pain can be controlled more readily if analgesia is provided pre-operatively or

intra-operatively (pre-emptive analgesia). Initiating treatment before acute insult is believed to inhibit peripheral and central sensitisation.

An exception exists with the use of buprenorphine in rats where there have been reports of unexpected and unexplained mortality associated with the pre-operative administration of buprenorphine to rats anaesthetised with ketamine/medetomidine. Therefore, for analgesia following surgery or a painful procedure in rats anaesthetised with either ketamine/medetomidine or ketamine/xylazine, it is recommended that buprenorphine be administered during the post-anaesthetic period, rather than pre-operatively.

Care must be taken with the administration of NSAIDs pre-operatively as their action in inhibiting prostaglandin production can result in renal dysfunction. Carprofen is the only drug of this class that can be used safely prior to surgery.

2. Multimodal or balanced analgesia

Perception of pain arises from a combination of peripheral and central hypersensitivity involving a multitude of pathways, mechanisms and transmitter systems. Thus it is unlikely that a single class of analgesic will completely alleviate pain, irrespective of the dose used. A combination of drugs with different modes of action can be used to produce sequential blocks in the nociceptive pathways, and achieve beneficial additive or synergistic analgesic effects. With this approach, lower doses of any one analgesic agent can usually be used, thereby reducing potential undesirable side effects while improving the control of pain.

For example, opioids can be combined with NSAIDs where the opioid acts to dampen peripheral and central afferent nociceptive transmission. In contrast, the NSAID acts peripherally to decrease the amount of local inflammation and hence the nociceptive information entering the CNS as a result of inflammation. Adding a local anaesthetic to this regime can provide additional analgesia by blocking transmission in individual nerves.

NMDA receptor antagonists (eg. ketamine in sub-anaesthetic doses) can be used to reduce central sensitisation. Sedatives and tranquillisers can also be used to decrease anxiety and stress that have been shown to heighten responses to pain.

3. Monitoring to assess the effects of treatment for pain

Because of the individual variation in response to analgesic agents, animals must be monitored carefully during the post-operative period to assess whether or not analgesia has been effective, and whether or not additional analgesia is required. The dose or frequency of administration should be modified according to the needs of the animal.

It is difficult to make firm recommendations regarding the routine use of analgesics, both the agents to use and the frequency of administration. As a general guide:

- Relatively minor procedure (eg. vascular catheterisation) - a single dose of analgesic is administered, either an opioid (eg. buprenorphine) or an NSAID (eg. carprofen).
- More invasive surgical procedures (eg. laparotomy) - analgesic administration may continue for 72 hours. A common regime is a combination of opioid with an NSAID for 24-36 hours, followed by an NSAID alone for a further 24-36 hours.

The Animal Care and Ethics Committee has developed guidelines on the recognition and assessment of pain in animals. These guidelines, and other resource documents on this subject, may be accessed via the animal ethics website at (http://www.newcastle.edu.au/research/animal/revised-anipol-general.html#Pain) or from the Research Office (telephone: 02-49215353; email: animal-ethics@newcastle.edu.au).

PART 7. SPECIES - Recommended Regimes

AMPHIBIAN

ANAESTHESIA

Pre-anaesthetic starving is not required. Acclimatisation of frogs or toads to water temperature of 20-22^{o}C for 2 days is essential prior to induction of anaesthesia. Wrap in damp cloth for transportation.

Keep animal moist during anaesthesia and recovery, and raise temperature during recovery to 24-26^{o}C.

Oxygen exchange is 25% percutaneous in frogs so the immersion method of anaesthetic administration using aqueous solutions or vapour is very effective. At the end of anaesthesia, amphibians should be washed in warm tap water and then placed into a moist environment for recovery.

Intramuscular injections can be given into the hind leg but do not use alcohol to swab as it is an irritant. Subcutaneous and intraperitoneal injection can be given to frogs. Injection into dorsal lymph heart is simple as they are located pulsating on either side of the urostyle.

1. Tricaine (MS222)

(i) Immersion in 0.1% Tricaine (MS222) solution at 21^{o}C. Induction takes 5-20 minutes and can be maintained by wrapping frog in cotton wool moistened with this solution. Analgesia and muscle relaxation is excellent. Recovery takes 25-70 minutes.

(ii) 13 mg/kg can be injected into dorsal lymph hearts, with subsequent substantial reduction in both induction and recovery time are reduced substantially.

This drug is safe and gives good relaxation and analgesia.

2. Isoflurane

1.1 Direct application of isoflurane liquid to the skin at the rate of 0.007-0.0015 mls/gm.

1.2 Application of liquid isoflurane and water mixture to the skin using 0.28 % isoflurane (0.35 mls isoflurane to 125 mls water).

1.3 Application of isoflurane/KY jelly and water mix to the skin, using a thick solution of 3 mls liquid isoflurane, 3.5 mls K-Y jelly and 1.5 mls water: 0.025-0.035 mls/gm.

1.4 Vaporised isoflurane in a water bath – 5 % isoflurane vaporised in oxygen is bubbled into the water bath in which the animal is placed.

1.5 Vaporised isoflurane in an air chamber – 5% isoflurane vaporised in oxygen, piped into the plastic chamber in which the animal is placed.

All methods provided adequate sedation and /or anaesthesia.

Isoflurane is poorly miscible with water so the addition of water-soluble jelly decreases the rate of vapourisation and allows increased dermal contact and absorption. Both isoflurane plus water, and isoflurane plus water plus K-Y jelly, provide consistent levels of surgical anaesthesia. The animals should be removed from the isoflurane mixture immediately after induction to prevent deep and prolonged anaesthesia.

Both the traditional methods of application – vaporisation in air or water – provide adequate sedation and anaesthesia, but have longer induction times and more rapid recovery rates, and are more cumbersome for use with surgical procedures.

The percutaneous absorption of isoflurane appears to be species dependent, the thicker skin of toads requiring higher dose rates.

3. Ketamine 2-50 mg/kg IM

ANALGESIA

Fentanyl	1.0 mg/kg SC (into dorsal lymph sac). Analgesia > 4 hours
Buprenorphine	75 mg/kg SC (into dorsal lymph sac). Analgesia > 4 hours
Dexmedetomidine	40 mg/kg SC (into dorsal lymph sac). Analgesia > 4 hours
	120 mg/kg SC (into dorsal lymph sac). Analgesia > 8 hours
Epinephrine	1-30 nmol/g SC (into dorsal lymph sac). Analgesia > 4 hours

BIRD

ANAESTHESIA

Large birds should be starved of food for 6 hours.
Small birds should be starved of food for 2 hours.
Maintain body heat during anaesthesia.
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1. Inhalation

Inhalant anaesthetics, compared to injectable anaesthetics, offer several advantages for patient management, including rapid induction and recovery, especially when inhalant anaesthetics of low blood/gas solubility are used (isoflurane and sevoflurane), easier control of anaesthetic depth, the improved oxygenation due to the concurrent use of oxygen, and recovery that is not dependent on metabolic or excretory pathways.

(i) Isoflurane is widely regarded as the anaesthetic agent of choice for birds. It provides smooth and rapid induction and rapid recovery that is usually free from involuntary excitement. Mask induction 4-5% isoflurane with oxygen can be followed by intubation and maintenance 2-3 % on a T-piece. Do not use a cuffed endotracheal tube. Maintenance may also be achieved using a mask. The depth of anaesthesia can be changed very rapidly by changing the inspired concentration, allowing birds to be maintained at an anaesthetic plane appropriate to the degree of surgical stimulation.

(ii) Halothane (induction 3-4%; maintenance 1.5-2 %) can be used to provide surgical anaesthesia, but the margin of safety appears to be considerably less than that provided by isoflurane. In addition, recovery may be more prolonged.

Cardiac arrhythmias frequently occur in birds anaesthetised with halothane. Cardiac stability is one of the perceived advantages of isoflurane and is one of the reasons why it has so readily gained wide acceptance in clinical avian practice. Cardiac arrhythmias do occur during isoflurane anaesthesia in birds, but they are not as severe or as life threatening as are those associated with halothane anaesthesia. Chickens anaesthetised with sevoflurane have not shown any evidence of cardiac arrhythmias during the anaesthesia.

