

The University of Newcastle Animal Care and Ethics Committee

Policies and Guidelines

Policy Number:	ACEC: 16
Policy Name:	Perception and measurement of pain
Date of ACEC Approval:	September, 1993
Date of Previous Editions:	N/A
Date of Next Review:	2006
Related Policies:	Monitoring of animals used for research or teaching purposes (ACEC: 20) Unexpected or adverse effects during the conduct of an approved project: Guidelines for action (ACEC: 33)
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INTRODUCTION

The New South Wales Animal Research Act, Regulations (1990) make provision for the control of the pain, suffering, or distress which may result from any experiment or scientific procedure carried out on an animal. It states that:

"pain and distress cannot be easily evaluated 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."

The regulations also direct that in an animal which develops signs of pain or distress of a kind not predicted in the proposal, the pain or distress must be alleviated promptly. In addition, animal pain may influence the outcome of an experimental protocol. Thus, there is considerable onus on the investigator to be able to recognise pain in the laboratory animals under his/her control. The aim of this paper is to provide some guidance to all those involved with laboratory animals, regardless of their experience, so that they may be able to recognise the situation where the experience of pain, distress, discomfort or fear may exist in these animals.

DEFINITION

Currently, the most accepted definition of pain has been that published by the International Association for the Study of Pain. They define pain as "an unpleasant sensory or emotional experience associated with actual or potential tissue damage, or described in terms of such damage". They further add that "pain is always subjective" and propose that there is an association between pain and tissue damage. It is clear that this definition applies, in the main, to those organisms that can verbalise their "unpleasant sensory and emotive experience". It has been suggested that for animals where a verbal description is not possible, the definition should include the statement **"that pain can be inferred from physiological and behavioural changes."** Given the complex and indiscriminate use of words such as "suffering", as well as the present state of biological knowledge, a description of pain in animals is likely to be of more value than its definition.

BACKGROUND

A. Pain

Pain has been described according to its site of origin (somatic, visceral or neurogenic) and its temporal characteristics (acute, acute recurrent, chronic). Further, the consideration of a wide spectrum of anatomical, physiological, behavioural, and psychological evidence has led to the recognition of two functional dimensions of pain: the "sensory-discriminative" and the "motivational-affective". The "sensory-discriminative" dimension is that which allows the subject to register the quality, quantity, intensity and site of the pain. The "motivational-affective" dimension is that which causes the subject to register emotional and aversive experiences, to learn to avoid repetition and to carry out complex protective reactions. Thus, when considering the various forms of pain that have been described, it can be seen that the reaction of the individual (being animal or human) may be modified by the duration and intensity of the stimulus, as well as by previous experience. Neurophysiologically, the process whereby a series of impulses are generated and transmitted to the spinal cord and brain is described by the term "nociception". The higher centres in the brain may then interpret these impulses as pain.

Criteria have been developed which would suggest that an animal may have similar subjective experiences to humans. These criteria were based on the analysis of an animal's behaviour and the examination of the anatomical and neurophysiological features of its nervous system. The fact that nociceptive systems (i.e. sensory, motor and memory systems) are found to exist in all vertebrates has led to the suggestion that animals have similar subjective experiences to humans. However, the quality of pain experiences generated by activity in these systems, and the level of awareness of such experiences, is unclear. In addition, the application of this approach is inadequate when invertebrate animals are considered.

B. Distress

Normal responses to stress arise in animals when external (environmental) or internal (physiological or psychological) stressors lead to particular physiological, biochemical, immunological, behavioural or other changes. These responses may be seen as adaptive responses and are mediated principally through the autonomic nervous system and endocrine system. They may include enhanced release of adrenalin and noradrenaline from sympathetic nerves resulting in increased heart rate and cardiac output; and increased output of hormones from the hypothalamus and pituitary gland resulting in 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.

"Distress" or "maladaptation" occurs when the animal is unable to adapt physiologically or psychologically in order to return its body to a state of comfort. Our concern should centre around the length of time it takes for an animal to adapt, as long-term persistence of the psychological and physiological adaptive responses continually compromise the health and well-being of the animal.

Obstruction of the protective, defence or adaptive mechanisms of an animal can result in aversion and a state of alertness, described as anxiety, apprehension, fear or terror. Like pain, these states can cause distress in the broader sense, and can lead to rapid responses via the sympathetic nervous system (including urination and defecation). Again, if the reaction is prolonged, a permanent physiological state of distress can be created.

