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# **Ways of minimising pain and distress in animals in research**

Practical information for research scientists  
and animal experimentation  
ethics committees

National Health and Medical Research Council

# **NHMRC**

**Animal Welfare Committee**

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Other publications by the Animal Welfare Committee of the NHMRC's Medical Research Committee:

- ┆ Australian Code of Practice for the Care and Use of Animals for Scientific Purposes (NHMRC, CSIRO and Australian Agricultural Council).
- ┆ An Introductory Guide to Minimising the Numbers of Animals Used in Research Projects.
- ┆ Background Paper: Strategies for Minimising the Numbers of Animals Used in Research Projects.
- R A Guide to the Use of Australian Native Mammals in Biomedical Research (Sections 1-4).
- ┆ Australian Animal Experimentation Ethics Committees 1987-1989: Protection for Animals in Biomedical Research.
- R NHMRC Policy on the Use of Non-human Primates in Medical Research.
- ┆ NHMRC Policy on the Care of Dogs for Medical Research.

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# 1. Purpose of this document

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One of the major purposes of animal experimentation for biomedical research is to understand fundamental biological mechanisms. This understanding will become the basis for the maintenance of health and the treatment of disease in both humans and animals.

Many diseases cause significant degrees of pain and distress in affected individuals. Therefore there is the potential to cause pain or distress in the animal under study. In order to prevent or minimise this pain or distress, the investigator needs to be attuned to the recognition of signs in the species under study and to be familiar with ways of preventing or relieving pain or distress.

The purpose of this document is to provide helpful information to:

- i. enable investigators to recognise manifestations of pain in their experimental animals and to be aware of appropriate methods of prevention and relief;
- ii. assist in the planning and conduct of experiments in ways that will minimise pain and distress; and
- iii. help Animal Experimentation Ethics Committees (AEECs) to evaluate applications in which procedures may cause pain or distress.

The document is based on the provisions regarding pain and distress in the *Australian Code of Practice for the Care and Use of Animals for Scientific Purposes*.

## 2. Current provisions governing pain and distress

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### The Australian Code of Practice for the Care and Use of Animals for Scientific Purposes

The Code has five general principles dealing specifically with pain and distress.

1. Experiments must be designed to avoid pain or distress to animals. If this is not possible, pain or distress must be minimised. (Code paragraph 1.12)
2. Pain and distress cannot be evaluated easily in animals and therefore investigators must assume that animals experience pain in a manner similar to humans. Decisions regarding the animals' welfare must be based on this assumption unless there is evidence to the contrary. (Code paragraph 1.13)
3. Experiments which may cause pain or distress of a kind and degree for which anaesthesia would normally be used in medical or veterinary practice must be carried out using anaesthesia appropriate to the species and the procedure. When it is not possible to use anaesthesia, such as in certain toxicological or animal production experiments or in animal models of disease, the end-point of the experiments must be as early as possible to avoid or minimise pain or distress to the animals. (Code paragraph 1.14)
4. Analgesic and tranquilliser usage must be appropriate for the species and should at least parallel usage in medical or veterinary practice. (Code paragraph 1.16)
5. An animal which develops signs of pain or distress of a kind and degree not predicted in the proposal, must have the pain or distress alleviated promptly. If severe pain cannot be alleviated without delay, the animal must be killed humanely forthwith. Alleviation of such pain or distress must take precedence over finishing an experiment. (Code paragraph 1.17)

**Section 3.3 of the Code provides specific details on limiting pain and distress, and is reproduced below.**

#### 3.3.1

*Pain and distress cannot be evaluated easily in animals, and therefore investigators must assume that animals experience pain in a manner similar to humans. Decisions regarding their welfare in experiments must be based on this assumption unless there is evidence to the contrary.*

### 3.3.2

*The investigator must anticipate and take all possible steps to avoid or minimise pain and distress, including:*

- (i) choosing the most humane method for the conduct of the experiment;*
- (ii) ensuring the technical skills and competence of all persons involved in animal care and use;*
- (iii) ensuring that animals are adequately monitored for evidence of pain and distress;*
- (iv) acting promptly to alleviate pain or distress;*
- (v) using anaesthetic, analgesic and tranquillising agents appropriate to the species and the experimental purposes;*
- (vi) conducting projects over the shortest time practicable; and*
- (vii) using appropriate methods of euthanasia.*

### 3.3.3

*The use of local or general anaesthetics, analgesics or tranquillisers must be appropriate to the species, and should at least parallel their use in current medical or veterinary practice.*

### 3.3.4

*Experiments which are liable to cause pain of a kind and degree for which anaesthesia would normally be used in medical or veterinary practice must be carried out under anaesthesia.*

### 3.3.5

*Distress can sometimes be avoided or minimised by non-pharmacological means. Before an experiment begins, animals should be appropriately conditioned to the experimental environment and procedures, and be familiar with handlers. During and after experiments, appropriate nursing procedures to minimise pain and distress and to promote the well-being of the animals, must be provided.*

### 3.3.6

*The monitoring of animals must at all times be adequate to prevent the occurrence, or allow prompt alleviation, of pain or distress.*

### 3.3.7

*If animals develop signs of severe pain or distress despite the precautions outlined above, they must have the pain or distress alleviated promptly or must be killed humanely and without delay. Alleviation of such pain or distress must take precedence over continuing or finishing the experiment.*

## legislation

Each State/Territory with animal welfare legislation has approached the issue of pain and distress in animals generally, as an aspect of cruelty to animals. Penalties are prescribed under each of these Acts. The *Australian Code of Practice* is incorporated under animal welfare legislation in New South Wales, Victoria, Queensland, South Australia, Tasmania and the Australian Capital Territory and is expected to be incorporated soon in revised West Australian legislation.

### New South Wales

The New South Wales *Animal Research Act* 1985 is currently under review. It specifies that:

- 4 *The regulations may prescribe a Code of Practice with respect to the conduct of animal research and the supply of animals for use in connection with animal research.*

Additionally,

62 (3) A regulation may create an offence punishable by a penalty not exceeding \$500.

The Code of Practice which is prescribed by the regulations is the *Australian Code of Practice for the Care and Use of Animals for Scientific Purposes* and therefore the definitions of pain and distress and the provisions in the Code have legal status in New South Wales.

## Victoria

Under the Victorian *Prevention of Cruelty to Animals Act 1986*:

36 (1) A person who knowingly or negligently does or omits to do any act with the result that unnecessary, unreasonable or unjustifiable pain or suffering is caused to any animal kept at a scientific or breeding establishment or used for the purpose of carrying out a scientific procedure is guilty of an offence.

36 (2) A person who carries out any surgical operation on an animal unless –

(a) during the entire length of the operation, the animal is under the influence of an anaesthetic so as to be insensible to any pain it might otherwise have suffered; and

(b) the operation is carried out in accordance with any relevant Code of Practice – is guilty of an offence.

36 (3) If an animal has been so injured in the course of a scientific procedure that it would seriously suffer if it remained alive, a person who fails to destroy the animal painlessly is guilty of an offence.

The penalty for a person who is a corporation is 100 penalty units. The penalty for a person other than a corporation is 10 penalty units or imprisonment for 3 months for a first offence, and 25 penalty units or imprisonment for 6 months for a second or subsequent offence.

## Queensland

The Queensland *Animal Protection Act 1925-1977* is currently under review. It uses the term 'ill-treat' which is defined as 'ill-treat, wound, mutilate, overdrive, over-ride, overwork, abuse, worry, torment, torture and cause any animal unnecessary pain or suffering; also overload or drive when overloaded, and overcrowd, and unreasonably beat or kick and "ill-treated", "ill-treating" and "ill-treatment" have corresponding meanings'.

Actions falling under this definition are offences of cruelty and subject to penalties ranging from \$50-\$1000 or imprisonment for up to 6 months.

Additionally, Section 23 Regulations:

(2) Regulations made under this Act may adopt, in whole or in part, any of the standards, rules, codes or specifications of any body identified in the regulations.

The Code of Practice which is prescribed by the regulations is the *Australian Code of Practice for the Care and Use of Animals for Scientific Purposes* and therefore the definitions of pain and distress and the provisions in the Code have legal status in Queensland.

## South Australia

Under the South Australian *Prevention of Cruelty to Animals Act 1985*:

13(1) *A person who ill-treats an animal shall be guilty of an offence.*

13(2) *Without limiting the generality of subsection (1) a person ill-treats an animal if that person –*

- (a) *deliberately and unnecessarily causes the animal undue or severe pain;*
- (b) *being the owner of the animal –*
  - i. *fails to provide it with appropriate, and adequate, food, water, shelter or exercise;*
  - ii. *fails to take reasonable steps to alleviate any pain suffered by the animal;*
  - iii. *abandons the animal; or*
  - iv. *neglects the animal so as to cause it pain;*
- (c) *having injured the animal (not being an animal of which that person is the owner) fails to take reasonable steps to alleviate any pain suffered by the animal;*
- (g) *kills the animal in a manner that causes the animal undue or severe pain.*

The penalty is \$10,000 or imprisonment for 12 months.

## Western Australia

The Western Australian *Prevention of Cruelty to Animals Act 1920 (1976)* is currently under review. It states that:

7(2) *An authorised person who perform an operation shall observe the following conditions which apply to that operation and to the animal the subject of the operation –*

- (a) *the animal subject to the operation shall, during the whole time thereof be so under the influence of some anaesthetic as to be insensible to pain;*
- (b) *when the animal has in the course of the operation been so injured that its recovery would involve serious suffering it shall be destroyed while still insensible; and*
- (c) *an animal which has suffered one operation shall not be subjected to another.*

Penalties are not specified.

## Tasmania

The Tasmanian *Animal Welfare Act 1993* states that:

8(1) *A person must not do any act, or omit to do any duty, which causes or is likely to cause unnecessary and unjustifiable pain or suffering to an animal.*

The penalty is a fine not exceeding 50 penalty units or imprisonment for a period not exceeding 12 months, or both.

## Northern Territory

The Northern Territory *Prevention of Cruelty to Animals Act 1980* uses the term 'ill-treat' which includes:

- (a) *cruelly assault, mutilate, overdrive, overwork, abuse, worry, torment or torture;*

- (b) knowingly overload or overcrowd;
- (c) unreasonably, wantonly or recklessly neglect or beat.

The penalty for ill-treatment is \$200 or imprisonment for 6 months. Additionally, 'causing unnecessary pain' carries similar penalties.

### **Australian Capital Territory**

The Australian Capital Territory *Animal Welfare Act* 1992 states that:

- 8(1) A person shall not, without reasonable excuse, deliberately cause an animal unnecessary pain.
- 8(2) A person in charge of an animal shall not, without reasonable excuse –
  - (a) fail to provide it with appropriate food, water, shelter, or exercise;
  - (b) fail to take reasonable steps to alleviate any pain suffered by the animal;
  - (c) neglect the animal so as to cause it pain;
  - (d) kill the animal in a manner that causes it unnecessary pain.

The penalty is \$10,000 or imprisonment for 1 year, or both.

### 3. What are pain and distress?

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It is difficult to provide a satisfactory definition of pain, even in human medicine (NFIIMRC *Report of the Working Party on Management of Severe Pain*, 1988). Pain is a subjective feeling: there are few objective ways of measuring it. In human beings, pain perception varies greatly between individuals and is influenced greatly by environmental conditions and the mental state of the person.

The Oxford Dictionary defines pain as 'the sensation which one feels when hurt', but goes on to cite the quotation that 'pain and pleasure are simple ideas incapable of definition'. A physiology textbook defines pain as 'that sensory experience evoked by stimuli that injure or threaten to destroy tissue, defined introspectively by every man as that which hurts' (Mountcastle, 1984). These definitions point to the highly subjective nature of pain in human beings. It is therefore even harder to find a definition that satisfactorily defines pain across all vertebrate species. Pain in animals has been defined by Zimmermann (1984) as 'an aversive sensory experience that elicits protective motor actions, results in learned avoidance and may modify species specific traits of behaviour including social behaviour'. In practical terms, the important issue is to be able to recognise that an animal is in an abnormal behavioural or physiological state.

The Australian Code is based on the view that pain in animals, at our current state of knowledge, cannot be easily evaluated, and therefore investigators must, for practical purposes, assume that animals experience pain in a manner similar to humans (see above, Code paragraph 33.1). Although this assumption will not always be true, it is a cautious position that provides a framework to allow research workers and ethics committee members to set reasonable limits.

*Pain in animals serves a similar function to pain in humans. Therefore animals' interest in avoiding pain should be respected even if their experience of pain is not equivalent to that of human beings.*

#### Responses to pain

A number of behavioural changes occur in response to pain and these will vary according to species, location and degree of pain, and between animals (Sanford et al., 1986).

- i. Conscious avoidance responses: These involve a learned modification in the animal's behaviour, enabling it to avoid further exposure to the painful stimulus.
- ii. Protective responses: These are designed to protect the animal or parts of it and may include withdrawal from the stimulus or removal of the stimulus. These responses are sometimes involuntary.
- iii. Responses that minimise pain and promote healing: In response to pain, animals may reduce their activity, for example, by lying down or standing very still. However, some animals may increase their activity in response to pain, for example horses will be restless and will roll during abdominal pain ie. colic.

- iv. Communicative responses: These communicate the painful experience to animals of the same or different species. The responses may involve pain-specific vocalisation or modifications to facial expression or posture.
- v. Physiological responses to pain: The anatomical and physiological mechanisms underlying pain sensation are dealt with in most standard textbooks of physiology and have been summarised by Sanford et al. (1986).

## Assessment of pain

The sensitivity of both human beings and animals to pain may not be a simple function of the intensity of the damaging stimulus or the severity of the illness or condition to which the individual is exposed. When it has been tested scientifically, sensitivity to pain is highly variable. It is thought that this variability may be related to the subject's prior experience, state of anxiety, and attention to the stimulus or condition.