2. Injectable

2.1 Methohexitone — 4-8 mg/kg by rapid IV using wing vein; 4-5 minutes light anaesthesia.

2.2 Saffan® — 10-14 mg/kg IV or IM (pectoral muscle) gives 5-7 minutes anaesthesia. Unreliable in some birds.

2.3 Ketamine combinations

(i) Ketamine+ xylazine

Ketamine in combination with xylazine will produce light to moderate surgical anaesthesia for 10-30 minutes. The effects vary with the body weight and species involved. Dose range is 10-30 mg/kg ketamine and 2-6 mg/kg xylazine, with smaller birds requiring higher dose rates per kilogram.

(ii) Ketamine + midazolam or diazepam

Ketamine (20-40 mg/kg) and diazepam (1-1.5 mg/kg) or midazolam (4 mg/kg), all given by intramuscular injection, produce medium surgical anaesthesia for 20-30 minutes. Dose rates vary with the body weight and species involved.

ANALGESIA

Little is known about analgesic agents in this species, with only very limited data available. Wide variation in responses to analgesics can occur between major groups of birds. Suggestions:

Meloxicam	0.1-0.3 mg/kg every 24 hours (wide applications)
Carprofen	0.5-2 mg/kg every 24 hours
Butorphanol	1-4 mg/kg IM every 6 hours. If somnolent or ataxic, reduce dose.

CAT

ANAESTHESIA

1. Inhalation

There are many combinations of injectable and gaseous anaesthetics for the cat. Several examples are described here.

1.1 Butorphanol/propofol/isoflurane

(i) Premedication: Butorphanol 0.1 mg/kg IV or 0.4 mg/kg IM or SC.

(ii) Induction: Propofol 6.0 mg/kg IV only.

(iii) Tracheal intubation. Lignocaine spray on the larynx can be considered to prevent laryngospasm, using a Caff needle attached to a tuberculin syringe. Because the Caff needle has a dead space of 0.1 ml, 0.3 mls lignocaine in the syringe results in the delivery of 0.2 mls onto the larynx. This dose is usually sufficient, with the maximum recommended dose being 0.4 mls.

(iv) Maintenance: Isoflurane/O_2 via an Ayres T-piece or a Bain coaxial circuit. Use 1.5 litres/minute of O_2 and isoflurane concentration no greater than 2.5%.

1.2 Butorphanol/medetomidine/halothane or isoflurane

(i) Premedication: Butorphanol (0.4 mg/kg IM or SC) with medetomidine (50 µg/kg IM or SC). At the completion of the surgery, medetomidine can be reversed using atipamezole ((125 µg/kg IM or SC). Note: Do not use atropine with this combination.

(ii) Induction: Mask induction with 4% isoflurane or 4% halothane.

(iii) Tracheal intubation. Use lignocaine spray as above.

(iv) Maintenance: Isoflurane/O_2 or halothane/O_2 via an Ayres T-piece or a Bain coaxial circuit. Use 1.5 litres/minute of O_2 and isoflurane or halothane concentration no greater than 2.5%.

1.3 Atropine/acepromazine/thiopentone/halothane or isoflurane

(i) Premedication: Atropine (0.4 mg/kg SC) and a sedative (eg. acetylpromazine 0.1 mg/kg SC).

(ii) Induction: Mask induction with 3.5% isoflurane or 4% halothane, or thiopentone (10-20 mg/kg IV of a 2.5% solution) given slowly to effect.

(iii) Tracheal intubation. Use lignocaine spray as above.

(iv) Maintenance: Isoflurane/O_2 or halothane/O_2 via an Ayres T-piece or a Bain coaxial circuit. Use 1.5 litres/minute of O_2 and isoflurane or halothane concentration no greater than 2%.

Note: Additional analgesia will be required with this regime.

2. Injectable

2.1 Saffan® (alphaxalone/alphadolone)

(i) Induction – 9 mg/kg IV or 12 mg/kg IM

(ii) Maintenance: Supplement with IV Saffan® to effect, continuous infusion at approximately 0.2 mg/kg/min, or use gaseous anaesthesia following endotracheal intubation.

This drug may cause histamine release resulting in oedema of the footpad and pinna.

2.2 Ketamine combinations

The combination of ketamine with an alpha-2 adrenergic agonist (medetomidine or xylazine) provides analgesia, anaesthesia and muscle relaxation for longer, more invasive surgery (approximately 20 - 40 minutes). Note: Because of the low pH of the solution, intramuscular injection of ketamine is painful.

(i) Ketamine + medetomidine

Ketamine (7 mg/kg IM) with medetomidine (80 µg/kg IM) produces 30-40 minutes of surgical anaesthesia.

Analgesia is improved when combined with butorphanol (0.4 mg/kg butorphanol IM + 80 µg/kg medetomidine IM + 5 mg/kg ketamine IM). Partial reversal is achieved using atipamezole (300-500 µg/kg IV or SC) When administered intravenously, the dose rates are reduced to 0.1 mg/kg butorphanol + 40 µg/kg medetomidine + 2.5 mg/kg ketamine.

(ii) Ketamine + xylazine

Xylazine (1.1 mg/kg SC or IM) should be given 10 minutes prior to ketamine (22 mg/kg IM). Produces surgical anaesthesia for approximately 20 minutes. Administration of the drugs should be in separate sites. When xylazine is used, premedication with atropine is essential.

Partial reversal of anaesthesia can be achieved with atipamezole (0.3-0.5 mg/kg IV or SC). Xylazine is an effective emetic with 0.5 mg/kg IM producing emesis in most cats. The degree of analgesia may be improved by pre-anaesthetic administration of an opioid such as butorphanol (0.4 mg/kg SC). In this instance, the doses of ketamine and xylazine must be reduced.

2.3 Propofol

5-8 mg/kg IV provides 10 minutes of surgical anaesthesia with rapid and smooth induction and rapid recovery. Propofol can be used repeatedly or as a constant infusion.

ANALGESIA

Analgesics should be used with caution in this species, with buprenorphine or butorphanol being the agents of choice.

Buprenorphine	0.005-0.01 mg/kg SC or IV 12 hourly
Butorphanol	0.4mg/kg SC or IM repeated as needed
Pethidine	3.5-10 mg/kg IM or 10-15 mg/kg SC 2-3 hourly
Carprofen	2-4 mg/kg SC or IV once only.
Meloxicam	0.2 mg/kg SC or PO, followed by 0.1 mg/kg 24 hourly.
Fentanyl	0.002-0.003 mg/kg IV bolus, repeated every 20-30 mins, or by continuous infusion (0.002-0.003 mg/kg/hr) Transdermal: 25 µg/hr every 3 days

DOG

ANAESTHESIA

1. Inhalation

There are many combinations of injectable and gaseous anaesthetics for the dog. Several examples are described here.

1.1 Butorphanol/propofol/isoflurane

(i) Premedication: Butorphanol 0.1 mg/kg IV or IM, + acepromazine 0.02 mg/kg IV or IM. These drugs can be mixed together in one syringe.)

(ii) Induction: Propofol 4.0 mg/kg IV only.

(iii) Tracheal intubation.

(iv) Maintenance – 1-2.5% isoflurane.

Isoflurane can only be used with a calibrated vaporiser and an anaesthetic machine. For small dogs (i.e. <10 kg) an Ayres T-piece or a Bain coaxial circuit should be used.

1.2 Butorphanol/medetomidine/halothane or isoflurane

(i) Premedication – Butorphanol 0.1 mg/kg IM or IV + medetomidine 25 µg/kg IM or IV. At the completion of the surgery, medetomidine can be reversed using atipamezole (125 µg/kg IM). Note: Do not use atropine with medetomidine.

(ii) Induction – Mask induction with 4 % isoflurane or 4% halothane + 4 l/m 0_2.

(iii) Tracheal intubation.

