GUIDELINES ON THE CARE OF LABORATORY ANIMALS AND THEIR USE FOR SCIENTIFIC PURPOSES

II

PAIN, ANALGESIA AND ANAESTHESIA

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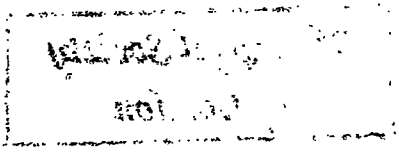
UNIVERSITIES FEDERATION FOR ANIMAL WELFA E



GUIDELINES ON THE CARE OF LABORATORY ANIMALS AND THEIR USE FOR SCIENTIFIC PURPOSES

II — PAIN, ANALGESIA AND ANAESTHESIA

UNIVERSITIES FEDERATION FOR ANIMAL WELFARE
8 Hamilton Close, South Mimms, Potters Bar, Herts EN6 3QD

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1. PREFACE

This is the second section of published guidelines initiated jointly by the Royal Society and the Universities Federation for Animal Welfare (UFAW) following a proposal by the Laboratory Animals Science Association. It is published by UFAW and represents a consensus of views of many directly concerned with the subject. In common with the first section, Housing and Care*, it takes into account the advice of the Animals (Scientific Procedures) Inspectorate.

It is felt there is a need for such a document for use by all persons responsible for laboratory animals and particularly by licensees, animal technicians and others working under the authority of the *Animals (Scientific Procedures) Act, 1986.* The contents should be regarded as guidelines and indications of practices and standards which should be generally understood and borne in mind before undertaking procedures on animals. It is not a code of practice although throughout, the term 'must' is used to remind the reader of legal or otherwise commonly accepted obligations. The term 'should' is generally adopted and used to encourage attainment of desirable standards.

The 1986 Act provides the framework in the United Kingdom for the protection of vertebrate animals used for experimental or other scientific procedures. Within the controls established by the system of personal and project licences, primary responsibility for the proper treatment of the animals rests with the licensee and those other members of staff who look after them before and after surgery. It is the hope and intention of the Universities Federation for Animal Welfare that these guidelines will assist such persons in meeting their obligations and thereby advance the welfare of such animals. Good science and animal welfare should continue to go hand in hand.

* Guidelines on the Care of Laboratory Animals and their Use for Scientific Purposes. I —Housing and Care. The Royal Society and Universities Federation for Animal Welfare 1987. Now superseded by the Home Office Code of Practice for the Housing and Care of Animals used in Scientific Procedures 1989. HMSO: London.

2. INTRODUCTION

There is an overriding obligation for those using animals in scientific procedures to be able to recognize the signs that an animal might be in pain, to minimize pain by preventive measures and to control it by use of analgesic and anaesthetic agents.

This obligation is reinforced in the United Kingdom by a legislative framework currently the *Animals (Scientific Procedures) Act, 1986.* This Act controls scientific procedures which may have the effect of causing an animal pain, suffering, distress or lasting harm. In the Home Office guidance published under the Act such effects are given the composite term severity and are considered in three categories:- *mild, moderate,* and *substantial* - so that any possible adverse effects on animals can be weighed against the benefits which are likely to accrue from the work (Home Office 1986).

Scientists must be able to recognize the behavioural and other signs that will indicate the limit of the particular severity band authorized for that procedure. They must be able to control the experiment so that the specified limit of severity will not be exceeded. If pain, suffering or distress cannot be constrained to the authorized level, the Home Office Inspector must be informed immediately. The Act requires that where an animal is in severe pain or severe distress which cannot be alleviated the licensee must ensure that the animal is painlessly killed forthwith.

The Home Office guidance states that the administration of an anaesthetic or analgesic or other substance to sedate or restrain or to dull perception, to an animal, or its decerebration or any other procedure rendering it insentient, if carried out for the purpose of any experimental or other scientific procedure, is itself a regulated procedure and thus can only be carried out by someone with a personal licence. However, the therapeutic use of analgesics or other medication is not so restricted, ie if it is for the benefit of the animal rather than a specific objective of the procedure.