"Mental stress" is a syndrome well-recognised in humans, but is a difficult concept to apply to animals. Although many of us can recognise when our pet animal is "happy" or "content", to date, there are no objective ways of measuring these aspects of mental health in animals.

SYSTEMATIC ASSESSMENT OF PAIN AND DISTRESS

Since assessment of pain and distress in animals is subjective, behavioural criteria probably provide the most obvious and reliable indications of an animal's condition. It is essential to be aware of the *normal* physical appearance, performance and pattern of behaviour of the species under consideration. *Signs vary, not only according to the species studied, but also between strains within the same species. Furthermore, individuals within the same strain will show differing responses.*

A. Principles

1. The overall assessment of welfare in individual cases can only be treated as a *value judgement based upon the experience* of those presented with the task. It is desirable that the experience and training of those making these judgements should be such that they are able to make use of all the relevant signs and information. When necessary, advice should be sought from those with necessary expertise. The practical assistance of animal attendants can be considerable and should be fully utilised.
2. **If any doubt exists as to the presence of pain or distress, the welfare of the animal must be considered paramount and further information and advice should be sought.**
3. A distinction must be made between what the animal may be feeling and what the human observer is feeling when attempting to assess the animal's condition. Ideally the assessment should not be influenced by the emotional state of the observer.

B. General Signs

The following signs, common to all species, may indicate the need to seek further advice from more experienced colleagues.

1. Appearance

Changes in the overall appearance of an individual or a group of animals may indicate the first signs of abnormality. Failure to groom may form the basis for many of these signs. If weight loss has been marked, the backbone will stand out and the animal will be light to handle. Clinical abnormalities may be evident e.g. ocular and nasal discharges, abnormal breathing, sunken eyes, enlarged pupils, abnormal stance. A sick animal is often on its own and may be less mobile.

2. Body Weight Changes

This criterion has the distinct advantage in that it can be objectively measured. Body weight usually reflects the amount of food and water consumed. Significant weight loss in adult animals, or failure to reach expected weight in growing animals may be one of the more important signs of a deterioration in the animal's condition.

3. Behaviour pattern

Abnormal activity may range from total inactivity to maniacal hyperactivity depending on the species and the severity and location within the body of the source of pain. Painful conditions in particular locations may result in a specific activity, e.g. pain in the mouth leading to pawing at this area, lameness resulting from pain in a limb. Other important changes in activity may be seen as changes in sleep/waking patterns, exploratory behaviour, eating and foraging behaviour, and social behaviour.

4. Clinical examination

Species-specific signs indicating the presence of pain in that animal are summarised in section C. Where an animal is suspected of suffering from a clinical disease as a result of infectious, toxic or allergic agents, deficient or abnormal diets or trauma, it should be subjected to appropriate veterinary investigation and treatment. Where this state results from the experimental procedure, it would be necessary to assess whether the severity of the pain experienced is as anticipated and therefore within the conditions of the Animal Research Authority and the legislation.

5. Mental status

The animal attendant is often the person best qualified to detect the presence of changes in the presumed mental state of an animal.

Assessment should be made by comparison with the previous behaviour of the animal and with the normal behaviour of the species, breed and strain. Mental states have been described in the following terms: dull, depressed, unresponsive, unaware, apprehensive, anxious, bright, alert, aware, excitable, hypersensitive, aggressive, timid, etc. It is of primary importance to assess the state of consciousness or awareness of the animal by subjecting it to the appropriate tests, such as response to visual or auditory stimuli. It is a necessary condition, however, that the animal should have the motor competence to respond to such tests. These responses are abolished by neuromuscular blocking agents and these drugs should not be administered to conscious animals.

6. Posture

Some species communicate their experiences by means of bodily attitude and other postural mechanisms. Particular changes in posture are often elicited by painful foci in particular parts of the body, e.g. dogs with abdominal pain may lie with their bellies on a cold floor, chickens with abdominal pain may adopt a penguin-like stance.

7. Facial expression

This is an important supplement to postural change as a means of communication in some species. The various

subtleties of facial expression have not been analysed for most species. However, people who work with particular species often become aware of subtle changes in expression without being able to describe them in detail.