(iv) Maintenance – 1-2.5% isoflurane or 0.75-2% halothane.

Isoflurane and halothane can only be used with a calibrated vaporiser and an anaesthetic machine. For small dogs (i.e. <10 kg) an Ayres T-piece or a Bain coaxial circuit should be used.

1.3..Atropine/acepromazine/thiopentone/isoflurane or halothane

(i) Premedication: Atropine (0.05 mg/kg SC) and a sedative (eg. acetylpromazine 0.1mg/kg SC).

(ii) Induction: Mask induction with 4% isoflurane or 4% halothane + 4 l/m 0_2 or ultra-short acting barbiturate (e.g. thiopentone 10-20 mg/kg) given slowly IV to effect.

(iii) Tracheal intubation.

(iv) Maintenance: 1 -2.5% isoflurane or 1-2% halothane.

Isoflurane and halothane can only be used with a calibrated vaporiser and an anaesthetic machine. For small dogs (i.e. <10 kg) an Ayres T-piece or a Bain coaxial circuit should be used.

Note: Additional analgesia will be required with this regime.

2. Injectable

2.1 Thiopentone

10-20 mg/kg IV provides 5-10 minutes of light anaesthesia. This drug is most useful for induction of anaesthesia prior to maintenance by inhaled agents.

2.2 Methohexitone

4-8 mg/kg IV provides 5 minutes of anaesthesia. Most useful for induction of anaesthesia prior to maintenance by inhaled agents.

2.3 Propofol

5-7.5 mg/kg IV Induction is rapid and smooth and recovery is rapid. Provides 7-10 minutes of surgical anaesthesia after a single dose. However, it can be used repeatedly as a constant infusion, or as an induction agent.

ANALGESIA

Morphine	0.1 – 1.0 mg/kg SC or IM 4 hourly
Pethidine	3.5 - 10 mg/kg IM or 10-15 mg/kg SC 2.5-3.5 hourly
Buprenorphine	0.005 - 0.02 mg/kg IM, SC, IV 4-8 hourly
Butorphanol	0.2-0.3 mg/kg IV, SC or IM. Repeat as required
Carprofen	4.0 mg/kg IV or SC, on induction. Then 2.2 mg/kg 24 hourly IV, SC, or PO
Meloxicam	0.2 mg/kg IV, SC, or PO. Then 0.1 mg/kg 24 hourly.

GUINEA PIG

Difficult to anaesthetise due to:

- Fragile veins.
- Variable responses to injectable agents.
- Calculating accurate dosages on a bodyweight basis is difficult since the gastro- intestinal tract may contribute significantly to total body weight.
- Adequate analgesia is difficult to achieve without deep anaesthesia.
- Narrow long airways produce resistance, and large amounts of dead space.
- A number of drugs given via the intramuscular route in guinea pigs cause myositis, neuritis and subsequent lose of limb use and self-mutilation.
- Post-anaesthetic complications such as respiratory infections, digestive disturbances and generalised depression and inappetence are frequently seen.

Pre-anaesthesia: Ingesta may contribute to 20% of the body weight of a guinea pig. Thus dose rates must be adjusted accordingly.

ANAESTHESIA

1. Inhalation

Premedicate with atropine (0.05 mg/kg SC) 30 minutes prior to inhalation anaesthesia.

(i) Halothane with oxygen administered with a suitable facemask, a calibrated vaporiser, and an Ayres T-piece or Bain coaxial circuit.

(ii) Isoflurane, as with halothane, but longer induction may be seen due to breath holding.

2. Injectable

2.1 Fentanyl/fluanisone (Hypnorm) + midazolam or diazepam

(i) Fentanyl/fluanisone (1.0 ml/kg IP) and diazepam (2.5 mg/kg IP) OR
(ii) Fentanyl/fluanisone with midazolam - 2 mls Hypnorm (0.315 mg fentanyl per ml; 10 mg fluanisone per ml) + 2 ml midazolam (5 mg per ml) + 4 mls Water For Injection - dose at 8 mls/kg IP

These combinations provide good surgical anaesthesia lasting about 45 minutes. Following completion of surgery, the fentanyl component of the anaesthesia can be reversed using nalbuphine (1 mg/kg IP or SC), butorphanol (1 mg/kg IP or SC) or buprenorphine (0.01 mg/kg IV or 0.05 mg/kg IP).

2.2 Ketamine + Medetomidine

Ketamine 40 mg/kg IP + Medetomidine 0.5 mg/kg IP. Anaesthesia can be partially reversed using atipamezole (1.0 mg/kg SC).

2.3 Ketamine + xylazine

Ketamine 40 mg/kg SC + xylazine 5 mg/kg SC This regime gives good surgical anaesthesia for about 30-40 minutes with good muscle relaxation and excellent recovery. The degree of analgesia may be insufficient for major surgery in some animals. Anaesthesia can be partially reversed using atipamezole (1.0 mg/kg SC).

2.4 Saffan® (alphaxalone/alphadolone)

12 mg/kg given IV slowly to effect or 40 mg/kg IP produces only light anaesthesia of short duration. Anaesthesia can be extended by giving 4 mg/kg increments every 10 minutes. However severe respiratory depression may be seen. Recovery is rapid.

It is not recommended for IM administration as responses are too variable.

ANALGESIA

Pethidine	10 mg/kg SC or IM 2-4 hourly
Morphine	2-5 mg/kg SC or IM 4 hourly
Buprenorphine	0.05 mg/kg SC or IV 8-12 hourly (recommended)
Carprofen	2-5 mg/kg SC 24 hourly.

MARSUPIAL

Stress is a major cause of mortality in marsupials. This can be limited by careful and efficient handling.

Regimes that have been used at this University include:

SEDATION OR PREMEDICATION

1. Diazepam (Valium®) 1-2 mg/kg IM

2. Saffan® (alphaxalone/alphadolone) 6-9 mg/kg IV or 9-12 mg/kg IM. Both routes provide light anaesthesia of short duration.

3. Atropine 0.1 mg/kg IM produces cardiovascular protective effects and reduces salivation.

GENERAL ANAESTHESIA

1. Inhalation

1. Isoflurane or halothane

Prior to any inhalation anaesthesia, premedication with a sedative may be considered. Premedication with atropine is recommended prior to halothane anaesthesia.

Mask induction using 4% halothane or isoflurane until the desired plane of anaesthesia is reached. Maintain via mask or endotracheal tube on 1- 2.5% Halothane or isoflurane. Chamber induction can be used in small marsupials such as dunnarts and planigales.

2. Injectable

* Note: Increased sensitivity to noise stimuli is normal.

2.1* Ketamine combinations

(a) Ketamine (2-3 mg/kg IM) + medetomidine (50-100 µg/kg IM). Medetomidine can be reversed with atipamezole (50-400 µg/kg IM).

(b) Ketamine (3 mg/kg IM) + diazepam (1-2 mg/kg IM) or xylazine (2 mg/kg IM). Xylazine can be reversed using atipamezole (50-400 µg/kg IM).

2.2* Saffan® (alphaxalone/alphadolone) 1ml/5kg IM or IV.

2.3 Tiletamine +zolazepam (Zoletil®)

20-30 mg/kg IM. Used for examination alone. Can be used as an induction agent (2.5 mg/kg IV) for intubation and gaseous anaesthetic with isoflurane or halothane and O_2. The use of nitrous oxide should be guarded.

2.4 Tiletamine + zolazepam (Zoletil®) + xylazine

Tiletamine +zolazepam (5mg/kg) + xylazine (0.5 mg/kg). Xylazine may be reversed using atipamezole (50-400 µg/kg)

ANALGESIA

Buprenorphine	0.01 mg/kg SC 12 hourly
Carprofen	2-4 mg/kg IV, SC, PO 24 hourly
Flunixin meglumine	1 mg/kg IV, IM, SC
Ketoprofen	1 mg/kg SC, PO 24 hourly
Pethidine	1 mg/kg IV, IM, SC

Long acting neuroleptic such as fluphenazine decanoate (2.5 mg/kg IM; duration of action 3-4 weeks) are often used as prophylactic agents against further injury and pain. Similarly, a variety of sedatives (eg. azaperone 0.5-2.0 mg/kg IM 6-8 hourly, tiletamine-zolazepam 5-10 mg/kg IM) are used to alleviate stress and prevent further injury and pain.