Investigators will be able to identify signs of pain or discomfort in experimental animals more readily if they are familiar with the normal behaviour of the species, and if they take into account as wide a range of behavioural, physiological and biochemical parameters as possible when monitoring an animal's well-being. The overall assessment of well-being in individual animals comes down to a value judgement based on the experience of those making the observation (Sanford et al., 1986).

Section 6 lists some of the signs that may enable investigators to identify the presence of pain or distress in particular species and gives information on the appropriate analgesic and anaesthetic agents. There are now a number of other very helpful publications dealing with the assessment and alleviation of pain and distress in experimental animals, farm animals and domestic animals, including Sanford et al. (1986), Flecknell (1984, 1986), Gibson (1985), Smith (1987), Stephens (1988), Duncan & Moloney (1986).

## Distress

The *Australian Code of Practice for the Care and Use of Animals for Scientific Purposes* defines distress as 'acute or chronic response of an animal caused by stimuli that produce biological stress which produces observable, abnormal physiological or behavioural responses.'

Normal responses to biological stress arise in human beings or other animals when environmental demands lead to particular physiological, biochemical, immunological, behavioural or other changes. These responses may be seen as adaptive responses, for example heat or cold stress, exercise-induced stress, psychological stress or immune system challenge. Distress does not occur if the animal is able to cope with these stressors by evoking a series of measurable physiological responses, mediated principally through the autonomic nervous system or endocrine system. These responses may include enhanced release of adrenaline and noradrenaline from sympathetic nerves leading to increases in heart rate and cardiac output; increased output of glucagon from the pancreas; increased output of hormones from the hypothalamus and pituitary which lead in turn to increased secretion of corticosteroids from the adrenal cortex. Where these adaptive changes have no adverse effects and the animal's behaviour is considered within the normal range, the stress may be regarded as physiological.

Where the stress becomes 'distress' however, it reaches levels that exceed the normal physiological range with detrimental effects on the health and well-being of the animal. The Australian Code requires that distress must be alleviated or minimised. The monitoring of animals must at all times be adequate to allow prompt alleviation of the symptoms.

# 4. A checklist for minimising pain and distress

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## General

### Planning the experiment (see also Section 3.2 of the Australian Code of Practice):

- c1 Determine whether alternative, non-animal techniques could be used;
- c1 Anticipate the extent of pain and distress and work out the ways in which it can be controlled;
- ┌ Choose the most humane experimental methods possible;
- Cl Balance the anticipated pain and distress to individual animals against the possibility of lesser pain to a greater number;
- ┌ Design the experiment to last for the shortest possible time, e.g. choosing the earliest practicable end-point;
- ┌ Learn the normal behaviour of the species and the signs of pain and distress;
- ☐ Consider whether the proposed techniques are the best possible ones which could be used;
- ┌ Provide comfortable housing appropriate to the species being used.

### Conducting the experiment:

- Cl Monitor animals for changes in behaviour and signs of pain and distress throughout the experiment;
- Cl Provide animals with adequate anaesthesia or analgesia;
- Cl Provide palliative treatment for pain and distress, e.g. post-operative nursing, comfortable bedding, optimal environmental temperature and humidity, minimal noise etc.;
- ┌ Kill humanely and without delay any animal which appears to be suffering unforeseen pain and distress which cannot be promptly alleviated;
- ┌ Continue to review techniques and refine them whenever possible.

## **AEEC checklist based on NHMRC categories of experiments**

It is difficult to provide a general guide to the minimisation of pain, as the likelihood of its occurrence and the degree of its severity varies greatly between types of experiments ranging from venepuncture procedures to orthopaedic surgery.

The NHMRC has developed a system of categorising experiments. This is not primarily based on the severity of the experiments, but on the techniques and procedures to be used.

AEECs may find the following questions of assistance when examining applications. The questions are grouped according to the category. Not all questions will be relevant for every experiment, and the list is not exhaustive.

### **NHMRC Category 1.1**

'No experimentation on living animals (i.e. animals are killed painlessly for biochemical analysis, or in vitro cell, tissue or organ studies).'

- U Do the procedures to be used to kill the animal avoid distress and produce rapid loss of consciousness without pain until death occurs?
- J Are the procedures compatible with the aims of the experiments?
- U Is the person who will perform the procedures competent?

### **NHMRC Category 1.2**

'Experiments under anaesthesia, without recovery (i.e. animals are fully anaesthetised for the duration of the experiment, and are killed at its conclusion without recovery from anaesthesia).'

- U Are the anaesthetic techniques to be used the most appropriate?
- J What monitoring of anaesthesia will be carried out (continuous supervision or intermittent checks)?
- CI What parameters will be checked (e.g. heart rate, blood pressure, pupillary diameter)?
- J What physiological parameters will be assessed to ensure the animal is dead at the end of the experiment?

### **NHMRC Category 2.1**

'No anaesthesia, minor procedures used (e.g. injections, blood sampling, antibody raising, minor dietary manipulations).'

- U Why is anaesthesia not to be used?
- J Should it be used?
- J Would anaesthesia decrease pain and distress?
- J Will any special handling techniques be used to minimise pain and distress during the experimental procedures?

### **NHMRC Category 3**

'Experiments or surgery under anaesthesia, with subsequent recovery of the animal.'

- U Are the anaesthetic techniques to be used the most appropriate?
- J What monitoring of anaesthesia will be carried out (continuous supervision or intermittent checks)?

- Cl What parameters will be checked (e.g. heart rate, blood pressure, pupillary diameter)?
- ┘ Is the general health of the animal such that the best possible outcome can be expected after surgery?
- Cl Will the animal be isolated while receiving anaesthetics?
- O What monitoring of fluid levels will be carried out during surgery?
- Cl Will the surgery be carried out under aseptic conditions?
- Cl Will an experienced and competent person be performing the surgical procedure?
- ┘ Should evidence be sought regarding the skills of the surgeon?
- ┘ Will any person learning the procedures be adequately supervised?
- ┘ Should additional help be sought from a person with established clinical expertise in the procedure?

### **NHMRC Category 3.1 and NHMRC Category 3.2**

'Minor post-operative sequelae (e.g. following biopsies or cannulations)'  
and

'Significant post-operative sequelae.'

- Cl What provisions will be made to ensure comfortable post-operative recovery (e.g. warmth, hygiene, fluid and food intake, control of infection)?
- Cl Will analgesics or tranquillisers be given? (Analgesic and tranquilliser usage should parallel that in current medical and veterinary practice.)
- Cl Is suitable housing available to enable animals to recover from surgery in isolation?
- ┘ What clinical records will be kept?
- ┘ What post-operative monitoring will be carried out and by whom?
- Cl How frequently will surgical wounds be checked?
- Cl What emergency procedures are in place?

### **NHMRC Category 4.1**

'Studies on the biology of pain or of the responses to physical stresses (e.g. heat, cold, burning, ionising radiation).'

- ┘ Can anaesthesia be used?
- ┘ If anaesthesia is not appropriate, what supportive measures (e.g. bedding) are to be used to help alleviate pain?
- ┘ Can the investigator demonstrate that any proposed painful stimulus will be confined to levels comparable to those which do not distress human beings?
- ┘ What is the basis for establishing the minimum pain levels necessary to achieve the aims of the experiments?
- Cl What analgesia is to be given to the animals?
- O Is there any opportunity for the animals to escape from painful stimuli?
- ┘ Are physical stresses to be applied to the whole animal or parts of the animal only?
- ┘ Is any proposed temperature variation within the limits to which the animal is able to adjust physiologically?
- Cl Will monitoring of the animal be sufficiently frequent to quickly detect unexpected pain and distress?

## NHMRC Category 4.2

'Studies on unanaesthetised animals of the toxic actions of drugs or other chemical agents or of infectious agents.'

- U Are there alternative methods that could be used for testing toxicity?
- Cl Is the minimum number of animals to be used to gain the maximum amount of information?
- 3 Are the doses to be used the lowest practicable?
- ┘ Is the duration of administration the shortest practicable?
- 3 Is any lethal dose test to be carried out? (Is it essential? Are minimum numbers to be used? Check legal situation.)

## NHMRC Category 4.3

'Experimental procedures on unanaesthetised animals requiring immobilisation or extended periods of restraint other than normal caging.'

- ┘ Why is a restraint device to be used?
- ┘ Is it necessary for the purposes of the experiment?
- ┘ Is restraint to be used for as short a time as possible?
- ┘ Is this an appropriate type of restraint for the animal species?
- ┘ Are tranquillisers or anaesthetics to be used in conjunction with the restraint device?
- ┘ What monitoring of recovery from tranquillisers or anaesthetics will be carried out?
- ┘ Where restraint is to be prolonged, what monitoring will be carried out, and by whom? (The person must not be participating in the experiment, and must be able to remove the animal from restraint or modify the method.)
- ┘ Are any of the drugs to be used in the experiment likely to interfere with any of the parameters to be monitored?

*It should be noted that where it is planned to use neuromuscular blocking agents or electroimmobilisation:*

- i. Neuromuscular blocking agents must not be used without adequate general anaesthesia or an appropriate surgical procedure which eliminates sensory awareness. Immobilisation of an animal solely with a neuromuscular blocking agent is not acceptable. When these agents are used with an anaesthetic, special care must be taken to ensure the maintenance of an adequate plane of anaesthesia. Since criteria such as character of respiration and corneal and flexor withdrawal reflexes cannot be used, continuous or frequent intermittent monitoring of physiological variables such as heart rate, blood pressure, pupil size and the electroencephalogram is necessary together with the effects on these of mild sensory stimuli. Care is required to ensure that drugs used in these experiments do not interfere with this monitoring. (Code paragraph 3.3.39)
- ii. Electroimmobilisation must not be used as an alternative to analgesia or anaesthesia. When its use is proposed for the restraint of animals, AECCs must carefully evaluate published evidence to assess whether it may cause distress. If so, an alternative restraint method must be used. (Code paragraph 3.3.40)

#### **NHMRC Category 4.4**

'Studies involving experimental induction of abnormal fetal growth.'

- Cl Does the investigator anticipate (based on present knowledge of physiology and neural development) that the fetus will be able to feel pain?
- O What anaesthesia and analgesia will be used to provide adequate pain relief to both the mother and the fetus?
- Cl Does the fetus have any special requirements for anaesthesia during the procedures?
- Cl Will the fetal experimentation or surgery compromise the ability of the neonate to survive without pain or distress?
- Cl Can such pain and distress be relieved? (If not, the Code of Practice requires that the animals must be humanely killed before or immediately following birth.)
- U Are eggs to be destroyed before hatching?

See Code paragraph 3.3.65 on Fetal experimentation.

#### **NHMRC Category 4.5**

'Experiments on individual animals that last for more than three months.'

- ┘ What monitoring of the animal's health and welfare will be carried out and by whom?
- Cl Is a periodic report planned, including assessments of good health, weight gain or loss, behavioural disorders, use of environment enrichment, adequacy of accommodation and exercise regimens (particularly for dogs)?
- ┘ Should a report from a person not involved with the experiment also be sought?

#### **NHMRC Category 4.6**

'Experiments involving the restriction of food or water intake, or other major dietary intervention.'

- ┘ Are animals to be monitored for pica (including eating their wiring and bedding), weight, general appearance, grooming and behaviour?
- ┘ What weight loss limits will be set?
- ┘ How often will the animals be monitored?

#### **NHMRC Category 4.7**

'Studies on animals prone to serious chronic disease (e.g. studies on mutant strains of animals such as stroke-prone rats, transgenic animals with experimentally induced disease).'

- Cl Does the strain chosen provide an appropriate model for the study?
- Cl Are any special husbandry methods required to maintain the animals (e.g. disease barrier methods)?
- ┘ Are appropriate housing facilities available?
- Cl Is the investigator confident of the genetic purity of the strain to be used?
- Cl If the project involves genetic manipulation, is it in accord with the guidelines issued by the Genetic Manipulation Advisory Committee and the relevant biohazards committee of the institution?

- U Is the result of genetic manipulation expected to affect the welfare of the animals and their offspring adversely? What are the expected adverse effects?
- Cl What monitoring of the clinical status of genetically manipulated animals will be carried out? (The Code of Practice requires that adverse effects must be reported to the AEEC.)

*See Code paragraphs 3.3.54-3.3.57 on Experimental manipulation of animals' genetic material.*

### **NHMRC Category 4.8**

'Laboratory studies designed to produce substantial and overt changes in behaviour by physical or chemical means.'

- Cl Will positive inducement be used to alter the animal's behaviour?
- U If not, will the degree of biological stress to be used be as mild as possible? Will it be used for as short a time as possible?

# 5. Signs of pain and distress in animals

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A thorough knowledge of the species involved is necessary before the state of well-being of the animal can be assessed.

## Examination of the animal

The animal's history and full details of any experimental procedures performed should be established prior to examination of the animal. A detailed clinical examination should be carried out and signs of pain and distress checked (such as changes in the overall appearance and behaviour of the animal). Recent articles have given detailed guidelines to assess and to quantify the levels of pain and distress produced in laboratory animals (Morton and Griffiths, 1985; Sanford et al., 1986) to aid particularly those inexperienced in assessing welfare. Pain and stress produce dramatic changes in physiological and biochemical parameters but the correlation of these with the level of the distress felt by an animal is by no means fully elucidated. The overall assessment of individual cases has to be a value judgement based on the experience of the person inspecting the animals (Sanford et al., 1986).