3. PAIN

Description and definitions

Pain is a complex phenomenon which can be perceived only by the conscious animal. It is caused by potentially damaging stimuli that produce an unpleasant sensation which may range from mildly unpleasant to intolerable. Between these extremes there will be a whole spectrum of pain which can be tolerated in varying degrees by individual animals with or without analgesic support. Awareness of pain may help animals avoid harmful stimuli; pain is not necessarily all bad.

Reaction to pain can be communicated to others through behaviour, vocalisation and, in man, speech. Perception of pain in animals may not be the same as in man, but that they perceive it as something to be avoided is beyond reasonable doubt.

A useful distinction can be drawn between what is the conscious perception of *pain* and the unconscious reflex response to *nociception*, ie stimulation of an injury receptor (Iggo 1985). Reference to consciousness implies the awake state when an animal can appreciate sensory stimuli rather than an introspective awareness which is better termed self-consciousness. See also Melzac and Wall (1982).

Pain is clearly difficult to define but there are three working definitions that may be found useful:-

1. Pain [in man] is an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage (IASP, 1979).
2. Pain in animals is an aversive sensory experience that elicits protective motor actions, results in learned avoidance and may modify species-specific traits of behaviour, including social behaviour (Zimmerman, 1986).
3. Pain is an aversive sensory experience caused by actual or potential injury which is accompanied by protective somatic and visceral reactions and induces changes in behaviour including social behaviour which can be specific for an individual animal (AVTRW, 1989).

Signs of pain

An animal's response to a nociceptive stimulus may be stereotyped or learned. Such a response may or may not penetrate to consciousness and if it does, may produce long-term effects. The initial avoidance responses to an acute stimulus are remarkably similar in all vertebrates and are not difficult to recognize. But responses to repeated or longer periods of pain are likely to be different between species and indeed between individuals. All scientists working with animals should, therefore, familiarize themselves with the normal behaviour of the species.

Signs of low-grade or prolonged pain may not be obvious to the occasional observer. It is the experienced scientist, the animal technician who looks after the animal daily, or a similarly experienced veterinary surgeon who is likely to notice early signs of pain. It is important, therefore, that before starting to use live animals, scientists should obtain advice from those experienced with that species in order to learn the ways in which animals can show signs of pain.

Any deviation from normal behaviour could indicate pain, suffering, distress or lasting harm, eg negative behaviour such as inactivity, failure to groom or to eat. A behavioural method of assessing the severity of common laboratory procedures on rodents by using a disturbance index is described by Barclay, Herbert and Poole (1988). For specific behaviour associated with pain see Morton and Griffiths (1985), Kitchell and Johnson (1985), Flecknell (1987) and AVTRW (1989).

Control of pain

The control of pain in animals is important, for humane reasons and because it makes good sense in the design of scientific research. Unless the study of pain is one of the objectives of the experiment, the effects of pain on the animal may confuse the results, eg by reason of restricting movement, reducing food and water intake, prolonging recovery from surgery and introducing other variables which might interfere with baseline data. Painful procedures should be avoided wherever possible in the design of any experiment using animals.

Where it is necessary to produce pain as part of the procedure, for example to study analgesic agents, it should be the minimum for the purpose, just sufficient to produce a measurable effect. If possible, the animal should be able to avoid or limit the pain stimulus, and the source of pain should cause minimal tissue damage, especially to sensitive structures such as the eye. In any case no more animals than are necessary should be exposed to the pain.

Pain can be minimized by allowing animals to acclimatize to new surroundings or methods of restraint, by ensuring skilled handling and by a high level of competence in the performance of techniques such as simple injections, oral gavage, etc. Post-operative pain can be reduced by high standards of surgery; by firm, decisive but gentle technique; by avoiding unnecessary trauma caused by stretching wound edges; by avoiding excessive manipulation of viscera and traction on sensitive organs, and, most important, by preventing infection and sepsis. Good nursing and medication should always be available.