MOUSE

ANAESTHESIA

Chronic Respiratory Disease in non-SPF mice increases the risk of mortality during anaesthesia.

1. Inhalation

Isoflurane or halothane - Induction using an anaesthetic chamber or facemask using 4% halothane or isoflurane. Maintenance using a facemask at 1-2.5% halothane or isoflurane.

2. Injectable

2.1 Fentanyl/fluanisone (Hypnorm®) + midazolam or diazepam

(i) Fentanyl/fluanisone (0.4 ml/kg IP) and diazepam (5 mg/kg IP) OR
(ii) Fentanyl/fluanisone with midazolam - 1 ml Hypnorm (0.315 mg fentanyl per ml; 10 mg fluanisone per ml) + 1 ml midazolam (5 mg per ml) + 2 mls Water For Injection - dose at 10 mls/kg IP

These combinations provide good surgical anaesthesia lasting about 30-40 minutes. Following completion of surgery, the fentanyl component of the anaesthesia can be reversed using nalbuphine (4 mg/kg IP or SC) or butorphanol (2 mg/kg IP or SC).

2.2 Intravenous anaesthesia

The advantage of intravenous anaesthesia is that repeated administration to prolong anaesthesia is not associated with prolongation of the recovery period.

(i) Saffan®: 10-15 mg/kg slowly IV via tail vein. Maximum effect is maintained for 5-8 minutes; recovery after 20-30 minutes.

(ii) Propofol: 26 mg/kg IV can be used to provide 10-15 minutes of anaesthesia.

(iii) Methohexitone: 10 mg/kg slowly IV 3-4 minutes anaesthesia

(iv) Thiopentone: 30 mg-40 mg/kg slowly IV 10-12 minutes anaesthesia.

2.3 Ketamine + medetomidine or xylazine

Ketamine (74 mg/kg IP) + medetomidine (1.0 mg/kg IP) OR ketamine (80-100 mg/kg IP) + xylazine (10 mg/kg IP) produce moderate surgical anaesthesia for 20-30 minutes. **However, the degree of analgesia is insufficient for major surgery such as laparotomy**. If major surgery is to be performed, additional analgesia should be provided. Anaesthesia can be partially reversed with atipamezole (1 mg/kg SC).

ANALGESIA

Buprenorphine	0.05-0.1 mg/kg SC 8-12 hourly
Carprofen	5 mg/kg SC 12 hourly

PIG

ANAESTHESIA

General considerations for general anesthesia

- Difficult to restrain in large size pigs.
- Lack of accessible superficial veins and arteries.
- Endotracheal intubation relatively difficult due to anatomic peculiarity
  - Inability to open mouth widely
  - Limited visibility of the larynx due to long distance between the snout and the larynx
  - Endotracheal tube tend to enter the middle ventricle in the floor of the larynx
  - Laryngospasm is easily induced. (similar to the cat)
- Will require longer needle (1.5-2") for IM injection. This is especially true for the large domestic pigs and potbellied pigs.
- Inhalation anaesthesia - A small number of pigs may develop malignant hypothermia in response to halothane anaesthesia. Whenever possible, animals should be sourced from herds that have a low incidence of this problem.

1. Inhalation

There are many anaesthetic regimens using combinations of sedative, analgesic, short-acting intravenous anaesthetic and inhalation anaesthetics. Several examples are provided here:

1.1 Azaperone/isoflurane

(i) Premedication: Azaperone 2-4 mg/kg IM.
(ii) Induction: Isoflurane by facemask (3-5%). Animal is then intubated.
(iii) Maintenance – Isoflurane 1-3%.

1.2 Ketamine/acepromazine/isoflurane

(i) Premedication – Ketamine (33 mg/kg IM) + acepromazine (1.1 mg/kg IM) + atropine (0.05 mg/kg IM).
(ii) Induction – Isoflurane by facemask (4-5%). Animal is then intubated.
(iii) Maintenance – Isoflurane (0.5-2%)/O_2/nitrous oxide (1:2, v/v).

1.3 Midazolam/fentanyl/isoflurane

(i) Premedication – Ketamine (15 mg/kg IM) + diazepam (2 mg/kg IM) + atropine (0.02-0.05 mg/kg IM).
(ii) Induction – Thiopentone (5 mg/kg IV). Animal is then intubated.
(iii) Maintenance – Continuous infusion of midazolam (0.5 mg/kg/hr) + fentanyl (7.5 µg/kg/hr), with supplemental isoflurane (0.25–5%) as required.

This protocol is reported as suitable for haemodynamic and fluid balance studies (Husby et al, 1997).

2. Injectable

2.1 Thiopentone

6.6-25 mg/kg IV given to effect, provides surgical anaesthesia of 5-10 minutes duration. Prolonged anaesthesia can be provided using continuous infusion (3-6 mg/kg/hr).

2.2 Propofol

(i) 2.5-3.5 mg/kg IV produces surgical anaesthesia lasting 10 minutes.
(ii) Bolus IV injection of 0.83-1.66 mg/kg, followed by continuous infusion (12-20 mg/kg/hr).

2.3 Tiletamine-zolazepam / combinations

(i) Tiletamine-zolazepam (2-4 mg/kg IM) + alphaxalone-alphadolone (4-8.8 mg/kg IM) produces general anaesthesia of short duration.

(ii) Tiletamine-zolazepam (4.4 mg/kg IM) + ketamine (2.2 mg/kg IM) + xylazine (2.2 mg/kg IM) produces anaesthesia of 20-30 minute duration.

2.4 Opioid infusions

Continuous IV infusions of opioids have been used with other anaesthetics to enhance analgesia and produce balanced anaesthesia. In higher doses, they can be used to produce anaesthesia for experimental cardiac surgery. Their main advantage is that they produce minimal depression of cardiac function and provide protection against cardiac arrhythmias.

Fentanyl and sufentanil are the most commonly used agents for opioid infusion in swine. The agents may be used alone for induction, or following light sedation to facilitate IV access. Commencing the IV infusion prior to a bolus injection prevents muscle rigidity, which is frequently associated with these drugs. Some animals require supplemental anaesthesia with other agents such as isoflurane.

Fentanyl	Commence continuous IV infusion 30-100 µg/kg/hr, followed by IV bolus 50 µg/kg.
Sufentanil	Commence continuous IV infusion 15-30 µg/kg/hr, followed by IV bolus 7 µg/kg.

ANALGESIA

Most analgesic agents have a short half-life in pigs. The combination of buprenorphine (short half-life, rapid increase in blood plasma concentration) with transdermal fentanyl (at least 12 hour delay in rise of plasma levels, continuous administration) provides effective post-operative analgesia.

Buprenorphine alone	0.01 mg/kg IM or IV 8-12 hourly.
Buprenorphine + fentanyl	0.1 mg/kg IV at induction of anaesthesia + transdermal fentanyl (100 µg/hr for 17-22 kg pig. Every 72 hours) (Wilkinson et al, 2001)
Fentanyl alone	Transdermal: 50-100 µg/hr, applied 8-12 hours prior to surgery. Every 72 hours.

RABBIT

ANAESTHESIA

1. Inhalation

(i) Induction:

Induction of anaesthesia using a facemask or induction chamber is hazardous because of the prevalence of breath holding in rabbits. Sedation does not block this response. Therefore, it is generally preferable to induce anaesthesia with an injectable agent and maintain the rabbit on an inhalation anaesthetic. If induction with an inhalation agent is required, the animal should be observed closely for episodes of breath holding.