A variety of specific clinical signs may be used as an indication that pain and stress are present. There may be locomotor effects such as twitching, fits or tremors, convulsions, paralysis, dilated pupils, shivering, hyperaesthesia, altered reflexes, gait alterations, guarding of the abdomen and reluctance to move the limbs. The presence of dehydration may be an additional sign of pain or stress. The cardiovascular system may be affected, with alterations in the pulse rate and quality, decreased peripheral circulation, cyanosis and congestion. Any reduction in abnormal signs following administration of analgesics or anxiolytic drugs indicates that pain or distress were present.

Attempts to rank procedures on a scale of severity in order to give an easy checklist of the level of pain produced have an inherent danger of inducing a feeling of complacency in the investigator. A potentially useful scoring system is that of Morton and Griffiths (1985) who proposed a 'quantitative assessment of independent variables' which may be used in order to give a reproducible indication of the presence of pain or stress. Scores are given for body weight, appearance, clinical signs, unprovoked behaviour and responses to stimuli. Total scores are then ranked from normal to evidence of severe pain. In the latter case, the animal is physiologically abnormal and pain relief should be given or the animal killed

The next section contains helpful information on the most commonly used laboratory species. Information on Australian native mammals can be found in the NHMRC publication *A Guide to the Use of Australian Mammals in Research*. Information regarding non-human primates should be sought from the NHMRC Policy on the Use of Non-Human Primates in Research and by contacting one of the NHMRC-supported colonies of these animals in Australia.

# 6. Species-specific data on effective anaesthetics

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## 6.1 Rodents

### Signs of pain and distress (Morton & Griffiths, 1985)

Rats and mice may show a dormouse posture and squeal on handling. They may become more docile, or aggressive and eat the bedding or neonates. There may be red staining around the eyes and nose in rats, and the presence of a square tail indicating dehydration. There may be a change in feeding activity and a change in the normal group behaviour.

### Anaesthesia

Anaesthetising rodents is difficult for a number of reasons:

- a. The small body size, and large surface area to body weight ratio of small rodents, makes them susceptible to rapid loss of body heat, particularly when they are anaesthetised. Some anaesthetic drugs cause hypothermia as a result of peripheral vasodilation, and by changing normal thermoregulatory mechanisms in the animal. Hypothermia results in a reduction in the metabolic rate and slows the metabolism of some anaesthetic drugs resulting in a prolonged recovery time. Every effort should be made to maintain body heat. Excessive clipping of hair and the use of alcoholic cleansing agents should be minimised. The use of thermostatically controlled blankets, heating lamps, and insulation with cotton wool or aluminium foil should be encouraged and should be continued into the post-operative phase until the animal has fully recovered.
- b. There are few accessible veins suitable for injecting anaesthetic drugs. For this reason the administration of injectable anaesthetic drugs in small rodents is usually by the intraperitoneal (i.p.), intramuscular (i.m.) or occasionally the subcutaneous (s.c.) route. The i.p. route is recommended since there is little muscle mass in most small rodents and the injection of any more than a small volume of any drug solution by the i.m. route is painful. Some drugs are irritant and are therefore painful on i.m. injection. The i.m. route should be avoided in these cases. When the i.p., i.m. or s.c. routes are used to administer a drug only the computed dose based on body weight can be given. When a drug is given by the intravenous route, the drug can be administered slowly 'to effect', that is, only enough drug is given to produce the required effect. Because of the often wide variation in response to drugs between animals, some animals may be underdosed and others may be overdosed when the i.p. or i.m. routes are used, so only drugs with a wide margin of safety should be used. Some of the older drugs such as pentobarbitone have a narrow margin of safety and should be avoided if possible.

Note: The information in this section is intended as a guide only. It should be used in conjunction with other published data and in the light of clinical experience. Expert advice should be sought prior to using new agents or techniques.

- c. Rodents frequently have a small and inaccessible larynx which makes intubation difficult and their relatively narrow airways make them susceptible to airway obstruction by excessive salivation or bronchial secretions. Some drugs cause an increase in these secretions per se (ketamine) or by irritation of the mucous membranes (ether). Administration of atropine prior to anaesthesia may be indicated to reduce these effects.
- d. Even apparently normal rodents may have some degree of lung disease even if they come from a specific pathogen free environment. This lung disease may be clinical or subclinical and should be taken into account in intraoperative and postoperative mortality.
- e. Vomiting does not occur in the small rodents. Therefore it is usually unnecessary to withhold food from these animals prior to anaesthesia in contrast to other laboratory animals. Guinea pigs may regurgitate and some workers recommend withholding food for 12 hours.

### 6.1.1 Rats

#### Premedication (sedatives, tranquillisers, drugs for restraint)

Most rodents can be readily and humanely restrained and their anaesthetic drug can be administered without the need for sedation. However, if an i.v. administration of the anaesthetic is to be attempted, then pre-anaesthetic medication should be administered by the i.m. or i.p. route. If general anaesthesia is to be induced via the intravenous route, some sedation will be necessary first. If premedicant drugs are used, they will tend to reduce the dose of anaesthetic agent required to produce general anaesthesia by 30-50%. (See Table 6.1.1 A for suggested drugs.)

#### General anaesthesia

The drugs detailed below can be used to produce general anaesthesia in rats with sufficient analgesia to perform surgical techniques. Some drugs, such as pentobarbitone, produce general anaesthesia but show poor analgesia at low doses; at higher doses marked respiratory and cardiovascular depression occurs. If possible, these drugs should be avoided since better alternatives are available.

The most convenient and easiest method to administer gaseous anaesthetic agents in small laboratory rodents is by means of the open jar/anaesthetic chamber technique or the drop technique. In the drop technique, liquid anaesthetic is poured onto a cotton wool ball in a funnel or syringe case and this is held against the nose of the restrained animal until anaesthesia is induced. This tends to be rather stressful as the animal will probably struggle. Most workers prefer to use the anaesthetic chamber for induction and use the drop technique to maintain anaesthesia. To use the anaesthetic chamber it should be filled with vapour by one of two methods:

- a. A small amount of the liquid anaesthetic is poured onto some cotton wool and the liquid is allowed to evaporate and fill the chamber. The anaesthetic soaked cotton wool is placed under a mesh so that the animals do not have direct contact with the liquid. This is a relatively safe method when using agents such as methoxyflurane but should not be used for very potent and volatile agents like halothane or isoflurane. The method described below is safer.

Note: The information in this section is intended as a guide only. It should be used in conjunction with other published data and in the light of clinical experience. Expert advice should be sought prior to using new agents or techniques.

- b. Air or preferably oxygen as a carrier gas is passed through a vaporiser on an anaesthetic machine and a known concentration of the vapour is supplied to the chamber via a length of tubing. This is the preferred technique for agents such as halothane and isoflurane. After induction, anaesthesia can be maintained by means of a face mask, again either with cotton wool soaked in anaesthetic or with vapour supplied from the anaesthetic machine.

**A fume cupboard or a system to scavenge excess anaesthetic gases should be used to decrease exposure of personnel to even low levels of the gases.**

### **Inhaled anaesthetic agents**

**Halothane:** This is a non-flammable vapour which is a potent anaesthetic. It is readily vaporised and therefore it should only be used in a closed system. For example, it should be used in an anaesthetic chamber using a calibrated vaporiser when a known concentration can be supplied. It can also be delivered via an anaesthetic machine and appropriate circuit. Induction and recovery is rapid if this is used as the sole intraoperative agent.

Note halothane is toxic to humans; see NHMRC document *Hazards of anaesthetic gases, 1977*.

**Methoxyflurane:** This vapour is non-flammable and is also a potent anaesthetic. However, it vaporises much less readily than halothane and so can be used in the open anaesthetic chamber technique or drop technique for laboratory rodents. Induction is slow but not unpleasant as the vapour is a non-irritant. Recovery may also be more prolonged than with halothane, however one of the major advantages of this vapour is that it is an excellent analgesic and this analgesia extends into the recovery period. One of its main disadvantages is that it is expensive. It is also nephrotoxic in man.

**Enflurane/Isflurane:** These are some of the newer anaesthetic vapours with similar properties to halothane and should be used in the same way. They show an even more rapid induction and recovery time. They are however very expensive. Although intubation of rats is possible, it is difficult (see Costa et al., 1986). Twelve–14 g. i.v. catheters can be modified and used as endotracheal tubes.

**Ether:** Ether is not recommended on both animal welfare and workplace safety grounds.

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**Table 6.1.1 A    Injectable drugs for premedication in rats**

Drug	Accepted Dose	Route of Administration	Comments
Fentanyl/ Droperidol	0.31 ml/kg	i m. or i p	Takes 3 minutes i p and 15 minutes i m. to produce sedation with analgesia. Recovery takes 1-2 hours. Some respiratory depression may occur. This can be reversed with naloxone (0.1 mg/kg).  Fentanyl/droperidol is commercially available as "Leptan" (a drug combination of fentanyl 0.4 mg and droperidol 20 mg in each ml) hence doses are given as ml/kg
Diazepam or Midazolam	2mg/kg 4mg/kg	i p.	Good sedation, no analgesia. Diazepam must be given in a separate syringe as it is not miscible with aqueous solutions.  i.m. diazepam is painful. Midazolam is water soluble.
Ketamine	25 mg/kg	i m.	Deep sedation, poor muscle relaxation, variable analgesia at this dose.
Azaperone	50-100 mg/kg	i m.	(Olson & Renchko, 1988) Sedation in approx. 2 minutes, duration (1-2 hours) and recovery (4-6 hours) dose dependent. Respiratory rate increased and little effect on cardiovascular system and wide safety margin.
Acetylpromazine	1 mg/kg	i m.	Moderate sedation, no analgesia.
Xylazine	1-3 mg/kg	i m.	Sedation and muscle relaxation. Analgesia/variable
Alphadolone/ Alphaxalone	9-12 mg/kg	i p	Variable sedation.
Atropine	0.05 mg/kg	i p	Given prior to anaesthesia this will decrease salivary and bronchial secretion due to drugs such as ketamine and xylazine and will protect the heart from vagal stimulation (from drugs such as fentanyl or xylazine). Some rats also possess a plasma atropinesterase which hydrolyses and inactivates atropine.

Note: The information in this section is intended as a guide only. It should be used in conjunction with other published data and in the light of clinical experience. Expert advice should be sought prior to using new agents or techniques.

**Table 6.1.1 B injectable anaesthetic agents**

Drug	Accepted Dose	Route of Administration	Comments
Methohexitone/ Pentobarbitone/ Atropine or Inavlin	40 mg/kg 30 mg/kg 0.5 mg/kg	i p	Dose based on 1 ml/200 g rat. Good medium term anaesthetic.
Fentanyl/ Droperidol	0.3-0.4 ml/kg	i.m. or i p.	Good surgical anaesthesia with poor muscle relaxation. Lasts 20-40 minutes. Can be reversed with Naloxone 0.1 mg/kg or Buprenorphine 0.1 mg/kg. Fentanyl/droperidol is commercially available as "Leptan" (a drug combination of fentanyl 0.4 mg and droperidol 20 mg in each ml) hence doses are given as ml/kg. To obtain reasonable muscle relaxation, diazepam (2.5 mg/kg i.p.) must be given prior to the fentanyl/droperidol. The latter dose can then be reduced to 0.2 ml/kg i.p. instead of 0.3-0.4 ml/kg.
Xylazine/Ketamine or or	X 12 mg/kg K 80 mg/kg  X 8 mg/kg K 44 mg/kg  X 10-20 mg/kg K 50-100 mg/kg	i p i p.  i p. i p.  i.p. i.p.	(Green, 1982) Sedation and muscle relaxation but analgesia poor.  (Bar, 1984) Surgical anaesthesia in 48 minutes lasting 45-60 minutes.  Surgical anaesthesia in 5-10 minutes lasting 30-40 minutes at highest dose. When topping up use only ketamine i.m. as respiratory depression may occur when both drugs are administered.
Xylazine/ Ketamine/ Diazepam	X + K as above D 2.5 mg/kg	i p i p	Diazepam must be given in a separate syringe as it is not miscible with aqueous solutions. Diazepam potentiates the analgesic effects of ketamine.
Azaperone/ Ketamine	A 50 mg/kg K 87 mg/kg	i.m. i.m.	(Olson & Renchko, 1988) Anaesthesia with good muscle relaxation and analgesia; duration 2-4 hours dose dependent. Recovery rather prolonged but respiration not depressed.
Tiletamine/ Zolazepam Pentobarbitone	20-40 mg/kg 30-50 mg/kg	i.m. or i p i p.	(Silkerson et al., 1983) Satisfactory analgesia and anaesthesia. Duration dose dependent. Peak effect 5-10 minutes after injection, lasts for 20-40 minutes, recovery is prolonged particularly if multiple doses are used. Poor analgesia at low doses and low margin of safety.
Tribromoethanol	300 mg/kg	i p. (2.5% soln)	Good anaesthesia and analgesia for 45 minutes but large volumes needed and possibility of peritoneal adhesions particularly if used a second time. Mortality also higher if used repeatedly.
Urethane	1.2-1.5 gm/kg	i p. (10-20% soln)	Long lasting stable anaesthesia (8-10 hours) with minor effects on respiratory or cardiovascular systems. BUT is carcinogenic and mutagenic and should only be used in rodent-recovery procedures with adequate precautions to protect safety of personnel. IT IS NOT RECOMMENDED.

Table continued over page

Note: The information in this section is intended as a guide only. It should be used in conjunction with other published data and in the light of clinical experience. Expert advice should be sought prior to using new agents or techniques.

Table 6.1.1 B cont.