4. ANALGESIA

Analgesic therapy

Analgesic agents are substances designed specifically to temporarily abolish awareness of pain; however, although that may be the primary purpose they also usually have side effects. In like manner, sedatives which are narcotic agents used to calm nervous or agitated subjects, may not have specific analgesic activity but they can be usefully employed to reduce the animal's awareness and anxiety associated with pain. Most sedatives cause drowsiness or may induce sleep. Analgesics can be classified into three main groups.

The opioides

These have a central effect by inhibiting the transmission of nociceptive traffic at different levels of the central nervous system. It is likely that they mimic the endogenous endorphine/enkephalin system, one function of which is likely to be an intrinsic mechanism of pain control. Apart from their analgesic activity, opioides have other effects, some of which are undesirable, eg vomiting in some animals, reduced bowel mobility leading to constipation, and respiratory depression particularly in primates.

Examples of opioides are morphine and its derivatives, pethidine, methadone, fentanyl, pentazocine, butorphanol and buprenorphine. Of these buprenorphine has attracted special interest for the control of pain in laboratory animals because of its apparent longer duration of activity. Because it is not, as yet, a controlled drug in the UK under the *Misuse of Drugs Act 1971*, it is more freely available for use in the laboratory.

All analgesic agents have been developed and tested in animals, and information on their use in controlling the variable and less predictable levels of pain in clinical and experimental circumstances is available. Recommended dose rates are given in standard texts (Green 1982, Flecknell 1987). In general it is often necessary to titrate the dose to the particular level of pain, and then expect some variation of effects between animals. At times it is also more effective to give a protective dose of analgesic before the onset of pain rather than after it has become established.

The unwanted side effects of opioides are dose dependent, yet appear to be less severe when the animal is in pain, for example, a dose of morphine that will control pain in an animal and not produce respiratory depression would, in the normal pain-free animal, have a significant effect on respiration.

Intense excitement can be produced by an overdose of opioides in species such as the cat and horse.

There is a strong case for administering opiate analgesics to protected animals to control pain. Because it is not possible to rely on a set dose of analgesic for all occasions, the scientist should normally seek information from the literature, or from the manufacturers or both, and obtain advice from colleagues who have experience of the specific medication. It would be wrong to assume that an obligation has been fulfilled just because an analgesic has been administered. The animal's behaviour must be observed during and after the procedure to be sure that the treatment has been effective and pain has been controlled.

Non-steroidal anti-inflammatory drugs (NSAID)

These act peripherally by inhibiting the synthesis of prostaglandins that can increase the frequency of impulses generated in the nociceptive endings. They are particularly effective in chronic painful conditions associated with inflammation. Examples include aspirin, phenylbutazone, indomethacin and ibuprofen. They have specific analgesic effects, as well as those on inflammation, and they will also control pyrexia. There are some undesirable side-effects, however, which are more or less severe depending on the agent and species, eg gastrointestinal irritation, even haemorrhage and ulceration, and interference with erythropoiesis producing anaemia and occasionally producing liver and kidney damage. NSAID are not controlled drugs.

Local analgesics

These block conduction of pain along the nerve trunk by a local anaesthetic action. This can be achieved either by a general infiltration of the area of pain or if it is anatomically possible, a specific block of the nerve supplying the painful

focus or the operation site or both. Lignocaine is a commonly used local analgesic which will control pain for up to 2 hours. Bupivacaine provides a longer duration of activity and may be usefully employed to control pain when infiltrated along the wound edges after the closure of surgical incisions. Local analgesics (such as amethocaine) are also used in eye-drops and mucosal sprays.

Subcutaneous infiltration is an effective way of desensitizing the skin before inserting a needle or cannula, or for making a stab incision and subcutaneous pocket for an implant.