(a) Methohexitone 4-10 mg/kg given rapidly IV

(b) Saffan® (alphaxalone/alphadolone) 4 mg/kg IV

(c) Propofol 5 mg/kg IV

(ii) Maintenance: Endotracheal intubation followed by inhalation anaesthesia (eg. halothane 1-1.5% + 0_2, isoflurane 2-2.5% + 0_2). Intubation can be performed blind, or using a paediatric laryngoscope and paediatric endotracheal tube (2-3 mm ID). Maintenance of gaseous anaesthesia by mask is not recommended in rabbits because of the prevalence of breath holding (apnoea).

2. Injectable

2.1 Fentanyl/fluanisone (Hypnorm) + midazolam or diazepam

Hypnorm at 0.3 ml/kg IM combined with midazolam or diazepam (2 mg/kg IM, IV or IP) provides good surgical anaesthesia and excellent muscle relaxation for 20-40 minutes. It is recommended that fentanyl/fluanisone is administered first to sedate the rabbit, followed 10-15 minutes later by midazolam or diazepam. Longer periods of anaesthesia can be achieved by the administration of additional doses of Hypnorm (approximately 0.1 ml/kg IV every 30-40 minutes). If anaesthesia of several hours duration is required, it is preferable to administer fentanyl (30-100 µg/kg/hr) alone to avoid undue accumulation of the fluanisone component of Hypnorm.

Following completion of surgery, the fentanyl component of the anaesthesia can be reversed using nalbuphine (0.1 mg/kg IV) or buprenorphine (0.01 mg/kg IV).

2.2 Ketamine + medetomidine or xylazine

Ketamine (25 mg/kg IM) and medetomidine (0.5 mg/kg IM), OR ketamine (35 mg/kg IM) and xylazine (5 mg/kg IM) both provide about 30 mins of surgical anaesthesia. The duration of anaesthesia can be prolonged to approximately 80 minutes by the addition of butorphanol (0.1 mg/kg) to the ketamine/xylazine mixture. With this regime, blood pressure drops significantly and reflexes are very slow to return.

Anaesthesia can be partially reversed using atipamezole (1 mg/kg SC or IV).

2.3 Fentanyl + medetomidine

Fentanyl (8µg/kg) and medetomidine (330 µg/kg) administered in combination by intravenous injection produces good surgical anaesthesia, but some animals may make spontaneous movements in response to non-painful stimuli. An advantage of this combination is that it can be completely reversed using atipamezole (1 mg/kg IV) and nalbuphine (1 mg/kg IV). Full recovery may occur in less than 1 minute.

2.4 Saffan® (alphaxalone/alphadolone)

6-9 mg/kg IV for short surgical procedures. Produces only light anaesthesia.
4 mg/kg IV for induction prior to the use of an inhalation agent.

2.5 Propofol

Propofol is less effective in the rabbit than other species, and produces only light anaesthesia (10 mg/kg IV). Can be used alone or prior to intubation.

ANALGESIA

Pethidine	10 mg/kg SC or IM 2-3 hourly
Morphine	2-5 mg/kg SC or IM 2-4 hourly
Buprenorphine	0.01-0.05 mg/kg SC or IV 6-12 hourly (recommended)
Carprofen	4 mg/kg SC 24 hourly or 1.5 mg/kg PO 12 hourly

RAT

ANAESTHESIA

Chronic Respiratory Disease in non-SPF animals makes these animals poor candidates for anaesthesia.

1. Inhalation

1.1 Isoflurane or halothane

Induction: 4% halothane or isoflurane using an anaesthetic chamber or facemask.

Maintenance: 1-2.5% halothane or isoflurane using a facemask or intubation with a catheter. Rats may be intubated, however this can enhance anaesthetic risks because of increased resistance from very small diameter endotracheal tube. Active ventilation (positive pressure ventilation) may be needed to ensure adequate administration of both gaseous anaesthetic and oxygen when intubated.

2. Injectable

2.1 Fentanyl/fluanisone + diazepam or midazolam

0.6 ml/kg of undiluted commercial solution IP combined with 2.5 mg/kg IP diazepam produces anaesthesia of 20-40 minutes duration.

When fentanyl/fluanisone is combined with midazolam, prepare a mixture of 1 ml fentanyl/fluanisone (0.315 mg/ml of fentanyl; 10 mg/ml of fluanisone)+ 2 mls water for injection + 1 ml midazolam (5mg/ml). Add WFI to Hypnorm *before* adding midazolam. Then administer at a dose rate of 2.7 ml/kg IP of combined mixture.

Following the completion of surgery, the anaesthesia can be partially reversed using nalbuphine (1.0 mg/kg IP or SC) or butorphanol (2 mg/kg IP or SC).

2.2 Fentanyl + medetomidine

Fentanyl (300 µg/kg IP) and medetomidine (300 µg/kg IP) can be mixed and administered as a single infection. The combination provides about 60 minutes of surgical anaesthesia.

Rapid recovery may be achieved via reversal of anaesthesia - administration of atipamezole (1 mg/kg SC or IP) to reverse the medetomidine, and either nalbuphine (0.1 mg/kg IV, 1.0 mg/kg IP or SC), butorphanol (0.1 mg/kg iv, 2 mg/kg IP or SC) or another mixed agonist/antagonist opioid analgesic to reverse the fentanyl.

2.3 Ketamine + medetomidine or xylazine

Ketamine (75 mg/kg IP) and either medetomidine (0.5 mg/kg IP) or xylazine (10 mg/kg IP) will provide good surgical anaesthesia for about 30 minutes, although the depth of anaesthesia may be insufficient for major surgery in some animals.

The combination may be partially reversed using atipamezole (1 mg/kg SC or IP).

2.4 Intravenous anaesthesia

If intravenous administration of drugs is feasible, then propofol (10 mg/kg iv) or alphaxalone/alphadolone (Saffan®) (10-12mg/kg iv) produce surgical anaesthesia. Both compounds are especially useful for administration via continuous infusion to provide stable, long-lasting anaesthesia.

Alternative agents for intravenous induction are thiopentone (30 mg/kg iv) or methohexitone (10-15 mg/kg IV, 1% solution), which can be used to produce 5-10 minutes of anaesthesia.

ANALGESIA

Carprofen	5 mg/kg SC 12-24 hourly
Buprenorphine	0.01-0.05 mg/kg SC, IV, 8-12 hourly Recent reports suggest that significantly higher dose rates may be required for

effective analgesia via oral administration (2-10 mg/kg 8-12 hourly) Oral administration using the sublingual preparation of buprenorphine may be achieved using jelly as the carrier (for recipe, see below).

NOTE: There have been reports of unexpected and unexplained mortality associated with the pre-operative administration of buprenorphine to rats anaesthetised with ketamine/medetomidine. Therefore, for analgesia following surgery or a painful procedure in rats anaesthetised with either ketamine/medetomidine or ketamine/xylazine, it is recommended that buprenorphine be administered during the post-anaesthetic period, rather than pre-operatively.

Buprenorphine has also been recorded as causing pica in some strains at higher doses (> 0.05 mg/kg SC).

Oral administration of buprenorphine using jelly (rats): (Volker D et al, 2000)

Acclimatise the rats to consumption of jelly over several days or weeks. Dissolve 85 gms of jelly crystals in 250 mls of boiling water. Place aliquots of 4 mls of jelly liquid in ice-block moulds for refrigeration. Rats will accept berry, orange, lime and strawberry flavours.

When analgesia is required, 3 buprenorphine sublingual tablets (Temgesic ®, Reckitts and Coleman, 0.2 mg/tablet) are crushed into the base of each ice-block mould and moistened with 0.5 mls warm water, prior to the addition of 3.5 mls of warm jelly (total 4 mls). The jelly disks are set at 4-8^{0}C. For acute pain, the number of disks given to each animal is calculated on a dose rate of 2 mg/kg.

Do not use injectable form of buprenorphine for oral preparation as it is too bitter.