Drug	Accepted Dose	Route of Administration	Comments
Alphaxalone/ Alphaxalone	6-9mg/kg	i.v.	Good for long-term intravenous <del>influx of</del> , stable anaesthesia and rapid recovery.
Thiopentone	30 mg/kg	i.v. (15% soln)	5-10 minutes of anaesthesia.
Fentanyl/ Fluanisone (Hypnovel) + Midazolam (Hypnovel) + water	1 part (Hypnovel) 2 parts water (2.7ml of mixture per kg)	i.p.	Good surgical anaesthesia with good muscle relaxation. Lasts 20-40 minutes. Slight respiratory depression can be reversed with Buprenorphine.
Methohexitone	10-15 mg/kg	i.v. (1% soln)	5-10 minutes of anaesthesia.

Table 6.1.1 C Inhaled anaesthetic agents

Drug	Accepted Dose	Route of Administration	Comments
Halothane <del>halothane</del>	Calibrated vapouriser required	inhaled	Rapid induction and recovery.
Methoxyflurane	Anaesthetic / open drip	inhaled	Excellent analgesia, but expensive.
Carbon dioxide/ Oxygen	2-3 L/min	inhaled	Carbon dioxide/oxygen in a ratio of 50/50 is piped into perspex oxygen anaesthetic chamber. Rats placed in the chamber will lose consciousness in less than 1 minute. Minor procedures such as injections or bleeding can be performed in the chamber. Animals are removed and recovery occurs in a further 2-3 minutes. The best recovery occurs if exposure after loss of the pedal reflex is for less than 1 minute.

Table 6.1.1 D Analgesics

Morphine	Pethidine	Codeine	Pentazocine	Buprenorphine	Aspirin
10 mg/kg s.c. 2-3 hourly	20 mg/kg s.c./i.v. 2 hourly	60 mg/kg s.c. 4 hourly	10 mg/kg s.c. 4 hourly	0.1-0.5 mg/kg s.c. 8-12 hourly	100-450 mg/kg p.o. once daily

\*Flecknell (1984) — 100 mg/kg. Canadian Council on Animal Care (1984) — 450 mg/kg.

Note: The information in this section is intended as a guide only. It should be used in conjunction with other published data and in the light of clinical experience. Expert advice should be sought prior to using new agents or techniques.

## 6.1.2 Mice

### Premedication

Mice, like rats, generally do not require premedication prior to anaesthesia. If general anaesthesia is to be induced via the intravenous route some sedation will be necessary first.

If premedicant drugs are used they will tend to reduce the dose of anaesthetic agent required to produce general anaesthesia by 30-50%. (See Tables 6.1.2 A and 6.1.2B)

The following drugs can be used to produce general anaesthesia in mice with sufficient analgesia to perform surgical techniques. Some drugs like pentobarbitone produce general anaesthesia but show poor analgesia at low doses; at higher doses, marked respiratory and cardiovascular depression occurs. If possible, drugs such as these should be avoided since better alternatives are available. Hypothermia is a particular problem with mice and steps should be taken to minimise this.

Intravenous agents are not recommended but if necessary try *alphaxalone/alphaxalone* at a dose to effect i.v. It gives stable anaesthesia, and can be topped up as necessary, with a rapid recovery. The same comments for inhaled anaesthetics apply to mice as for rats. (See 6.1.1, page 18.)

**Table 6.1.2 A      Injectable drugs for premedication in mice**

Drug	Accepted Dose	Route of Administration	Comments
Fentanyl/ Droperidol	0.005 ml/kg	i.m. or i.p.	Takes 3 minutes i.p. 15 minutes i.m. to produce sedation with analgesia, recovery in 1-2 hours. Some respiratory depression may occur; this can be reversed with naloxone 10 µg/kg. For ease of administration the solution can be diluted 1 in 10 with normal saline.
Azaperone	50-100 mg/kg	i.m.	(Olson & Renchko, 1988) Sedation in approximately 2 minutes, no analgesia, duration and recovery dose dependent. Respiratory rate increased initially, later depressed. Little effect on cardiovascular system and wide safety margin.
Diazepam	5 mg/kg	i.p.	Good sedation, no analgesia. Diazepam must be given in a separate syringe as it is not miscible in aqueous solutions. I.m. is painful.
Acetylpromazine	2-5 mg/kg	i.p.	Moderate sedation, no analgesia.
Xylazine	10 mg/kg	i.p.	Sedation and muscle relaxation.
Atropine	0.04 mg/kg	i.p. or s.c. or i.m.	Given prior to anaesthesia this will decrease salivary and bronchial secretion due to drugs such as ketamine and xylazine and will protect the heart from vagal stimulation (from drugs such as fentanyl or xylazine).

Note: The information in this section is intended as a guide only. It should be used in conjunction with other published data and in the light of clinical experience. Expert advice should be sought prior to using new agents or techniques.

**Table 6.1.2 B Inhaled anaesthetic agents**

Drug	Accepted Dose	Route of Administration	Comments
Methoxyflurane	Anaesthetic chamber open drip	inhaled	Excellent analgesia but expensive
Halothane	Calibrated vapouriser required	inhaled	Rapid induction and recovery
Carbon dioxide/Oxygen	2-3 L/min	inhaled	Carbon dioxide/oxygen in a ratio of 50/50 piped into a perspex oxygen anaesthetic chamber. Mice placed in the chamber will lose consciousness in less than 1 minute. Minor procedures such as injections or bleeding can be performed in the chamber. When animals are removed, recovery occurs in a further 2-3 minutes.  For a high percentage of recoveries in mice, exposure following loss of pedal reflex should not exceed 15 seconds

**Table 6.1.2 C Injectable anaesthetic agents**

Drug	Accepted Dose	Route of Administration	Comments
Fentanyl/Droperidol + Diazepam	0.1 ml/30gm 5mg/kg	i.p.	Give diazepam five minutes prior to fentanyl/droperidol mixture. Dilute fentanyl/droperidol 1 in 10 and give 0.1 ml/30gm mouse. Good surgical anaesthesia with good muscle relaxation. Lasts 20-40 minutes. Can be reversed with naloxone 0.1 mg/kg or buprenorphine 0.2 mg/kg  Fentanyl/droperidol is commercially available as "Leptan", a drug combination of fentanyl 0.4 mg and droperidol 20 mg in each ml hence doses are given as ml/kg
Fentanyl/Flunitrazepam + Midazolam (Hypnovel) + water	1 part (Hypnorm)  1 part (Hypnovel) 6 parts water 110 parts of mixture per kg	i.p.	Good surgical anaesthesia with good muscle relaxation and analgesia.
Xylazine/Ketamine	X 16 mg/kg K 80 mg/kg	i.p.	Good muscle relaxation but analgesia poor
or	0.1 ml of mixture per 30 g mouse	i.p.	Mix equal volumes of xylazine and ketamine, 0.1 ml of mixture is made up to 1 ml with saline and 0.1 ml is the dose for each 30 gm mouse given i.p. Surgical anaesthesia in 4-8 minutes lasting 45-60 minutes.
or	X 10-20 mg/kg K 50-100 mg/kg	i.p.	Surgical anaesthesia in 5-10 minutes lasting 30-40 minutes. At highest dose, when topping up use only ketamine i.m. as respiratory depression may occur when both drugs are administered.

Table continued over page

Note: The information in this section is intended as a guide only. It should be used in conjunction with other published data and in the light of clinical experience. Expert advice should be sought prior to using new agents or techniques.

Table 6.1.2 C cont.

Drug	Accepted Dose	Route of Administration	Comments
Xylazine/ Ketamine	A 75 mg/kg K 100 mg/kg	i p i m	(Olson & Renchko, 1988) Anaesthesia with good muscle relaxation and analgesia, duration 1-2 hours) dose dependent. Recovery rather prolonged but respiration is slightly depressed, unless higher doses used.
Pentobarbitone	40 mg/kg	i p	Dilute solution 1 in 10 for ease of administration. Peak effect 5-10 minutes after injection, lasts for 20-40 minutes. Recovery is prolonged particularly if multiple doses are used. Very variable sleep times. Poor analgesia at low doses and low margin of safety.
Tribromoethanol	125-350 mg/kg	i p (2.5% soln)	Good anaesthesia and analgesia for 45 minutes but large volumes needed and possibility of peritoneal adhesions, particularly if used a second time. Mortalities also higher if used repeatedly.
Urethane	1.2-1.5 g/kg	i p (10-20% soln)	Long lasting stable anaesthesia (8-10 hours) with minor effects on respiratory or cardiovascular system. BUT is carcinogenic and mutagenic and should be used only in non-recovery procedures with adequate precautions for the safety of personnel. IT IS NOT RECOMMENDED.
Chloral hydrate	0.1 ml/10 gm mouse	i p (3.6% soln)	Make-up fresh solution in water or saline prior to use. Give 0.1 ml/10 gm mouse. Anaesthesia lasts for up to 1 hour. Can be topped up via i p route. Analgesia good, recovery quick depending on surgical procedure undertaken.

Table 6.1.2 D Analgesics

Morphine	Pethidine	Codeine	Pentazocine	Buprenorphine	Aspirin
10 mg/kg s.c. 2-4 hourly	20 mg/kg s.c. i p 2-3 hourly	20 mg/kg s.c. 60-90 mg/kg p.o.	10 mg/kg s.c. 3-4 hourly	2.5 mg/kg i p 6-8 hourly	120-300* mg/kg s.c. once daily, F.P.

\* Canadian Council on Animal Care (1984) — 400 mg. Flecknell (1984) — 120-300 mg/kg

Note: The information in this section is intended as a guide only. It should be used in conjunction with other published data and in the light of clinical experience. Expert advice should be sought prior to using new agents or techniques.

## 6.1.3 Guinea Pigs

### Specific signs of pain and distress (Morton & Griffiths, 1985)

Guinea pigs may show shallow breathing with grunting on expiration. There may be signs of cyanosis, congestion or jaundice. Other signs of distress are urgent repetitive squealing, being abnormally quiet and dragging the back legs. They may be much cleaner in the cage than normal with no spilling of food and water.

### Premedication

Guinea pigs tend to be nervous and will run around the cage if frightened. However, if approached carefully and quietly, they can be handled relatively easily in order to inject an anaesthetic drug. The intraperitoneal or intramuscular route can be used without premedication but if the intravenous route is to be used, then one of the drugs shown in Table 6.1.3A should be chosen.

If premedicant drugs are used, they will tend to reduce the dose of anaesthetic agent required to produce general anaesthesia by 20-50%.

### General anaesthesia

Guinea pigs are difficult to anaesthetise safely. Although they are larger than rats and mice, they have fewer accessible veins. The ear vein is probably the most accessible. In addition, their response to many drugs is variable and they are prone to post-operative problems such as respiratory infections, digestive disturbances, general depression and inappetance. It is also easy to overestimate the weight of the guinea pig as a mature animal will have a significant part of the weight in the gut.

Inhaled anaesthetic agents recommended for rats and mice may be used in the guinea pig. They can be administered either in an anaesthetic chamber or via a face mask with an Ayres T-piece. Methoxyflurane is the agent of choice, but halothane may be used if it is delivered using an anaesthetic machine, vaporiser and appropriate circuit. Ether is not recommended because of its irritant effects on the respiratory tree and airway blockage from increased secretions or bronchospasm may occur. Preservation of the airway is particularly important in the guinea pig as salivary and respiratory secretions become very viscid during anaesthesia. Green (1982) recommends that these secretions should be frequently aspirated with catheters attached to suction. If necessary oxygen can be supplied by insufflation with a catheter directed into the oropharynx, since intubation is difficult (Costa et al., 1986). (See Table 6.1.3 B and 6.1.3 C)

Note: The information in this section is intended as a guide only. It should be used in conjunction with other published data and in the light of clinical experience. Expert advice should be sought prior to using new agents or techniques.

**Table 6.1.3 A     Injectable drugs for premedication in guinea pigs**

Drug	Accepted Dose	Route of Administration	Comments
Fentanyl/ Droperidol	0.08 ml/kg	i m. or i p	Variable response. There are some reports of self-mutilation following the i r. route, so this route is best avoided. Fentanyl/Droperidol is commercially available as "Leptan", a drug combination of fentanyl 0.4 mg and droperidol 20 mg in each ml, hence doses are given as ml/kg
Diazepam	5mg/kg	i m	Sedation and immobilisation but no analgesia
Ketamine	100mg/kg	i m	Immobilisation but analgesia is poor.
Alphaxalone/ Alphaxalone	40 mg/kg	i m.	Large volumes required, therefore may be painful on injection, but good sedation.
Atropine	0.05 mg/kg	s.c.	Given prior to anaesthesia this will decrease salivary and bronchial secretion due to drugs such as ketamine and xylazine and will protect the heart from vagal stimulation (from drugs such as fentanyl or xylazine). Particularly useful as guinea pigs have relatively narrower airways than other rodents. However, some workers say atropine is contraindicated.

**Table 6.1.3 B     Inhaled anaesthetic agents**

Drug	Accepted Dose	Route of Administration	Comments
Carbon dioxide/ Oxygen	2-3 l/min	inhaled	Carbon dioxide/oxygen in a ratio of 50/50 is piped into a perspex anaesthetic chamber. Guinea pigs placed in the chamber will lose consciousness fairly rapidly. Minor procedures such as injections or bleeding can be performed in the chamber. After removal, recovery occurs in a further 2-3 minutes.

**Table 6.1.3 C     Injectable anaesthetic agents**

Drug	Accepted Dose	Route of Administration	Comments
Pentobarbitone	25 mg/kg	i p	This dose will give sedation and immobilisation. Alternative drugs should be used for surgical anaesthesia and maintenance, for example inhalation agents, as higher doses of pentobarbitone are associated with significant mortalities.
Fentanyl/ Droperidol	0.66-0.88 ml/kg	i m or i p	(Rubright & Thayer, 1970) Surgical anaesthesia. Lasts 45 minutes. Can be reversed with naloxone 0.1 mg/kg or buprenorphine 0.05 mg/kg. Avoid i.r.n. route as necrotic lesions are sometimes produced.
or			Fentanyl/droperidol is commercially available as "Leptan", a drug combination of fentanyl 0.4 mg and droperidol 20 mg in each ml hence doses are given as ml/kg

Table continued over page

Note: The information in this section is intended as a guide only. It should be used in conjunction with other published data and in the light of clinical experience. Expert advice should be sought prior to using new agents or techniques.