Regional nerve blocks can be used to prevent or control pain in an appendage, regions of the head and, most usefully, the chest or abdominal wall by intercostal or paravertebral nerve block. With a sound knowledge of anatomy, regional nerve blocks are not difficult, but before starting the technique scientists should read an appropriate text (eg Hall & Clark 1983) and seek advice from someone with experience of the method.

5. ANAESTHESIA

General principles

Anaesthetic agents are substances which produce in a controllable and reversible manner both loss of consciousness and an absence of motor response to noxious stimuli. Anaesthetics should be administered in such a way as to minimize excitement or distress at induction, to maintain a stable level of anaesthesia sufficient for the procedure, yet avoid gross depression, and, when it is intended that the animal should recover, to ensure a smooth, tranquil recovery. Only simple and relatively straightforward skills are required to administer established anaesthetic agents such as ether, barbiturates, chloralose or urethane to the usual laboratory animals for procedures from which it is not intended that they should recover. However there is a danger of fire or explosion with ether and urethane is a known carcinogen. On the other hand, a high level of professional skill is required to administer a balanced anaesthetic to an animal in which it is necessary to maintain a patent airway, support pulmonary ventilation and the circulation, avoid severe physiological and metabolic changes and, no matter what the level of surgical trauma, ensure a pain-free recovery. Such skill may be difficult to achieve, even in human anaesthetic practice. Nevertheless, it should be the objective in the practice of laboratory animal anaesthesia.

Administration of an anaesthetic should not cause more discomfort than that likely to ensue without its use.

A number of anaesthetic agents and techniques are available. Scientists should refer to the literature and seek advice from those with experience of the proposed method of administration which must be humane and safe for the animal, as well as safe and within the competence of the operator. Care must be taken to select an anaesthetic technique that will not interfere with the

particular body system being studied or the animal's response to the experiment. The short and long term actions and interactions of the compounds being used during anaesthesia should be understood in case they might influence the objectives of the study.

Balanced anaesthesia

This is now an established approach to general anaesthesia since a single dose of any single compound is unlikely to produce the three essential components of:-*narcosis* (unconsciousness), *analgesia* (control of pain) and *skeletal muscle relaxation* in appropriate balance and without undue side effects on the cardiovascular and respiratory systems.

All three components may not be required for all occasions. Animals are often anaesthetized merely for restraint for a non-painful procedure. Muscle relaxation may not be essential or desirable on all occasions. Some procedures can be carried out on a conscious animal using a local analgesic technique. A single anaesthetic can produce all three components of narcosis, analgesia and muscle relaxation but only at the cost of a level of central depression which may abolish protective reflexes and greatly extend recovery time.

Pre-anaesthetic preparation

An animal should always be allowed to adapt to its surroundings and, if possible, to become accustomed to being handled. It will then be less likely to be disturbed or stressed at the time of induction. Undue excitement or stress will increase the hazards of anaesthesia. Animals should be examined for overt signs of disease that might make them likely to succumb to anaesthesia. In particular small rodents and rabbits should be obtained from colonies known to be free of disease.

It is common practice with certain species to withhold food and sometimes water for a time to reduce the chance of vomiting and possible inhalation at the time of induction and during recovery. The period of deprivation will vary with size and metabolic activity of the species but, as a general rule, it should be shorter for the smaller animals, and in any case, it must be kept to the minimum necessary. Unless specifically contra-indicated, water should be available in order to maintain a reasonable level of hydration. Special care must be taken when preparing ruminants for anaesthesia and specialist advice should always be sought by less experienced operators.

Pre-anaesthetic medication

Medication may be necessary before anaesthesia to achieve a calm animal that will not show excessive excitement. Pre-anaesthetic medication should be aimed at control of fear and excitement by the use of sedatives and at the reduction of parasympathetic tone by agents such as atropine. Atropine should be used selectively as a drying agent when excessive salivation may occur, or to control vagal tone, but must not be given routinely.