SHEEP

ANAESTHESIA

Potential problems associated with recumbancy and general anesthesia are rumenal tympany or bloat, regurgitation, and aspiration pneumonia. Rumenal tympany occurs when fermentation of rumenal contents continues and eructation ceases. The large volume of rumenal contents and bloat will severely compress the diaphragm and impair pulmonary ventilation and venous return. Active regurgitation or vomiting occurs in a lighter plan of anesthesia. It is a complicated and coordinated series of unsuppressed reflex mechanisms intent on rejecting unwanted material from the pharynx and other upper digestive tract. Passive regurgitation or silent regurgitation occurs in a deeper plan of anesthesia through relaxation of the oesophageal sphincter and an increased transruminal pressure gradient.

Use of anticholinergics to prevent salivation in ruminants is controversial. Ruminants produce large quantities of saliva (sheep: 6-16 liters/24 hr) that continue to flow even after induction of anesthesia (at which time they lose their swallowing reflex). It has been suggested that use of atropine as an antisialagogue is of little value because it does not reduce the amount of saliva secreted. Rather, atropine causes an increase in saliva viscosity, rendering it more difficult to remove from the respiratory passages if inhaled.

Recommendations:

- Opinions vary as to whether sheep should be routinely starved before general anaesthesia. Fasting and water deprivation may have little effect on the volume of digesta present in the rumen, and whether or not regurgitation of rumenal contents occurs. However, fasting may reduce the incidence of rumenal tympany by decreasing the volume of fermentable ingesta. This appears to be a greater problem in animals that are grazing. Even with these precautions, some animals will develop rumenal tympany while others will regurgitate.
- Use of a balanced analgesic regime during anaesthesia, with the resultant decrease in the concentration of the gaseous anaesthetic agent, should be considered as passive regurgitation of rumenal contents is more common at deeper levels of anaesthesia.
- Tracheal intubation is recommended to provide a secure airway and prevent aspiration of salivary and rumenal contents if regurgitation occurs.
- A stomach tube must always be available to treat rumenal tympany should it develop. Opinion varies as to the routine placement of a stomach tube, particularly with animals that have been on pasture.
- Following induction of anaesthesia, the sheep should be positioned with its head below its body to facilitate drainage of fluid from its oropharynx.

- Nitrous oxide should not be used as an anaesthetic agent in this species as its use will promote the development of rumenal tympany.
- If necessary, any regurgitant may be washed out of the mouth and nostrils while the endotracheal tube is in place and inflated.
- To prevent the possible development of aspiration pneumonia, antibiotics should be administered if there is regurgitation of rumenal contents.
- Potential problems are reduced if the procedure can be performed in the standing animal, following the use of sedatives/tranquilisers and local or regional anaesthesia.

1. Thiopentone

15 mg/kg rapidly IV followed by intubation and gaseous anaesthesia (e.g. halothane 1-2% with O_2). Do not give to animals less than 3 months old.

2. Methohexitone

4 mg/kg IV 5-7 minutes anaesthesia. Can be used as an induction agent.

3. Ketamine/diazepam or midazolam

Diazepam (2 mg/kg IV or 1 mg/kg IV) or midalozam (1 mg/kg IV) prior to ketamine (10-15 mg/kg IM or 2-4 mg/kg IV). Produces light to moderate anaesthesia of 20-30 minutes duration.

4. Ketamine/xylazine

Ketamine (4 mg/kg IV or 5-12 mg/kg IM) plus xylazine (0.1-0.2 mg/kg IV) produces light to moderate anaesthesia of 20-30 minutes duration.

The effect of xylazine can be reversed using atipamezole (0.02 mg/kg IV or 0.06 mg/kg IM).

5. Xylazine

0.1-0.2 mg/kg IM will provide heavy sedation and good analgesia. It can be used alone for restraint and performance of minor surgical procedures involving minimal invasion. It can be used in combination with acetylpromazine (0.05 mg/kg) or diazepam (2 mg/kg) to give muscle relaxation and sedation. Local infiltration with lignocaine can then be used to effect in the surgical area.

The effect of xylazine can be reversed using atipamezole (0.02 mg/kg IV or 0.06 mg/kg IM).

The advantage with this regime is that the animals continue to eructate and will not bloat.

ANALGESIA

Buprenorphine 0.005 – 0.010 mg/kg SC, IM 4 hourly
Carprofen 1.5-2.0 mg/kg SC or IV daily

Because of the short half-life of buprenorphine in this species, a combination of buprenorphine (0.006 mg/kg IV) and carprofen (1.4 mg/kg IV) administered after induction of anaesthesia has been reported to provide good analgesia.

Ruminants have a high density of alpha-2 adrenoreceptors compared to opioid receptors. Hence, alpha-2 agonists (eg. Xylazine) are likely to be more effective analgesics in these species.

Xylazine 0.08 mg/kg IM, followed by 0.03-0.04 mg/kg IV continuous infusion. Reported to provide effective prolonged analgesia. However, care must be taken because of the severe hypoxia that can be produced.

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Appendix 1: SAMPLE ANAESTHETIC RECORD

Premedication:	**Induction:**	**Maintenance:**
Time:	Time:	Details:
Drug(s):	Drug(s):	
Dose:	Dose:	

x---x---x---x **Heart rate** **●---●---●---●** **Oxygen saturation**
--- --- --- **Breathing Frequency** **◆---◆---◆----◆** **Arterial blood pressure**

Pedal reflex (Y/N) *																			
Palpebral reflex (Y/N) *																			
Tail pinch reflex (Y/N) *																			
Ear pinch reflex (Y/N) *																			
Mucous membrane colour P=Pink. B=Blue																			
Isoflurane % #																			

** Reflexes - delete those that are not applicable OR include reflexes that are applicable* *Variable / Time intervals (15 minutes)*

 # Note volatile anaesthetic agent concentration if used

Appendix 2: Analgesia in rodents and rabbits: Non-steroidal Anti-inflammatory Drugs (NSAIDs)

Suggested dose rates for **Non-Steroidal Anti-Inflammatory Drugs** in SMALL laboratory animals. Note that considerable individual and strain variation in response may be encountered and that it is therefore essential to assess the analgesic effects in each individual animal.

Drug	Rat	Mouse	Guinea Pig	Rabbit
Aspirin (Acetylsalicylic acid)	100 mg/kg PO	120 mg/kg PO	80-90 mg/kg PO	100 mg/kg PO
Carprofen	5 mg/kg SC 12-24 hourly	5 mg/kg SC 24 hourly	2.5 mg/kg SC 24 hourly	1.5 mg/kg PO 12 hourly 4 mg/kg SC 24 hourly
Diclofenac	10 mg/kg PO 24 hourly	8 mg/kg PO 24 hourly	2 mg/kg PO 24 hourly	-
Flunixin	2.5 mg/kg SC ? 12-24 hourly	2.5 mg/kg SC ? 12-24 hourly	-	1.0 mg/kg SC ? 12-24 hourly
Ibuprofen	15 mg/kg PO 24 hourly	30 mg/kg PO 24 hourly	-	-
Indomethacin	2 mg/kg PO ? frequency	1 mg/kg PO ? frequency	8 mg/kg PO ? frequency	12.5 mg/kg PO ? frequency
Ketoprofen	5 mg/kg SC,PO 24 hourly	-	-	3 mg/kg SC 24 hourly
Meloxicam	1 mg/kg SC, PO 24 hourly	-	-	0.2 mg/kg SC 24 hourly? Up to 3 days
Paracetamol (Acetaminophen)	200 mg/kg PO ? 24 hourly	200 mg/kg PO ? 24 hourly	-	-
Piroxicam	3 mg/kg PO ? 24 hourly	3 mg/kg PO ? 24 hourly	6 mg/kg PO ? 24 hourly	-

Appendix 3: Analgesia in rodents and rabbits: Opioids

Suggested dose rates for **Opioid analgesics** in SMALL laboratory animals. Note that considerable individual and strain variation in response may be encountered, and that it is therefore essential to assess the analgesic effects in each individual animal.