**Table 6.1.3 C Injectable anaesthetic agents cont.**

Drug	Accepted Dose	Route of Administration	Comments
Fentanyl/ Droperidol + Diazepam	0.5 ml/kg 2.5 mg/kg	i.m. or i.p. i.p.	The addition of diazepam improves the anaesthesia produced by increasing muscle relaxation.
Xylazine/ Ketamine	X 5-10 mg/kg K 50-60 mg/kg	i.p. or i.m. i.p. or i.m.	Produces 30 minutes of anaesthesia, said to be sufficient for surgery. Any less is said to be insufficient for surgery.
Urethane	1.2-1.5 g/kg	i.p. (10-20% soln)	Long lasting stable anaesthesia (8-10 hours) with minor effects on respiratory or cardiovascular system. BUT is carcinogenic and mutagenic and should be used only in non-recovery procedures with adequate precautions for the safety of personnel. IT IS NOT RECOMMENDED.
Alfaxalone/ Alphaxalone	12 mg/kg	i.v.	Given slowly to effect this will produce anaesthesia of short duration. It is not recommended for i.m. administration as the responses are too variable. It can be given in 4 mg/kg increments every 10 minutes to extend anaesthesia. Recovery is rapid.
Fentanyl/ Fluanisone (Hypnorm) +	1 ml/kg	i.m.	Good anaesthesia but requires a top-up every 30-40 minutes with 0.5 ml/kg Hypnorm
Midazolam (Hypnovel) or	2.5 ml/kg*	i.v.	*Hypnovel can be administered i.v. but the dosage should then be halved.
1 part Hypnorm 1 part Hypnovel 2 parts H <sub>2</sub> O	8 ml/kg	i.v.	
Methohexitone	10 mg/kg	i.v. (1% soln)	5-10 minutes of anaesthesia

**Table 6.1.3 D Analgesics**

Morphine	Pethidine	Codeine	Pentazocine	Euprenorphine	Aspirin
10 mg/kg s.c. i.m. 2-3 hourly	20 mg/kg s.c. i.m. 2-3 hourly	— — —	— — —	— — —	270 mg/kg i.p. once daily

Note: The information in this section is intended as a guide only. It should be used in conjunction with other published data and in the light of clinical experience. Expert advice should be sought prior to using new agents or techniques.

## 6.2 Rabbits

### Specific signs of pain and distress

Rabbits may look anxious, face the back of the cage, emit a piercing squeal and either kick and scratch or become drowsy. There may be no spillage of food and water in contrast to their usual habits, and they may eat their neonates (Morton & Griffiths, 1985). Although most rabbits are timid and docile, acts of aggression such as biting, scratching and kicking can be expected in a frightened animal. Rough or inappropriate handling may increase the concentration of circulating catecholamines. The animal is then more susceptible to cardiac arrhythmias which could make anaesthesia more hazardous. Rabbits are also more prone to posterior paralysis due to spinal damage, especially in those animals caged for long periods. A gentle approach to handling rabbits is essential. This should include talking to the animal, stroking it and picking it up in the correct way. Premedication may also be useful in calming a rabbit.

### Premedication (sedatives, tranquillisers, drugs for restraint)

In the rabbit, premedicant drugs can be administered subcutaneously under the loose skin of the neck or alternatively by the intramuscular route. If premedicant drugs are used, they will tend to reduce the dose of anaesthetic agent required to produce general anaesthesia by 30-50%. (See Table 6.2 A)

### General anaesthesia

Like rodents, rabbits frequently have either subclinical or clinical respiratory disease which increases anaesthetic risk. Clinical signs of respiratory disease include snuffling and sneezing, nasal and ocular discharges and encrusted discharges on the forelegs. Animals with these signs should not be anaesthetised. As in all other species, post-operative care is important. If barbiturates are used as the anaesthetic agent, the recovery may be prolonged particularly if hypothermia is not avoided. Frequently, rabbits show post-operative inappetance resulting in gastrointestinal upsets and a delayed return to normal health. Vomiting does not occur in the rabbit, so withholding of food prior to anaesthesia is not necessary. The rabbit has accessible veins for injection of intravenous anaesthetic drugs (marginal ear veins and cephalic vein in the foreleg), therefore this route can be used in addition to the subcutaneous, intramuscular and intraperitoneal routes. Some drugs, such as pentobarbitone, produce general anaesthesia but show poor analgesia at low doses. At higher doses marked respiratory and cardiovascular depression occurs. If possible, drugs such as these should be avoided since better alternatives are available. Ideally, anaesthetics should be administered intravenously. This route allows sufficient drug to be administered to produce the depth of anaesthesia required and the amount administered is not just a calculated dose based on body weight alone. This is often the case with i.m. or i.p. injection of anaesthetic agents. It is preferable to administer the i.v. drug only to produce unconsciousness. Anaesthesia is maintained using an inhaled agent. In this way, anaesthetic depth can be monitored continuously and varied as required. (See Table 6.2 B)

### Inhaled anaesthetic agents

The use of anaesthetic chambers to anaesthetise rabbits may be stressful and it may be preferable to use an injectable agent given i.v. for induction followed by maintenance with an inhaled agent. If an i.d.e.d agent is used to induce anaesthesia by mask, the rabbit must be restrained firmly to ensure that it does not injure itself through struggling.

Note: The information in this section is intended as a guide only. It should be used in conjunction with other published data and in the light of clinical experience. Expert advice should be sought prior to using new agents or techniques.

Since intubation is possible in the rabbit, it is preferred for long procedures to ensure maintenance of the airway and permit the use of assisted or artificial ventilation if necessary. A 3-4 mm O.D. (outside diameter) endotracheal tube would be suitable for most rabbits (Fick and Schalm, 1987). Inhaled agents recommended for rodents are also recommended for rabbits. Methoxyflurane is a particularly safe and useful agent in the rabbit because it provides good intraoperative and post-operative analgesia. However, there is some cardiovascular and respiratory depression, the latter being more significant. Anaesthesia can be maintained at concentrations of 0.4-1%. Mask induction with this agent may be slower than with halothane, but it is probably less stressful as the vapour is less pungent. Halothane is also recommended but it should be administered via an anaesthetic machine and vaporiser. The cardiovascular depression is dose-related and is more marked than with methoxyflurane. Anaesthesia can be maintained at concentrations of 1.5-2% of halothane. Because of its irritant nature, ether is not recommended. Rabbits are prone to laryngeal spasm, particularly if it is used at high concentrations for induction. Ether will also stimulate profuse bronchial and salivary secretions.

**Table 6.2 A injectable drugs for premedication in rabbits**

Drug	Accepted Dose	Route of Administration	Comments
Fentanyl / Droperidol	0.17 ml/kg	i.m. or i.p.	Produces sedation and some analgesia and respiratory depression. This can be reversed with naloxone 0.01-0.1 mg/kg
Diazepam or Midazolam	2mg/kg 4mg/kg	i.v. i.m. or i.p.	Sedation but no analgesia, diazepam is not water soluble and so must not be mixed in the same syringe with other drugs. I.v. diazepam is painful. Midazolam is water soluble.
Ketamine	25 mg/kg	i.m.	Sedation, poor muscle relaxation
Acetylpromazine	1 mg/kg	i.v. or s.c.	Moderate sedation, no analgesia. When given s.c. it takes slightly longer to act.
Xylazine	1-3 mg/kg	i.m. or s.c.	Sedation and muscle relaxation. Analgesia variable.
Atropine/Alphaxalone	9-12mg/kg	i.m.	Variable sedation at this dose and analgesia is also variable.

Atropine is relatively ineffective in the rabbit due to the presence of an active atropinase. If it is used, repeated doses are necessary.

**Table 6.2 B injectable anaesthetic agents**

Drug	Accepted Dose	Route of Administration	Comments
Fentanyl / Droperidol	0.3 ml/kg	i.m. or i.p.	Good surgical anaesthesia with good muscle relaxation. Lasts 20-40 minutes. Can be reversed with naloxone 0.1 mg/kg or buprenorphine 0.01 mg/kg
+ Diazepam	2 mg/kg	i.m., i.p. or i.v.	Fentanyl / droperidol is commercially available as "Leptan", a drug combination of fentanyl 0.4 mg and droperidol 2.0 mg in each ml, hence doses are given as ml/kg

Table continued over page

Note: The information in this section is intended as a guide only. It should be used in conjunction with other published data and in the light of clinical experience. Expert advice should be sought prior to using new agents or techniques.

**Table 6.2 B      Injectable anaesthetic agents cont.**

Drug	Accepted Dose	Route of Administration	Comments
+ Hypnorm [Fentanyl/ fluanisone)	0.3 ml/kg	i.m.	Good surgical anaesthesia with good muscle relaxation. Lasts approx. 30 mins. Can be "topped up" by increments of hypnorm 0.01-0.05 ml/kg
+ Midazolam	2 mg/kg or 1 mg/kg	s.c. i.v.	
Xylazine/ Ketamine	X 1-3 mg/kg K 10 mg/kg	i.m. or s.c. i.v.	Xylazine is given initially followed by the ketamine 10 minutes later i.v. This gives 10-20 minutes of surgical anaesthesia.
or	X 1-3 mg/kg K 35 mg/kg	i.m. or s.c. i.m.	Given as a single injection. This produces good surgical anaesthesia
Pentobarbitone	30-45 mg/kg	i.v.	Its use is NOT RECOMMENDED.  The pentobarbitone should be diluted to 30 mg/kg prior to use. Respiratory arrest often occurs prior to onset of surgical anaesthesia, so high mortalities may be associated with its use. Prolonged recovery particularly if multiple doses are used. Poor analgesia at low doses and low margin of safety.
Alphaxalone/ Alphaxalone	6-9 mg/kg, or 30 mg/kg	i.v. i.m.	Produces general anaesthesia. At the higher doses required for major surgery, it may produce sudden apnoea and cardiac arrest. Treatment with supplemental oxygen and artificial ventilation may help in some cases
Acepromazine/ Propofol	1 mg/kg 10 mg/kg	s.c. or i.m. i.v.	Premedicate with acepromazine and follow with Propofol to effect after 10 minutes (suggested dose is given as a guide). Produces brief anaesthesia followed by very rapid recovery.
Thiopentone	30 mg/kg	i.v. (1.5% soln)	5-10 mins of anaesthesia. Good for induction followed by maintenance with inhaled agents.
Chloralose + Urethane	50-80 mg/kg 0.5 gm/kg	i.v. i.v. or i.p.	Chloralose and Urethane have been used for long-term experiments and non-recovery experiments.

**Table 6.2 C      Analgesics**

Morphine	Pethidine	Codeine	Pentazocine	Buprenorphine	Aspirin
5 mg/kg s.c., i.m. 2-3 hourly	10 mg/kg s.c., i.m. 2 hourly	—	10-20 mg/kg s.c., i.m. 4 hourly	0.02-0.05 mg/kg s.c., i.v. 8-12 hourly	up to 500 mg/kg p.o. once daily

Note: The information in this section is intended as a guide only. It should be used in conjunction with other published data and in the light of clinical experience. Expert advice should be sought prior to using new agents or techniques.

## 6.3 Cats

### Specific signs of pain and distress

It is difficult to distinguish between illness and the presence of pain. A positive response to the administration of analgesia confirms the presence of pain. Cats are usually silent even when in pain, but there may be excessive vocalisation if disturbed. The presence of purring is not necessarily an indication that no pain is present. They may have a hunched appearance and may try to hide. There may be continuous licking or the cat may have a dirty ungroomed coat. Panting is a common sign.

### Premedication (sedatives, tranquillisers, drugs for restraint)

If premedicant drugs are used, they will tend to reduce the dose of anaesthetic agent required to produce general anaesthesia by 30-50%. (See Table 6.3 A)

### General anaesthesia

Most cats respond to firm but gentle restraint, enabling subcutaneous, intramuscular or intravenous injections to be made, if skilled assistance is available. In some cases, cats should be wrapped up in a blanket prior to injection. The s.c. or i.m. route can be used if a drug is to be given for sedation or minimal chemical restraint. The i.v. route is usually used to induce general anaesthesia, though some drug mixtures can be given i.m. to produce surgical anaesthesia (e.g. xylazine/xetamine). Cats may vomit in the induction and post-operative period and so should be fasted for 12 hours prior to induction of anaesthesia. As with other species, minimising hypothermia will aid recovery. Good post-operative care is essential. Some drugs like pentobarbitone produce general anaesthesia but show poor analgesia at low doses and at higher doses marked respiratory and cardiovascular depression occurs. If possible, drugs such as these should be avoided as better alternatives are available. (See Table 6.3 B)

### Inhaled anaesthetic agents

Ideally, anaesthesia should be induced with short-acting injectable anaesthetic agents and then maintained with an inhaled agent. However, a wild or uncontrollable cat can be anaesthetised by piping anaesthetic gases in oxygen directly into the cat cage which has been placed in a clear plastic bag. It is possible to induce anaesthesia in some cats with a face mask, though struggling may occur. The rate of induction by mask can be increased by concomitant use of nitrous oxide with the anaesthetic agent/oxygen mixture. Nitrous oxide is a colourless odourless gas used widely for humans as an anaesthetic supplement. It is less potent in animals than in humans. It is a weak anaesthetic and so can only be used satisfactorily in animals which have received premedication and in which consciousness has been abolished by another agent. It is essential that it is administered with at least 20-25% oxygen and so requires special administration. Care must be taken to ensure asphyxia or diffusion hypoxia do not occur. (For more details on its use, see Hall and Clarke, 1983.) With all of these methods, adequate scavenging of waste gases is essential. Cats can be quickly intubated with the aid of a laryngoscope but cats will exhibit potentially fatal laryngospasm if an endotracheal tube is passed without first desensitising the larynx with local anaesthetic spray (2% lignocaine spray). Size 3, 4 or 5 mm endotracheal tubes are suitable for most cats. Anaesthetised cats can be maintained on an Ayres T-piece or a Bain coaxial circuit.