Potent analgesics can be administered prior to anaesthesia, when an animal may already be suffering from pain or is about to undergo a painful procedure. Early control of pain under such circumstances will smooth out the course of anaesthesia and will mean that central depression will be more easily achieved with a lower dose of anaesthetic agent.

Neuroleptanalgesia (NLA)

This technique uses a combination of neuroleptic (ataractic/tranquilliser) agent with a potent analgesic, usually an opiate type, to produce a state of moderate to profound sedation and relative freedom from pain. Depending on the circumstances, NLA can be used either to prepare an animal for further anaesthesia or, in a higher dose, to induce a state similar to full surgical anaesthesia.

Many combinations of neuroleptic and analgesic can be used and scientists are advised to refer to the standard texts for dose rates in different species (Green 1982, Flecknell 1987).

The effects of an opioid analgesic component of the NLA can be reversed by specific antagonists such as naloxone; but it should be appreciated that while the undesirable side effects are reduced the analgesic activity will also be abolished.

Induction of anaesthesia

The main objective for induction of anaesthesia should be that the animal will pass from a calm and relaxed pre-anaesthetic period to a state of unconsciousness with the minimum of distress or discomfort. This does not necessarily mean that speed is essential because the animal that becomes quietly unconscious some time after a simple injection, may show no signs of distress.

There are two commonly used methods for induction of anaesthesia — by injection of anaesthetic agents or by inhalation of gases and/or vapours. It is rarely necessary to use other methods.

Injectable anaesthetics

An *intravenous* route of administration is generally preferred as it allows titration of the dose to produce the desired effect. If the size of the animal or lack of suitable superficial veins precludes the use of this route, then injections can be given *intraperitoneally, intramuscularly* or *subcutaneously* with a decreasing speed of onset of effect because of a slower rate of absorption. Whereas the intravenous dose can be titrated to effect, by the other routes a single dose calculated on body weight has to be given with the disadvantages of individual variation in response and variability in speed of uptake. For this reason, anaesthetic agents with a wide safety margin are used.

In addition to safety and efficacy, the volume of injection needed to administer the dose of anaesthetic compound is critical; for example, in small rodents, intramuscular injection of large volumes relative to their muscle mass can produce damage which will not only cause pain, but can reduce absorption of the agent and interfere with the results of the experiment.

The structure of the muscle group may also affect the absorption of the anaesthetic agent. In the cat, for example, the caudal muscles of the thigh are separated by large intermuscular spaces so that it is difficult to make an injection which is truly intramuscular at this site. Use of the quadriceps group of muscles cranial to the thigh is much more reliable and carries less risk of damaging major nerves such as the sciatic.

Fine 'butterfly' needles are useful in small veins as the plastic tubing allows considerable flexibility between the syringe and the animal. Fine needles block easily and can damage the vein as the animal is moved. Plastic cannulae and longer plastic catheters are used to maintain reliable access for incremental doses of anaesthetic agent or infusions.

There is a wide individual species and strain variation of response, so scientists are therefore advised to consult experienced colleagues and the standard anaesthetic texts regarding choice of agents. Selection will depend very much on the purpose for which it is being used, but the overriding principle is that it should be humane and safe for the animal. Scientists should aim to avoid compounds which may cause pain on injection or a prolonged period of induction. Thiobarbiturates are irritant, because of their high pH, and should only be used intravenously and then with great care. They should be diluted to a low concentration to allow greater control over the rate of administration and less damage if the material leaks into perivascular tissues. A short acting induction agent can be used if the main maintenance anaesthetic agent by itself requires a long induction phase.