Drug	Rat	Mouse	Guinea Pig	Rabbit
Buprenorphine	0.01-0.05 mg/kg SC, IV 8-12 hourly 0.10-0.25 + mg/kg PO 8-12 hourly	0.05-0.10 mg/kg SC 8-12 hourly	0.05 mg/kg SC 8-12 hourly	0.01-0.05 mg/kg SC, IM or IV 6-12 hourly
Butorphanol	1.0-2.0 mg/kg SC 2-4 hourly	1.0-2.0 mg/kg SC 4 hourly	-	0.1-0.5 mg/kg IV 4 hourly
Morphine	2-5 mg/kg SC 4 hourly Sustained release formulation **#**: 4.8 mg/kg SC 6 hourly	2-5 mg/kg SC 4 hourly	2-5 mg/kg SC or IM 4 hourly	2-5 mg/kg SC or IM 4 hourly
Nalbuphine	1-2 mg/kg IM 4 hourly	2-4 mg/kg IM. ? 4 hourly	1-2 mg/kg IV, IP or IM 4 hourly	1-2 mg/kg IV 4 hourly
Pentazocine	5-10 mg/kg SC 3-4 hourly	5-10 mg/kg SC 3-4 hourly	-	5-10 mg/kg SC, IM, IV 4 hourly
Pethidine	10-20 mg/kg SC or IM 2-3 hourly	10-20 mg/kg SC 2-3 hourly	10 mg/kg SC or IM 2-4 hourly	10 mg/kg SC or IM 2-3 hourly

Morphine - Sustained release formulation. In N,O-carboxymethylchitosan (NOCC) and chitosan (Tasker RAR et al, 1997)

Appendix 4: Analgesia in other laboratory animals: Non-steroidal Anti-inflammatory Drugs (NSAIDs)

Suggested dose rates for **Non-Steroidal Anti-Inflammatory Drugs** in LARGE laboratory animals. Note that considerable individual and strain variation in response may be encountered and that it is therefore essential to assess the analgesic effects in each individual animal.

Drug	Cat	Dog	Pig	Sheep	Bird	Wallaby
Aspirin (Acetylsalicylic acid)	10-25 mg/kg PO every 48 hours	10-25 mg/kg PO 8-12 hourly	10 mg/kg PO 4 hourly	50-100 mg/kg PO 6-12 hourly	5-10 mg/kg 8-24 hourly	-
Carprofen	2-4 mg/kg SC or IV once. 2 mg/kg PO for 4 days, then every other day.	4 mg/kg IV or SC on induction. Then 2.2 mg/kg 24 hourly IV, SC or PO	2-4 mg/kg IV or SC 24 hourly	1.5-2.0 mg/kg IV or SC 24 hourly	0.5-2 mg/kg 24 hourly	2-4 mg/kg IV. SC, PO 24 hourly
Flunixin	1 mg/kg SC, PO single dose.	1 mg/kg IV or SC single dose 1 mg/kg PO, daily for up to 3 days	1-2 mg/kg IV or SC 24 hourly	2 mg/kg, IV or SC 24 hourly	-	1 mg/kg IV, IM, SC
Ibuprofen	-	10 mg/kg PO 24 hourly	-	-	1 mg/kg 12 hourly	-
Ketoprofen	2 mg/kg SC, once daily for up to 3 days 1 mg/kg PO, once daily for up to 5 days	2 mg/kg SC, once daily for up to 3 days 1 mg/kg PO, daily for 5 days	3 mg/kg IM Once only	-	1-2 mg/kg 24 hourly	1 ,g/kg SC, PO 24 hourly
Meloxicam	0.2 mg/kg SC, PO Then 0.1 mg/kg daily	0.2 mg/kg IV, SC or PO. Then 0.1 mg/kg PO daily.	-	-	0.1-0.3 mg/kg 24 hourly	-
Paracetamol (Acetaminophen)	**Contraindicated**	15 mg/kg PO 6-8 hourly	-	-	-	**-**
Piroxicam	-	-	-	-	-	-

Appendix 5: Analgesia in other laboratory animals: Opioids

Suggested dose rates for **Opioid analgesics** in LARGE laboratory animals. Note that considerable individual and strain variation in response may be encountered, and that it is therefore essential to assess the analgesic effects in each individual animal.

Drug	Cat	Dog	Pig	Sheep	Bird	Wallaby
Buprenorphine	0.005-0.01 mg/kg SC or IV 4-8 hourly	0.005-0.02 mg/kg IM, SC, IV 4-8 hourly	0.01 mg/kg IM or IV 6-12 hourly	0.005-0.010 mg/kg IM or IV, 4 hourly	0.01-0.05 mg/kg IM	0.01 mg/kg SC 12 hourly
Butorphanol	0.4-0.8 mg/kg SC or IM 2-4 hourly	0.2-0.4 mg/kg SC or IM 2-3 hourly	0.1-0.3 mg/kg IM 4 hourly	0.5 mg/kg IM, SC 2-3 hourly	1-4 mg/kg IM 6 hourly	-
Morphine	0.1-0.2 mg/kg SC, IM, IV 4 hourly	0.1-1.0 mg/kg SC, IM, IV 4-6 hourly	0.2-1.0 mg/kg IM ?4 hourly	0.2-0.5 mg/kg IM ?4 hourly	-	-
Nalbuphine	0.3-0.5 mg/kg SC, IM, IV 3 hourly	0.3-0.5 mg/kg SC, IM 3-4 hourly	-	-	-	-
Oxymorphone	0.05-0.40 mg/kg SC, IM, IV 2-4 hourly	0.05-0.22 mg/kg IM, SC, IV 2-4 hourly	0.02 mg/kg IM	-	=	-
Pentazocine	1-4 mg/kg IM, IV 2-3 hourly	1-4 mg/kg IM or IV 2-4 hourly	2 mg/kg IM or IV 4 hourly	-	-	-
Pethidine	3.5-10.0 mg/kg IM or 10-15 mg/kg SC 2-3 hourly	3.5-10 mg/kg IM or 10-15 mg/kg SC 2.5-3.5 hourly	2 mg/kg IM or IV 2-4 hourly	2 mg/kg IM or IV 2 hourly	3-5 mg/kg IM 6 hourly	1 mg/kg IV, IM SC
Fentanyl	0.002-0.003 mg/kg IV bolus, repeated every 20-30 mins, or by continuous infusion (0.002-0.003 mg/kg/hr) Transdermal: 25 µg/hr every 3 days	0.001-0.005 mg/kg IV bolus, repeated every 20-30 mins, or by continuous infusion (0.003-0.010 mg/kg/hr) Transdermal: 3-10 kg: 25µg/hr 10-20 kg: 50µg/hr 20-30 kg: 75 µg/hr >30 kg: 100µg/hr	Transdermal: 50-100 µg/hr applied 8-12 hrs prior to surgery. Reapply every 72 hours.	-	-	

Appendix 6: Inhalation Anaesthesia

Induction and maintenance concentrations of inhalational anaesthetics in laboratory animals

	Induction %	Maintenance %
Halothane	**4**	**0.75-2**
Isoflurane	**4**	**1-2.5+**
Enflurane	**3-5**	**1-3**
Sevoflurane	**5-8**	**2.5-4**

Appendix 7: Injectable Anaesthesia in rodents and rabbits

Note that these dose rates provide only a general guide. Considerable between-strain and between-animal variation occurs.