Note: The information in this section is intended as a guide only. It should be used in conjunction with other published data and in the light of clinical experience. Expert advice should be sought prior to using new agents or techniques.

**Table 6.3 A      Injectable drugs for premedication in cats**

Drug	Accepted Dose	Route of Administration	Comments
Acetylpromazine	0.5mg/kg	i.m. or s.c.	Most cats will object to i.v. injection which should be given s.c. in the scruff of the neck 15-20 minutes prior to induction. Occasionally the response is variable and the cat may show some excitement instead of sedation. No analgesia.
Xylazine	1-2mg/kg	i.m. or s.c.	Sedation for 30-40 minutes. Usually associated with vomiting during onset of sedation. Analgesia variable.
Ketamine	10-20mg/kg	i.v.	This is painful when given i.m. [particularly the 100 mg/ml solution] Moderate analgesia and sedation lasting up to 45 minutes in higher doses. No muscle relaxation; in fact increased muscle tone. Pharyngeal and laryngeal reflexes said to be retained and eyes remain open. Because of this a protective coating of ophthalmic ointment may be useful during long procedures.
Tiletamine/ Zolazepam	7mg/kg	i.v.	Atropine recommended 15 minutes s.c. prior to use of the drug mixture. Said to show rapid onset of action in 2-5 minutes, with good sedation and muscle relaxation and analgesia.
Alphadalone/ Alphaxalone	9mg/kg	i.m.	Variable sedation when given by this route and this dose. It must be given into the muscle mass and not the fascia to ensure adequate absorption.
Atropine	0.05mg/kg	i.m. or s.c.	Given prior to anaesthesia this will decrease salivary and bronchial secretion due to drugs such as ketamine and xylazine. Will protect the heart from vagal stimulation (from drugs such as xylazine).
Pethidine	3-5mg/kg	i.m. or s.c.	Some analgesia and variable sedation.

**Table 6.3 B      Injectable anaesthetic agents**

Drug	Accepted Dose	Route of Administration	Comments
Xylazine/ Ketamine	X 1-2mg/kg K 10-20mg/kg	i.m. or s.c. i.v.	Xylazine can be given first, followed 5 minutes later by ketamine, though some inject both together. Reasonable surgical anaesthesia for approximately 20 minutes, good muscle relaxation and analgesia.
Tiletamine/ Zolazepam	15mg/kg	i.m.	Premedicate with atropine. Good surgical anaesthesia for 20-30 minutes can be topped up with half initial dose.
Alphadalone/ Alphaxalone	9mg/kg	i.v.	Best given slowly to effect required. Provides 10 minutes of surgical anaesthesia, can be topped up as required without prolonging recovery too much. May cause an allergic reaction in some cats but this can be prevented by pre-medication with Niramine (Chlorpheniramine) 10mg/ml and chlorobutol 0.5%

Table continued over page

Note: The information in this section is intended as a guide only. It should be used in conjunction with other published data and in the light of clinical experience. Expert advice should be sought prior to using new agents or techniques.

**Table 6.3 B      Injectable anaesthetic agents cont.**

Drug	Accepted Dose	Route of Administration	Comments
Thiopentone	10-15 mg/kg	i.v. (1.25% soln)	5 minutes of light anaesthesia, useful for induction of anaesthesia prior to maintenance by inhaled agents.
Chloralose	80-90 mg/kg	i.v. (1% soln)	6-10 hours of stable light anaesthesia, not sufficient for surgery. Additional analgesia required if surgical or other painful procedures are to be undertaken. Usually anaesthesia is induced with a short-acting barbiturate initially as induction is slow. (Green, 1982).
Pentobarbitone	35-40 mg/kg	i.p./i.v.	Recommended only for long-term (non-recovery) anaesthesia. Slow to cross blood-brain barrier and may cause some excitement during induction, therefore should be used in a well-oxygenated animal. Half the calculated dose should be fairly rapidly followed by the rest to effect, over the next couple of minutes. Surgical anaesthesia will last 30-45 minutes with prolonged recovery particularly if topping up occurs. High doses cause marked respiratory depression, cardiovascular depression and high mortality. IT IS NOT RECOMMENDED.
Propofol	7.5 mg/kg	i.v.	(Watkins et al., 1987) 10 minutes of surgical anaesthesia, induction rapid and smooth and recovery rapid. Can be used repeatedly or as a constant infusion, recovery still rapid.
Methohexitone	4-8 mg/kg	i.v. (1% soln)	5 minutes of anaesthesia, useful for induction of anaesthesia prior to maintenance by inhaled agents.

**Table 6.3 C      Analgesics (use with caution)**

Morphine;	Pethidine	Codeine	Pentazocine	Buprenorphine	Aspirin
0.1 mg/kg s.c. 4 hourly	2-10 mg/kg s.c./i.m. 2 hourly	—	2-3 mg/kg i.p. 4 hourly	0.005-0.01 mg/kg s.c./i.v. 12 hourly	—

\*Morphine can be used as analgesia, however it is essential that the dosage is absolutely accurate. Refer to Davis and Donnelly (1988).

Note: The information in this section is intended as a guide only. It should be used in conjunction with other published data and in the light of clinical experience. Expert advice should be sought prior to using new agents or techniques.

## 6.4 Dogs

### Specific signs of pain and distress

Dogs may growl or whimper and show lameness or stiff body movement. They may inflict damage upon themselves and may be restless or immobile. They may bite unexpectedly (Taylor, 1985). There may be inappetence and shivering with increased respiration and panting.

### Premedication

Premedication and prior training of the animal enables injections to be given without difficulty. Some dogs require sedation or chemical restraint. To ensure smooth induction and recovery from general anaesthesia, premedication is advisable. The subcutaneous, intramuscular and intravenous routes all may be used. There are accessible veins in the fore legs (cephalic), hind legs (recurrent tarsal), the neck (jugular) and, when anaesthetised, the lingual on the under surface of the tongue. Like cats, dogs should be fasted for 12 hours prior to induction of anaesthesia. The use of premedicant drugs will reduce the dose of anaesthetic agent required to produce general anaesthesia by 30-50%. (See Table 6.4 A)

### General anaesthesia

Some drugs like pentobarbitone produce general anaesthesia but show poor analgesia at low doses. At higher doses marked respiratory and cardiovascular depression occurs. The injectable drugs are normally given by the intravenous route. (See Table 6.4 B)

### Inhaled anaesthetic agents

Apart from brachycephalic breeds, anaesthesia can be induced in all types of dogs via a face mask following sedation. Many dogs will tolerate the mask well, particularly if nitrous oxide is used with the anaesthetic agent/oxygen mixture and if the concentrations of vapours are increased slowly. It is, however, preferable to induce anaesthesia with a short acting injectable agent and then maintain anaesthesia with an inhaled agent. Intubation is easy and the agents described for cats, rabbits and rodents can be used with a variety of circuits including the Bain, Maggill or circle circuit depending on the size of the dog and procedure to be undertaken. Maintenance concentrations for the inhaled agents are: halothane 1-2%, methoxyflurane 0.5-1.5%, isoflurane 2-3% and enflurane 0.8-2%. If nitrous oxide is added to the anaesthetic mixture (as 70:30 nitrous oxide: oxygen) lower concentrations of the inhaled vapour are required. Ensure that the oxygen concentration does not drop below 28-30%.

### Analgesia

See Table 6.4 C, also Davis & Donnelly, 1968; Haskins, 1987; Hughes & Lang, 1983; Taylor, 1985; Wright et al., 1985; Yoxall, 1978.

Note: The information in this section is intended as a guide only. It should be used in conjunction with other published data and in the light of clinical experience. Expert advice should be sought prior to using new agents or techniques.

**Table 6.4 A      Injectable drugs for premedication in dogs**

Drug	Accepted Dose	Route of Administration	Comments
Acetylpromazine	0.1-0.2 mg/kg	i.m. or s.c.	This drug will take up to 15-20 minutes to act particularly if given s.c. Sedation lasts 2-4 hours. There is no analgesia and large doses should be avoided as hypotension will result.
Droperidol	0.1 mg/kg	i.m., i.v. or s.c.	Reasonable sedation with less effect on the cardiovascular system.
Fentanyl / Droperidol	0.1-0.15 ml/kg	i.m.	Good analgesia and sedation. Produces bradycardia, therefore use atropine first. Good for aggressive dogs.
Buprenorphine / Acetylpromazine	0.009 mg/kg / 0.07 mg/kg	i.m.	Moderate to deep sedation.
Xylazine	2 mg/kg	i.m. or s.c.	Sedation for 30-40 minutes. May be associated with vomiting during onset of sedation. Analgesia mild. Atropine should be used prior to this drug to counteract the induced bradycardia. Animals may be stimulated by loud noises and it is unreliable in aggressive dogs.
Tiletamine / Zolazepam	7 mg/kg	i.m.	Atropine recommended 15 minutes s.c. prior to use of the drug mixture. Said to show rapid onset of action in 2-5 minutes, with good sedation and muscle relaxation and analgesia.
Pethidine	3-5 mg/kg	i.m. or s.c.	Some analgesia and variable sedation.
Atropine	0.05 mg/kg	i.m. or s.c.	Given prior to anaesthesia this will decrease salivary and bronchial secretion due to drugs such as ketamine and xylazine and will protect the heart from vagal stimulation (from drugs such as xylazine and fentanyl)

**Table 6.4 B      Injectable anaesthetic agents**

Drug	Accepted Dose	Route of Administration	Comments
Tiletamine / Zolazepam	15 mg/kg	i.m.	Premedicate with atropine. Good surgical anaesthesia for 20-30 minutes, can be topped up with half initial dose.
Alfaxalone / Alphaxalone	Contraindicated in the dog as the solvents may precipitate an anaphylactic response.		
Thiopentone	10-20 mg/kg	i.v. (2.5% soln)	5-10 minutes of light anaesthesia, useful for induction of anaesthesia prior to maintenance by inhaled agents.
Methohexitone	4-8 mg/kg	i.v. (1% soln)	5 minutes of anaesthesia, useful for induction of anaesthesia prior to maintenance by inhaled agents. A short period of apnoea may be seen at induction.
Propofol	5-7.5 mg/kg	i.v. (1% soln)	7-10 minutes of surgical anaesthesia, induction rapid and smooth and recovery rapid. Can be used repeatedly or as a constant infusion and recovery is still rapid. Premedication with acetylpromazine will greatly reduce dose required and will allow a smoother induction.

Table continued over page

Note: The information in this section is intended as a guide only. It should be used in conjunction with other published data and in the light of clinical experience. Expert advice should be sought prior to using new agents or techniques.

**Table 6.4 B      Injectable anaesthetic agents cont.**

Drug	Accepted Dose	Route of Administration	Comments
Chloralose	80-110 mg/kg	i.v. (1% soln)	6-10 hours of stable light anaesthesia, not sufficient for surgery. Additional analgesia required if surgical procedures are to be undertaken. Usually anaesthesia is induced with a short-acting barbiturate initially as induction is slow. The same technique may be used in the cat.
Pentobarbitone	0.4 ml/kg	i.v. 160 mg/ml	Slow to cross blood-brain barrier and may cause some excitement during induction, therefore should be used in a well-sedated animal. Half the calculated dose should be fairly rapidly followed by the rest to effect over the next couple of minutes. Surgical anaesthesia will last 30-45 minutes with prolonged recovery <del>potentially</del> if topping up occurs. High doses cause <del>marked</del> respiratory depression, and cardiovascular depression. Dose varies according to strain of dog and amount of body fat. <b>IT IS NOT RECOMMENDED.</b>

**Table 6.4 C      Analgesics**

Morphine	Pethidine	Codeine	Pentazocine	Buprenorphine	Aspirin
0.5-5.0 mg/kg s.c./i.m. 2-4 hourly	3-5 mg/kg s.c./i.m. 2-3 hourly	2 mg/kg s.c. 6 hourly	2 mg/kg i.m. 4 hourly	0.01-0.02 mg/kg s.c./i.m. 8-12 hourly	10 mg/kg p.o. 8 hourly

Note: The information in this section is intended as a guide only. It should be used in conjunction with other published data and in the light of clinical experience. Expert advice should be sought prior to using new agents or techniques.

## 6.5 Pigs

### Specific signs of pain and distress

Pigs may squeal persistently when the affected part of the body is handled, and may become aggressive. They may attempt to escape and may self-mutilate (Oldham, 1985). They show changes in gait and posture and may try to huddle in bedding. There may be a change in normal social behaviour.