Inhalation anaesthetics

These may be either volatile liquids which have to be vaporized, eg halothane, methoxyflurane and ether, or gases stored under pressure in cylinders, eg nitrous oxide and cyclopropane. Ether is best avoided in longer-recovery operations because of unpleasant after effects, and the increased risk of pulmonary infection. An advantage of inhalation anaesthetic techniques is that a greater control of effect can be achieved. The agents are taken up by the pulmonary vascular bed to affect the brain; they can then be eliminated by the same route following a concentration gradient. As far as inhalation agents are concerned, redistribution in the body and metabolic breakdown of the active agent are much less important than with injectable agents.

Gaseous anaesthesia can be induced either in a chamber containing the vapour of a volatile agent placed on a reservoir of absorbent material, or, the animal can breathe, through a face mask, air which is drawn over a reservoir of volatile anaesthetic. The advantage of simplicity is outweighed by the disadvantage that the concentration of the agent cannot be controlled. In addition, it is essential that there is no direct contact between the animal and the liquid volatile anaesthetic as it may be irritant. Such methods are only

recommended for brief periods of anaesthesia with agents which have a wide margin of safety such as methoxyflurane.

Controlled inhalation anaesthesia can be achieved by preparing the correct mixture of gases and vapours using an anaesthetic machine. This will mix gases through flow meters, provide oxygen to supplement that available in atmospheric air and vaporize a volatile anaesthetic to a set concentration. The mixtures of anaesthetic gases and vapours are then administered through a delivery system compatible with the animal's breathing characteristics.

The delivery system can be as simple as a perspex box that has input and output ports or as complex as an electronically controlled ventilator able to produce a wide range of breathing patterns suitable for a variety of species.

Potential hazards

Scientists should not use anaesthetic equipment unless they have been specially trained and know how it should be applied efficiently and safely for the animal in question. There are potential hazards for operating personnel using inhalational agents which create flammable and explosive mixtures and precautions must be taken to prevent sparks and flames in the area. There is also a danger of pollution of operating rooms by waste anaesthetic gases and vapours. An effective scavenging system should be installed to remove inhalation agents from the area where people work.

Maintenance of anaesthesia

The principle for maintenance of anaesthesia is to ensure that the animal is sufficiently deeply unconscious for the procedure. Anaesthesia should be maintained for any operative interference so that the animal does not respond to a painful stimulus. A light level of anaesthesia is often all that is required to maintain unconsciousness for procedures that in themselves cause no pain, eg for physiological measurements to be made or exposure to ionising radiation.

Another important objective must be to maintain, as far as possible, all vital body systems and homeostatic mechanisms. A patent airway must be ensured and when necessary, pulmonary ventilation and the circulation must be supported. Most anaesthetics not only induce unconsciousness but they are also respiratory, myocardial and circulatory depressants in a dose dependent manner. Prolonged exposure to high concentrations of anaesthetics will produce gross distortion of homeostatic control mechanisms. Special care has to be taken to maintain body heat, particularly in the small animals in which a precipitous fall in body temperature is an early feature of general anaesthesia.

The anaesthetic method must be designed to take care of any special features of the procedure such as placement of the animal in a fixed unusual position or the need for skeletal muscle relaxation, immobility or planned periods of apnoea. Animals require a high level of attention during the course of an anaesthetic, including the recovery period. For anything more than minor interferences, it is advisable to have someone else to look after the anaesthetic and monitor the progress of the animal. It is not possible to concentrate on an intricate piece of surgery and to control anaesthesia at the same time. Under no circumstances must anaesthetized animals be left unattended.

Assessment of depth of anaesthesia

There are empirical criteria to assess depth of anaesthesia. Appropriate stimuli should be used to judge the depth of central depression that will allow surgical interference. Examples are deep needle penetration over the site of incision to elicit a visible response, or pinching the web between the toes to produce withdrawal of the foot, or touching the eyelids and lashes to observe the blink reflex. If an animal shows brisk movement in response to an operative procedure, surgery should be stopped and anaesthesia adjusted to sufficient depth to allow continuation without response.