Species **Drug**	Rat	Mouse	Guinea pig	Rabbit
Alphaxalone/alphadolone (Saffan®)	10-12 mg/kg IV	10-15 mg/kg IV	40 mg/kg IP (light anaesthesia only)	6-9 mg/kg IV
Alpha-Chloralose	55-65 mg/kg IP	-	70 mg/kg IP	80-100 mg/kg IV
Alpha-Chloralose + urethane	50-60 mg/kg IP + 500-800 mg/kg IP (administer urethane 20-30 min prior to alpha-chloralose)	-	-	80 mg chloralose IV + 400-800 mg/kg Urethane IV
Fentanyl/fluanisone (Hypnorm) + diazepam	0.6 ml/kg IP + 2.5 mg/kg IP	0.4 ml/kg IP + 5 mg/kg	1 ml/kg IM or IP + 2.5 mg/kg IP	0.3 ml/kg IM + 1-2 mg/kg IV, IM or IP (diazepam 10-15 mins after the Hypnorm)
Reverse fentanyl with an opioid	2 mg/kg SC or IP (butorphanol)	2 mg/kg SC or IP (butorphanol)	1 mg/kg IP or SC (butorphanol) 0.01 mg/kg IV or 0.05 mg/kg IP (buprenorphine)	0.01 mg/kg IV (buprenorphine)
Fentanyl/fluanisone/midazolam	2.7 ml/kg IP *	10.0 ml/kg IP *	8.0 ml/kg IP*	0.3 ml/kg IM + 1-2 mg/kg IV or IP (midazolam -10 to15 mins after the Hypnorm)
Reverse fentanyl with an opioid	2 mg/kg SC or IP (butorphanol)	2 mg/kg SC or IP (butorphanol)	1 mg/kg IP or SC (butorphanol); 0.01 mg/kg IV or 0.05 mg/kg IP (buprenorphine)	0.01 mg/kg IV (buprenorphine)
* Fentanyl/medetomidine	300 □g/kg IP + 300 □g/kg IP	Not Recommended	-	8 µg/kg IV + 330 µg/kg IV
Reverse medetomidine with atipamezole, and fentanyl with an opioid	1 mg/kg SC or IP + 2 mg/kg SC or IP (butorphanol)			1 mg/kg IV + 1 mg/kg IV (nalbuphine)
Inactin	80 - 100 mg/kg IP	80 mg/kg IP	-	47.5 mg/kg IV
Ketamine + acepromazine	75-80 mg/kg IP + 2.5 mg/kg IP	100 mg/kg IP + 5 mg/kg IP	125 mg/kg IP or IM + 5 mg/kg IP or IM	50 mg/kg IM + 1 mg/kg IM

Species Drug	Rat	Mouse	Guinea pig	Rabbit
Ketamine + Diazepam	75 mg/kg IP + 5 mg/kg IP	100 mg/kg IP + 5 mg/kg IP	100 mg/kg IP or IM + 5 mg/kg IP or IM	25 mg/kg IM + 5 mg/kg IM
* Ketamine + medetomidine Reverse medetomidine with atipamezole	75 mg/kg IP + 0.5 mg/kg IP 1 mg/kg SC or IP	75 mg/kg IP + 1 mg/kg IP 1 mg/kg SC or IP	40 mg/kg IP + 0.5 mg/kg IP 1 mg/kg SC	25 mg/kg IM + 0.5 mg/kg IM 1 mg/kg SC or IV
Ketamine + Midazolam	75 mg/kg IP + 5 mg/kg IP	100 mg/kg IP + 5 mg/kg IP	-	-
* Ketamine + xylazine Reverse xylazine with atipamezole	75-100 mg/kg IP + 10 mg/kg IP 1 mg/kg SC or IP	80 - 100 mg/kg IP + 10 mg/kg IP 1 mg/kg SC	40 mg/kg IM + 5 mg/kg SC or IM 1 mg/kg SC	35 mg/kg IM + 5 mg/kg IM 10 mg/kg IV + 3 mg/kg IV 1 mg/kg SC or IV
Methohexitone	10 mg/kg IV 40 mg/kg IP	10 mg/kg IV	31 mg/kg IP	10 mg/kg IV
Pentobarbitone	40-50 mg/kg IP	40 - 50 mg/kg IP	37 mg/kg IP	30-45 mg/kg IV
Propofol	10 mg/kg IV	26 mg/kg IV	-	10 mg/kg IV
Tiletamine/zolazepam	40 mg/kg IP	80 mg/kg IP (restraint only)	40 - 60 mg/kg IM (sedation)	-
Tiletamine/zolazepam + medetomidine	–	–	40 mg/kg IM + 0.5 mg/kg IM	
Thiopentone	30 mg/kg IV	30-40 mg/kg IV	-	15-30 mg/kg IV
Urethane	1000-1500 mg/kg IP	-	1500 mg/kg IV or IP	1000-2000 mg/kg IV or IP

* Dose in ml/kg of a mixture of 1 part fentanyl/fluanisone plus 2 parts water for injection, and 1 part midazolam (5 mg/ml initial concentration)

Appendix 8: Injectable Anaesthesia in other laboratory animals

Note that these dose rates provide only a general guide. Considerable between-strain and between-animal variation occurs.

Species **Drug**	Cat	Dog	Pig	Sheep	Bird	Wallaby
Alpha-chloralose (**non-recovery**)	70 mg/kg IP or 60 mg/kg IV	80 mg/kg IV	-	-	-	-
Alphaxalone/alphadolone (Saffan®)	9-12 mg/kg IV 12-18 mg/kg IM	-	6 mg/kg IM, then 2 mg/kg IV	2-3 mg/kg IV (adult) 6 mg/kg IV (lamb)	10 - 14 mg/kg IV	1 ml/5 mg IM or IV
Azaperone (sedation)	-	-	2-8 mg/kg IM	-	-	-
Ketamine + acepromazine	20 mg/kg IM + 0.11 mg/kg IM	-	33 mg/kg IM + 1.1 mg/kg IM	-	-	-
Ketamine + Diazepam	-	-	10 – 15 mg/kg IM + 0.5 – 2 mg/kg IM	10-15 mg/kg IM + 2 mg/kg IM 4 mg/kg IV + 1 mg/kg IV	20-40 mg/kg IM + 1-1.5 mg/kg IM	3 mg/kg + 1-2 mg/kg
Ketamine + Medetomidine Reverse with atipamezole	7 mg/kg IM + 0.08 mg/kg IM or SC 0.3-0.5 mg/kg IV or SC	2.5 – 7.5 mg/kg IM + 0.05 mg/kg IM	10 mg/kg IM + 0.08 mg/kg IM	1 mg/kg IM + 25 µg/kg IM	-	2-3 mg/kg IM + 50-100 Φg/kg IM 50-400 Φg/kg
Ketamine + Midazolam	10 mg/kg IM + 0.2 mg/kg IM	-	10 – 15 mg/kg IM + 0.5 – 2 mg/kg IM	10-15 mg/kg IM or 2-4 mg/kg IV + 1 mg/kg IV	20-40 mg/kg IM + 4 mg/kg IM	-
Ketamine + Xylazine Reverse with atipamezole	22 mg/kg IM + 1.1 mg/kg IM or SC 0.3-0.5 mg/kg IV or SC	5 mg/kg IV + 1-2 mg/kg IV or IM	-	4 mg/kg IV + 0.2 mg/kg IV	10-30 mg/kg IM + 2-6 mg/kg IM	3 mg/kg IM + 2-3 mg/kg IM
Methohexitone	4-8 mg/kg IV	4-8 mg/kg IV	5 mg/kg IV	4 mg/kg IV	-	10 mg/kg IV
Pentobarbitone	20 - 30 mg/kg IV	20-30 mg/kg IV	20 - 30 mg/kg IV	30 mg/kg IV	-	-
Propofol	5 - 8 mg/kg IV	5-7.5 mg/kg IV	2.5 - 3.5 mg/kg IV	4-5 mg/kg IV	-	-

Species Drug	Cat	Dog	Pig	Sheep	Bird	Wallaby
Tiletamine/zolazepam (Zoletil®)	7.5 mg/kg IM + 7.5 mg/kg IM	-	2-4 mg/kg IM (restraint) 6-8 mg/kg IM (light anaesthesia)	-	-	20-30 mg/kg IM 2.5 mg/kg IV (for induction)
Tiletamine/zolazepam + xylazine Reverse xylazine with atipamezole	-	-	-	-	-	5 mg/kg IM + 0.5 mg/kg IM 50-400 µg/kg
Thiopentone	10-15 mg/kg IV	10-20 mg/kg IV	6.6-25 mg/kg IV	10-15 mg/kg IV	-	20 mg/kg IV
Urethane (**non-recovery**)	750 mg/kg IV 1500 mg/kg IP	1000 mg/kg IV	-	1000 mg/kg IV	-	-