### Premedication

Premedication prior to anaesthesia is recommended. The intramuscular and intravenous routes are preferred. In large pigs greater than 30 kg, deep IM injections are required since the layer of subcutaneous fat may be up to 3 cm thick. There are some accessible veins, the most useful is the marginal ear vein or possibly the cephalic. The jugular is difficult to find in large fat pigs. If premedicant drugs are used, they will tend to reduce the dose of anaesthetic agent required to produce general anaesthesia by 30-50%. (See Table 6.5 A)

### General anaesthesia

Some drugs like pentobarbitone produce general anaesthesia but show poor analgesia at low doses; at higher doses marked respiratory and cardiovascular depression occurs. Drugs such as these should be avoided since better alternatives are available. Injectable agents are usually given intravenously, via the ear veins. (See Table 6.5 B)

### Inhaled anaesthetic agents

Anaesthesia can be induced with any of the inhaled agents via a face mask following sedation. Pigs will tolerate this well, particularly if nitrous oxide is used with the anaesthetic agent/oxygen mixture and if the concentrations of vapours are increased slowly. Ideally, anaesthesia should be induced with a short-acting injectable agent and then maintained with an inhaled agent. Intubation is difficult and consequently anaesthesia in pigs is frequently maintained via face masks. However, artificial ventilation cannot be performed adequately with a face mask and pollution with waste gases is high. The Bain, Maggill or circle circuits can be used for pigs. Maintenance concentrations for the t i d e d agents are: halothane 1-2%, methoxyflurane 0.5-1.5%, isoflurane 2-5%, enflurane 0.8-2%. If nitrous oxide is added to the anaesthetic mixture (as 70:30 nitrous oxide oxygen) lower concentrations of the inhaled vapour may be required. The oxygen concentration should not drop below 28-30%.

Note: The information in this section is intended as a guide only. It should be used in conjunction with other published data and in the light of clinical experience. Expert advice should be sought prior to using new agents or techniques.

**Table 6.5 A      Injectable drugs for premedication in pigs**

Drug	Accepted Dose	Route of Administration	Comments
Azaperone	5 mg/kg	i.m.	Sedation but no analgesia. Ensure injection is into muscle not fat. Animals should be left alone after injection until full effects are apparent.
Droperidol/ Atropine sulphate/ Acetylpromazine	10 mg/kg 2.5 mg/kg 8 mg/kg	i.m.	Pigs become agitated 3-5 minutes after premedication, then become tractable and sedated (see Ramsey et al., 1993).
Diazepam/ Ketamine	0.2 mg/kg K 10 mg/kg	i.m.	Large volume needs to be injected except in small pigs. Use restricted to them.
Ketamine	10 mg/kg	i.m.	Immobilises the pig but spontaneous movements are possible. Expensive.
Alphaxalone/ Alphaxalone	6 mg/kg	i.m.	Good sedation, but again large volumes limit its use.
Atropine	0.05 mg/kg	i.m.	If necessary.
Acetylpromazine	0.2 mg/kg	i.m.	Moderate sedation, no analgesia

**Table 6.5 B      Injectable anaesthetic agents**

Drug	Accepted Dose	Route of Administration	Comments
Methohexitone	5 mg/kg	i.v.	5-10 minutes anaesthesia, usually used as an induction agent. Anaesthesia maintained using an inhaled agent.
Thiopentone	6-9 mg/kg	i.v.	5-10 minutes anaesthesia, usually used as an induction agent. Anaesthesia maintained using an inhaled agent.
Alphaxalone/ Alphaxalone	1-2 mg/kg	i.v.	Usually given to effect. Produces surgical anaesthesia and good muscle relaxation with minimal respiratory depression. Can be used as a continuous infusion. Expensive.
Pentobarbitone	20-30 mg/kg	i.v.	Light surgical anaesthesia but at the higher dose produces severe cardiovascular depression. Anaesthesia only lasts 20-30 minutes. Full recovery in 3-4 hours

**Table 6.5 C      Analgesics**

Morphine	Pethidine	Codeine	Pentazocine	Buprenorphine	Aspirin
up to 20 mg	2 mg/kg	—	2 mg/kg	0.005-0.01 mg/kg	10 mg/kg
	i.t.	—	i.t.	i.m.	
total dose	4 hourly	—	4 hourly	12 hourly	4 hourly

Note: The information in this section is intended as a guide only. It should be used in conjunction with other published data and in the light of clinical experience. Expert advice should be sought prior to using new agents or techniques.

## 6.6 Sheep

### Specific signs of pain and distress

Sheep may be dull and depressed and show obvious discomfort on handling the affected part. They may have an abnormal posture, a disinclination to move and lameness. Other signs may include grinding of teeth, grunting and a lack of ~~grunting~~ (Edwards, 1985).

### Premedication

Premedication facilitates handling, enabling injections of anaesthetic drugs to be administered readily. There are a number of accessible veins including the jugular and cephalic. Withdrawal of food for 24 hours and water for 12 hours is particularly important to try to decrease gut contents and lessen the problems associated with regurgitation and mhalation during surgery and to decrease the likelihood of ruminal tympany. If possible, local anaesthetic blocks with sedation are recommended m sheep to avoid the complications associated with general anaesthesia. If premedicant drugs are used, they will tend to reduce the dose of anaesthetic agent required to produce general anaesthesia by 30-50%. (See Table 6.6 A)

### General anaesthesia

Some drugs like pentobarbitone produce general anaesthesia but show poor analgesia at low doses; at higher doses marked respiratory and cardiovascular depression occurs. If possible drugs such as these should be avoided since better alternatives are available. The injectable agents are usually given intravenously, via the jugular or cephalic veins. (See Table 6.6 B)

### Inhaled anaesthetic agents

Anaesthesia in the sheep can be induced via a face mask following sedation. Sheep will tolerate the face mask well if the concentrations of the vapours are increased slowly, however, they must be intubated for maintenance. Ideally, anaesthesia should be induced with a short-acting injectable agent and maintained with an inhaled agent. htubation can be difficult, but is vital to prevent inhalation pneumonia during general anaesthesia. To decrease the incidence of ruminal tympany, a stomach tube can be passed with the animal lying on its side with the head sloping down. The Bain, Maggill or circle circuits may be used in sheep. Observation in the recovery phase is very important and the animal should not be left until it can maintain itself in sternal recumbency. Maintenance concentrations for the inhaled agents are: halothane 1-2%, methoxyflurane 0.5-1.5%, isoflurane 2-3%, enflurane 0.8-2%. Nitrous oxide is probably best avoided in ruminants.

### Analgesia

See review by Jenkins (1986), and Table 6.6 C.

Note: The information in this section is intended as a guide only. It should be used in conjunction with other published data and in the light of clinical experience. Expert advice should be sought prior to using new agents or techniques.

**Table 6.6 A      Injectable drugs for premedication in sheep**

Drug	Accepted Dose	Route of Administration	Comments
Xylazine	1 mg/kg	i.m.	Heavy sedation, good analgesia, but variable in response. Lasts 30-35 minutes.
Acetylpromazine	0.05-0.1 mg/kg	i.m.	Sedation with no analgesia.
Diazepam	2 mg/kg 1 mg/kg	i.m.	Useful tranquilliser.

Atropine – of little use. In fact makes saliva more viscid.

**Table 6.6 B      injectable anaesthetic agents**

Drug	Accepted Dose	Route of Administration	Comments
Methohexitone	4 mg/kg	i.v.	5-10 minutes anaesthesia, usually used as an induction agent. Anaesthesia maintained using an inhaled agent.
Thiopentone	10-15 mg/kg	i.v.	5-10 minutes anaesthesia, usually used as an induction agent. Anaesthesia maintained using an inhaled agent.
Xylazine/ Ketamine	X 1 mg/kg K 4 mg/kg	i.m. i.v.	tight surgical anaesthesia.
Diazepam/ Ketamine	D 2 mg/kg K 4 mg/kg	i.m. i.v.	Light surgical anaesthesia.
Alphaxalone/ Alphaxalone	3 mg/kg (adults) 6 mg/kg (lambs)	i.v. infusion	Stable anaesthesia and can be extended by continuous infusion. See Eales & Small (1982), Waterman (1981).
Pentobarbitone	30 mg/kg	i.v.	Gives only 15-30 minutes of anaesthesia but with marked respiratory depression.

**Table 6.6 C      Analgesics**

Morphine	Pethidine	Codeine	Pentazocine	Euprenorphine	Aspirin
up to 10 mg i.m.	up to 200 mg i.m.	—	—	0.005 mg/kg i.m.	900 mg/kg
total dose	total dose	—	—	12 hourly	once daily, p.o.

Note: The information in this section is intended as a guide only. It should be used in conjunction with other published data and in the light of clinical experience. Expert advice should be sought prior to using new agents or techniques.

## 6.7 Birds

### Specific signs of pain and distress

Very little is known about pain perception in birds, however studies have indicated that birds do have receptors which respond to noxious stimuli and these have similar properties to those found in mammals (Breward, 1984).

A bird subjected to acute pain stimuli may vocalise, exhibit excessive movement and try to escape. At the same time there will be an increase in heart rate and respiratory rate. When the bird is distressed it may show freezing behaviour or tonic 'immobility'. If the bird is in chronic pain there will be inactivity, inappetance and decreased preening and the bird will generally appear droopy and miserable (Sanford et al., 1986).

Unlike mammals, birds experiencing pain or distress, or diseased birds tend only to exhibit symptoms and behaviour outlined above when they are close to death. Therefore it is very important for researchers to be familiar with a bird's normal behaviour and appearance in order to pick up warning signs of pain, distress or illness as soon as possible. Two key indicators of a sick or distressed bird are:

- a. Fluffed feathers: birds have a very high metabolic rate and when in a state of stress they will fluff their feathers in order to increase insulation and maintain body temperature.
- b. Excessive sleep especially during the day: if a bird is sleeping when it is normally active or feeding, this is usually an indication that it is unwell.

### Premedication

There is rarely a need for premedication in birds, in fact it may be detrimental by slowing down recovery. However, some raptors may be very difficult to handle (refer to Tribe and Middleton's paper *Anaesthesia of raptors and birds*, (1988) for details concerning anaesthesia of raptors).

### General anaesthesia

The following points should be remembered when anaesthetising birds. Birds have a small body size, relatively large surface area and a high metabolic rate. Consequently they lose body heat rapidly. For this reason, great care must be taken to keep them warm during anaesthesia and surgery. Heating mats are useful, as is keeping the bird covered (whilst still allowing adequate monitoring). Alcoholic disinfectants should be avoided and any other liquid disinfectants should be used sparingly. As with other animals, any abdominal surgery will result in heat loss particularly if associated with the use of cold flushing solutions. There will also be heat loss and fluid loss associated with high flows of anaesthetic gases which may lead to hypothermia and dehydration. In small birds, even the loss of a few drops of blood is significant as it may be a large proportion of the total blood volume (e.g. 5 drops of blood is 10% blood volume of a budgerigar and can cause problems).

It is very important to weigh birds accurately as they can be overdosed easily when injectable anaesthetics are used. Food and water should probably not be withheld prior to anaesthesia, *especially* because of their high metabolic rate.

Note: The information in this section is intended as a guide only. It should be used in conjunction with other published data and in the light of clinical experience. Expert advice should be sought prior to using new agents or techniques.

## Inhaled anaesthetic agents

Induction and maintenance by gaseous techniques are probably the methods of choice, allowing quick induction, easily varied depth of anaesthesia as required and a quick recovery. However, the patient must be constantly monitored as respiratory depression can be a problem if the anaesthetic concentration is too high. Isoflurane is now preferred over halothane but either can be used. It has been suggested that if halothane is used, then the concentration for a mask induction should be gradually increased (but keeping below 4%) at induction and then lowered again for maintenance. A T-piece or Bain circuit (oxygen flow rate of 1-2 l/min depending on the size of bird) is suitable for most birds. Intubation is simple and recommended if possible as this does allow a more stable anaesthesia if maintenance is by a gaseous method. Even if an injectable anaesthetic is used, intubation will allow supplemental oxygen to be provided and this is often beneficial. It also means that excessive dead space is avoided.

## Analgesia

Because so little is known about pain perception in birds, analgesia is a very difficult area. Aspirin is sometimes administered, however the dose will vary considerably according to the species and the size of the bird.

**Table 6.7 A**      **Injectable drugs for premedication in birds**

Drug	Accepted Dose	Route of Administration	Comments
Diazepam	0.5-2 mg/kg	i.m.	Tribe and Middleton (1988) suggest as a sedative for fractious stressed birds.

**Table 6.7 B**      **Inhaled anaesthetic agents**

Drug	Accepted Dose	Route of Administration	Comments
Isoflurane	Calibrated vapouriser required	inhaled - mask induction	Rapid induction and recovery. Often preferred over injectable anaesthetic agents.

**Table 6.7 C**      **Injectable anaesthetic agents**

Drug	Accepted Dose	Route of Administration	Comments
Xylazine/ Ketamine	2-6 mg/kg 10-30 mg/kg	i.m.	Smaller birds require relatively larger doses (ie. at the top of the range) compared with larger birds.
Alphaxalone/ Alphaxalone	8 mg/kg	i.v.	incremental doses may be given up to a total of 25 mg/kg (Cooper 1984). May show excitement during recovery. Birds may benefit from wrapping in aluminium foil (small birds) or cardboard tubes.

Note: The information in this section is intended as a guide only. It should be used in conjunction with other published data and in the light of clinical experience. Expert advice should be sought prior to using new agents or techniques.

# 7. Analgesics

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These drugs are used primarily to relieve or minimise pain. They may also produce some calming effect and sleep in some species (e.g. dog) whereas in other species at comparable doses they produce restlessness or excitement (e.g. cat or pony).

There are basically two main groups of analgesics: centrally-acting agents e.g. narcotic/ opioid analgesics, and peripherally-acting agents, e.g. non-steroidal anti-inflammatory agents and para-aminophenol derivatives.

## Centrally-acting analgesics

### Narcotics/Opioids — agonists

This group includes the best established veterinary analgesics, morphine and pethidine. The drugs are potent analgesics but do show some undesirable side effects on the central nervous system, respiratory depression and bradycardia being the most clinically significant. Most side effects are dose related. These drugs are said to raise intracranial pressure by decreasing respiration, increasing  $\mu\text{CO}_2$  and so increasing cerebral blood flow. Opioid analgesics are normally administered parenterally as often by the oral route they have a high first pass metabolism by the liver. Codeine is the exception to this and so can be given orally.