In order to maintain a steady level of anaesthesia, heart rate and, if possible, arterial blood pressure should be monitored. When skeletal muscle has been paralyzed by a neuromuscular blocking agent, such monitoring is essential. An increase in heart rate or blood pressure in response to stimuli indicates the need for more anaesthetic.

Certain anaesthetics, such as the neuroleptanalgesic mixtures and chloralose, allow some animals to remain responsive to noise. A sharp tap on the table can cause arousal and may indicate a need for deepening the plane of anaesthesia. This also means that loud sudden noises should be avoided in the area where animals are being anaesthetized.

Neuromuscular blocking agents

Depolarizing agents such as suxamethonium and non-depolarizing agents such as curare, gallamine and pancuronium are used in clinical anaesthesia to paralyze skeletal muscle, thus producing a profound level of relaxation.

These agents do not produce unconsciousness. If given to an animal that is either inadequately anaesthetized or not anaesthetized at all, the animal will not only be unable to breathe, but will also be aware of any painful procedure and the helplessness of being paralyzed.

Specific permission must be obtained from the Home Office *before* neuromuscular blocking agents are used for a scientific purpose on live animals. The Home Office has published guidelines (Home Office 1988) for the use of such agents but, if there is any doubt scientists are strongly advised to consult their Home Office Inspector.

6. POST-ANAESTHETIC CARE

There is a special need for post-operative care to ensure the welfare of the animal when it is intended that it shall recover from anaesthesia. Attention must not cease when the surgical or other procedure is finished. The anaesthetized animal needs close supervision until it is conscious and capable of looking after itself. This is usually taken as being when it is aware of its surroundings; when it can swallow and its airway is protected; when it is breathing normally and has an adequate circulation, and its temperature is returning to normal.

It is preferable to provide a special area for recovery so that the animal can be observed in a quiet, warm environment with subdued lighting. Dry absorbent materials should be used as bedding, not sawdust or other particulate material which can stick to eyes, nose and mouth during recovery.

The animal must be examined at regular intervals, and a record kept of its progress. If an endotracheal tube has been used, it should remain in place until pharyngeal reflexes have returned. Fluid therapy should be given to prevent or correct dehydration. but the animal will be uncomfortable if it has a full bladder, so this should be drained.

Prolonged recovery from anaesthesia should be avoided but this does not necessarily mean that the aim should be to have a fully active animal as soon as possible after the operative procedure. Great care must be taken to control pain during the recovery period and this may best be achieved by:

— use of an appropriately refined anaesthetic technique;
— attention to the best principles of surgery during the procedure;
— provision of a comfortable environment during recovery;
— judicious use of analgesics and sedatives as appropriate.

Ideally, the animal should recover consciousness and regain its protective reflexes, be responsive and yet relaxed and quiet, with no signs of pain. Such an animal will feel warm to touch, be willing to take fluids and, where appropriate, respond to attention.

7. CONCLUSION

It is an underlying principle of the 1986 Act that animals used for scientific purposes should be cared for in accordance with the best standards of modern animal husbandry, and that the effects of pain, suffering, distress or lasting harm should be controlled by the most suitable analgesic and anaesthetic methods.

These recommendations cover only the general principles and the standard texts should be consulted for specific dose rates for different species. However, from the animal's point of view the care and attention given by the staff before and after the procedure are likely to be the most important factors in minimizing any pain, suffering or distress.

Knowledge of the effects of surgical procedures and of the efficacy of the various analgesic and anaesthetic agents is continuously growing and it is important that such information is shared. Manufacturers are always willing to provide details of their products; experienced scientists, their assistants and veterinary surgeons responsible for the day-to-day care of the animals, should be encouraged to pass-on their knowledge and if needs be to seek advice from the Home Office Inspectorate. It is up to all concerned with the care and use of laboratory animals to keep themselves fully aware of developments that might improve their ability to recognize the signs that an animal is in pain, to minimize it by appropriate preventive measures and to control it by use of effective analgesic and anaesthetic agents. It is hoped that these guidelines will help to achieve this.

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