Most of the side effects can be reversed by the use of specific antagonists (naloxone, ('Narcan') or nalorphine), however this will also reverse the analgesia which has been produced. Some workers recommend the use of a respiratory stimulant, such as doxapram ('Dopram'), if required. This will not reverse the analgesia but will stimulate respiration.

The opioid analgesics show marked species variation in response: primates, dogs, rats and rabbits show CNS depression, miosis, hypothermia and bradycardia. Cats, horses, ruminants and swine show CNS stimulation with mydriasis, panting, tachycardia, sweating (in horses) and hyperkinesia.

The side-effects are dose dependent and so can often be avoided with low doses. Also, the excitement can be reduced by the use of other drugs in conjunction with the narcotic analgesic. For example, the combination of acetylpromazine and pethidine produces good sedation with analgesia in the horse while droperidol combined with a narcotic is more appropriate in swine.

**Morphine:** Effective but there is some species variation as indicated above. In most species this drug is short-lived and so repeated doses are needed to maintain analgesia.

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- Pethidine:** 100 mg = 10-15 mg morphine. Widely used in veterinary practice, but does produce respiratory depression which may be significant in the post-operative period and has a much shorter duration of action than in man; in cats it lasts only two hours.
- Methadone:** This synthetic analgesic has been used as a premedicant in dogs and in combination with acetylpromazine in the horse (Lumb and Jones, 1984; Pritchard and Lumb, 1979).
- Codeine:** Morphine derivative used to a limited extent in small animals. Used orally for mild pain in the dog at a dose of 2 mg/kg (Taylor, 1985).

The maximum pharmacological effect of most opioids is observed 30-60 minutes after i.v. or s.c. injection and the duration is less than 2 hours.

- Fentanyl/Etorphine:** These are two extremely potent analgesics. Fentanyl has a short duration which limits its usefulness when given by intermittent injection, but it could be used for continuous intravenous infusion. These particular drugs are often used in combination with a neuroleptic to produce a state of neuroleptanalgesia in which the CNS is sufficiently depressed to enable surgical operations to be performed without the patient being aware of pain. The neuroleptic component counteracts many of the adverse side effects of the analgesic given at high doses (nausea, vomiting, respiratory depression).
- 'Innovar Vet':** This is no longer commercially available but has been replaced by 'Leptan' and is a mixture containing fentanyl and droperidol (Green, 1982). One of the advantages of this combination is that a reversal agent, naloxone, is available. It should be remembered however, that naloxone will only reverse the fentanyl-induced respiratory depression (and the analgesia), but not the sedating effect of the droperidol. Buprenorphine is a mixed antagonist/agonist and may actually be more useful as a reversing agent as some analgesia will be retained while the respiratory depression will be reversed (Flecknell et al., 1989).

### **Narcotics/Opioids — partial agonists**

These drugs have mixed morphine-like analgesic and antagonist activity. They were developed primarily in an attempt to produce analgesic drugs free from morphine's undesirable side effects.

- Buprenorphine:** 'Temgesic' - This drug is potent and long lasting, in most species up to 8 hours (sheep 2-4 hours), and has few side effects. It may well be one of the most useful analgesics in rodents. It is, however, difficult to obtain despite being a Schedule 4 drug as it has been assessed to be a drug of dependence and subject to abuse.
- Nalbuphine:** Again, this is not currently available in this country. It may be useful in the dog because of its long half-life (8.3 hours, Fahmy, 1983) and also useful in mice and rats (Blumberg et al., 1968).
- Pentazocine:** 'Fortral' - Useful in the dog (Taylor and Houlton, 1984) and in non-human primates (Flecknell, 1986).
- Butorphanol:** Available in the UK and USA as 'Torbutol'. Similar to pentazocine but with somewhat greater potency.

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## Peripherally-acting analgesics

This group comprises a wide range of either moderate or low potency analgesics. They have analgesic, antipyretic and anti-inflammatory properties and are used in humans in the treatment of arthritic and related inflammatory conditions. They can be taken orally and can be given via drinking water and so may be useful for long-term administration.

### 1. Non steroidal anti-inflammatory drugs (NSAIDs)

These drugs have a number of side effects which vary between species but in most produce gastro-intestinal erosion and ulceration with subsequent anaemia and hypoproteinaemia. They often produce impaired platelet adhesion leading to a tendency to bleed. Nephropathy, particularly in patients who are compromised (due to dehydration, hypovolaemia, etc) can also occur. Occasionally a hypersensitivity to the drugs may occur.

As previously stated, these drugs are really only effective against low to moderate intensity pain – particularly that associated with inflammation or the release of prostaglandins. Usually somatic and integumentary pain rather than visceral pain are relieved, however, one exception is flunixin which is effective in visceral pain associated with colic in horses.

**Salicylates and related drugs:** e.g. Aspirin: irritant to gastric mucosa and rapidly toxic to cats.

**Fenamates:** e.g. Meclofenamic acid ('Arquel'), mefenamic acid.

**Nicotinic acid derivatives:** e.g. Aspirin: irritant to gastric mucosa and rapidly toxic to cats. Also ketoprofen, diclofenac.

**Phenylacetates:** (Propionic acid derivatives) e.g. Ibuprofen ('Brufen'), useful in the dog (Yoxall, 1978). 'Brufen' in dog 30 mg/kg in divided dose as a loading dose followed by maintenance with 16 mg/kg.

**Indole acetates:** e.g. Indomethacin ('Indocid') and sulindac ('Clmoril').

**Pyrazolon derivatives:** e.g. Phenylbutazone ('Nabudone IM' and 'Nabudine P'). This drug is useful in the control of musculoskeletal pain in the dog and horse but has the same undesirable side effects as other drugs in this group (Yoxall, 1978). Tachyphylaxis is also a problem.

**Benzothiazines:** e.g. Fentanyl ('Feldene').

### 2. Para-aminophenol derivatives

Also known as coal tar analgesics. They have moderate analgesic and anti-pyretic activity to the NSAIDs but anti-inflammatory activity is weak.

**Acetaminophen phenacetin:** These are the most important drugs in this group and they are useful as a substitute for aspirin. However, they are still toxic to cats (due to metabolising enzyme deficiency). They do not produce gastrointestinal erosion or bleeding and have weak effect on platelet function but are still potentially toxic to animals.

Note: The information in this section is intended as a guide only. It should be used in conjunction with other published data and in the light of clinical experience. Expert advice should be sought prior to using new agents or techniques.

## Clinical use of analgesics

The most frequent use of analgesics is likely to be post-operative pain relief; narcotic analgesics are the most effective in this respect and may have to be administered for up to 72 hours. Some of the milder analgesics, e.g. aspirin and paracetamol, may be useful after certain procedures which may later produce inflammation and pain. These could be given in drinking water for continuous administration.

The short duration of most analgesics is a major problem and therefore repeated administrations may be necessary. In such cases long lasting buprenorphine may be useful as it is said to last at least six hours in most species (Cowan et al., 1977). Other alternatives have been suggested: continuous drug delivery systems (Teiger, 1974), depot preparations (Flecknell, 1984) or infusion pumps (Mather, 1983). One problem, however, is the development of tolerance and dependence to the narcotic drugs and it should be remembered that overdosage may produce severe respiratory depression.

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## 8. Anaesthetic drugs

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### Generic names, trade names and manufacturers

Acepromazine	'Promes 2', 2 mg/ml acepromazine. Apex Laboratories Pty Ltd, 30 Christie Street, St Marys NSW 2760. 'A.C.I. 2 Injection', 2 mg/ml acepromazine. Delta Veterinary Laboratories, P.O. Box 289, Hornsby NSW 2077.
Alphaxalone/ Alphacalcium	'Saffan', alphacalcium 9 mg/ml, alphaxalone 3 mg/ml. Pitman Moore Australia Pty Ltd, 71 Epping Road, North Ryde NSW 2133.
Atropine	'Atropine injection', 0.6 mg/ml atropine sulphate. Apex Laboratories Pty Ltd, 30 Christie Street, St Marys NSW 2760.
Azaperone	'Stresnil', 40 mg/ml azaperone. Boehringer Ingelheim Pty Ltd Animal Health Division, 50 Broughton Road, Artarmon NSW 2064.
Buprenorphine	'Temgesic', 0.3 mg/ml buprenorphine hydrochloride. Reckitt and Colman Pty Ltd, 12 Wharf Road, West Ryde NSW 2114.
Diazepam	'Valium', 10 mg in 2 ml diazepam. Roche Diagnostics, 4 Inman Road, Dee Why NSW 2099.
Doxapram	'Dopram-V injectable', 20 mg/ml doxapram hydrochloride. Robins Bomac Laboratories Pty Ltd, Unit 22, 5 Hudson Avenue, Castle Hill NSW 2174.
Droperidol	'Droleptan injection', 1.0 mg in 2 ml. Janssen-Cilag, 706 Mowbray Road, Lane Cove NSW 2066.
Enflurane	'Efloran'. Abbott Australasia Pty Ltd., Captain Cook Drive, Kurnell NSW 2231.
Fentanyl/ Droperidol	'Anovan-Vet'. Each ml contains fentanyl 10.4 mg and droperidol 20 mg. Pitman-Moore, Or Eltham Pty Ltd, Veterinary Division, 1-S Khartoum Road, North Ryde NSW 2113. No longer available; however an equivalent product is available from Parrell Laboratories. 'Leptan'.
Fentanyl/ Flunitrazepam	'Hypnorm'. Janssen-Cilag, 706 Mowbray Road, Lane Cove NSW 2066.
Flunixin	'Finadyne', flunixin meglumine 50 mg/ml. Heriot Agrivet Pty Ltd, 9 Edina Road, Ferntree Gully VIC 3156.
Halothane	'Halothane M&B'. May & Baker Australia Pty Ltd., 19-23 Paramount Road, West Footscray VIC 3012.
Isoflurane	'Forane'. Abbott Australasia Pty Ltd., Captain Cook Drive, Kurnell NSW 2231.
Ketamine	'Ketalar Vet', 100 mg/ml ketamine hydrochloride. Parke-Davis and Co., 32-40 Cassara Road, North Carringbah NSW 2229.

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Methohexitone	'Brietal', 2.5 gm. Eli Lilly Australia & Co., Wharf Road, West Ryde NSW 2114.
Methoxyflurane	'Fenthanoc'. Abbott Australasia Pty Ltd, Captain Cook Drive, Kurnell NSW 2231.
Midazolam	'Evepower'. Available from F.H. Faulding (Queensland), 56 Edmonstone Street, Mayne QLD 4016.
Morphine	'Morphine sulphate', 30 mg/ml. David Bull Laboratories Pty Ltd, 11-15 Lexia Place, Mulgrave VIC 3170.
Naloxone	'Narcan Injection', 0.4 mg/ml. Dupont Australia Ltd, 168 Walker Street, North Sydney NSW 2060.
Pentazocine	'Fortral', 60 mg in 2 ml pentazocine lactate. Winthrop Laboratories, Sydney.
Pentobarbitone	'Sagatal', 60 mg/ml pentobarbitone sodium. May & Baker Australia Pty Ltd, 19-23 Paramount Road, West Footscray VIC 3012. 'Nembital', 60 mg/ml pentobarbitone sodium. Abbott Australasia, Captain Cook Drive, Kurnell NSW 2231.
Pethidine	'Pethidine Injection', 50 mg/ml pethidine hydrochloride. Parnell Laboratories Australia Pty Ltd, 21-28 Vore Street, Silverwater NSW 2141.
Phenylbutazone	'Nabudone', phenylbutazone 200 mg/ml. Ilbarrat Tray Laboratories Pty Ltd, 98 Long Street, Smithfield NSW 2164.
Propofol	'Diprivan', 10 mg/ml. KCI Operations Pty Ltd, Pharmaceutical Division, 1 Nicholson Street, Melbourne VIC 3000.
Thiopentone	'Pentothal Veterinary Sterile Powder', Vials 2.5 gm and 5 gm. Abbott Australasia, Captain Cook Drive, Kurnell NSW 2231, or Bomac Laboratories Pty Ltd, 111 Pacific Highway, Hornsby NSW 2077.
Tiletamine / Zolazepam	'Zoletil 20', tiletamine 50 mg, zolazepam 50 mg. 'Zoletil 50', tiletamine 150 mg, zolazepam 150 mg. 'Zoletil 100', tiletamine 250 mg, zolazepam 250 mg. Virbac Australia Pty Ltd, 15 Parkland Place, Leichhardt NSW 2210.
Xylazine	'Rompun', 20 mg/ml xylazine hydrochloride. Bayer Australia Ltd., 46-67 Wilson Street, Botany NSW 2019.
Yohimbine	'Reverzine', yohimbine hydrochloride 10 mg/ml. Parnell Laboratories Australia Pty Ltd, 21-28 Vore Street, Silverwater NSW 2141.
4-aminopyridine	'Xylex', 4-aminopyridine 24 mg/ml. Parnell Laboratories Australia Pty Ltd, 21-28 Vore Street, Silverwater NSW 2141. 'Reverzine SA', yohimbine 1.25 mg/ml and 4-aminopyridine 2 mg/ml. Parnell Laboratories Australia Pty Ltd, 21-28 Vore Street, Silverwater NSW 2141.

Note: The information in this section is intended as a guide only. It should be used in conjunction with other published data and in the light of clinical experience. Expert advice should be sought prior to using new agents or techniques.

## 9.

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## Further Reading

*Animal Pain: Ethical and Scientific Perspectives* (1992), (Eds., T. Kuchel, M. Rose and J. Burrell). Proceedings of a two-day conference hosted by the Australian and New Zealand Council for the Care of Animals in Research and Teaching (ANZCCART) in 1990. Copies available from ANZCCART, PO Box 19, Glen Osmond SA 5064.