8. Reluctance to accept handling

Animals may show changes in their normal response to handling and to being manipulated. Since this change may be indicative of an underlying abnormality, the animal should be examined closely whenever a behavioural modification of this nature is noted.

9. Vocalisation

Noises associated with pain and distress of more than momentary duration are usually repeated and should be differentiated from those normally made by the animal. They may be voluntary or involuntary, or may occur during a particular physiological function or behavioural act, eg a dog with a damaged bladder may yelp when urinating. Vocalisation may be described as growling, snarling, grunting, groaning, whimpering, whining, howling, yelping, screeching, and crying.

10. Physiological signs

Physiological signs are not necessarily the same for all species and may occur singly or in more complex combinations. Responses commonly seen include the following:

Dilatation of the pupils, wide opening of the eyelids, transient increases or decreases in blood pressure, increased heart rate, increased rate and alteration of the character of breathing (gasping or panting), movements of whiskers, piloerection, increased body temperature, increased muscle tone, sweating, changes in skin temperature, evacuation of rectum or para-anal sacs.

11. Biochemical signs

Increased plasma levels of ACTH and various adrenocortical hormones have been used in the assessment of stress. However, clear correlation of such increases with pain remains to be demonstrated.

12. Response to analgesics

The ability of analgesic or anti-inflammatory drugs to reverse signs of pain can provide a powerful diagnostic tool. Where the intensity of pain is disproportionate to the injury or is serving no discernible useful purpose, effective analgesic treatment should be considered obligatory.

C. Species-specific signs

Species-specific signs of pain and distress should be taken into account when making an assessment of an animal. Such signs are often associated with what is believed to be a painful condition. However no sign can, by itself, be regarded as diagnostic of pain and may also occur in conditions in which pain is unlikely to be a feature. The following notes of signs of pain in species of animals used for research purposes may be helpful. (Please note that the information provided here relates mainly to those species used by researchers within the University of Newcastle. Further information regarding other animal species is available from the Animal Welfare Officer or the University Veterinarians.)

1. Amphibian

The external features of a frog are important when assessing its well-being. A dry or dull skin, blood spots or a dry, dull appearance to the tongue, and staring, dry eyes may be an indication of stress. The animal may also become lethargic with poor responses to simple stimuli. The heart rate and breathing frequency can be easily monitored by placing the animal on a glass plate or in a glass container. Muscle wastage, especially in the thigh region, is readily observed as a result of decreased feed intake, or in an animal who has been inactive.

2. Bird

When a bird is in pain or is distressed, it may show escape reactions with vocalisation and excessive movement.

Head movements may increase in extent and frequency. Prolonged pain may result in inappetence and inactivity with a drooping miserable appearance. The eyes may be partially closed, the wings held flat against the body, and the neck retracted. When handled, the escape reaction may be replaced by a state of tonic immobility. Birds with limb pain may avoid use of the affected limb and may "guard" it from extension.

3. Cat

Cats in pain are generally quiet and may exhibit an apprehensive facial expression. The forehead may appear creased. There may be crying or yowling and the cat may hiss and growl if approached or made to move. There may be inappetence and a tendency to hide or to separate themselves from other cats. The posture may become stiff or abnormal, varying with the site of the pain. Incessant licking may sometimes be associated with localised pain. Purring may not necessarily indicate that no pain is present.

A cat in severe pain may show demented behaviour and make desperate attempts to escape. If a painful area is touched or palpated, there may be an instant and violent reaction. There may be panting with an increased pulse rate and pupillary dilatation. Chronic pain may result in a generally miserable and ungroomed appearance with a marked change from its normal behaviour. This general lack of well-being is an important indicator of pain in this species.

4. Dog

Dogs in pain generally appear quieter and less alert with stiff body movements or an unwillingness to move. However, the immediate response to acute, but low intensity pain may be restlessness or an increased alertness. With severe pain, dogs may lie still or adopt an abnormal posture to minimise its discomfort. There may be inappetence and shivering and increased breathing frequency with panting. While spontaneous barking is unlikely, dogs may whimper or howl, especially if unattended. They may also growl without apparent provocation. Dogs may bite or scratch at painful regions. When handled, they may be abnormally apprehensive or aggressive. It should be noted that dogs in pain or distress may still wag their tails when petted.

5. Fish

It is difficult to determine the nature of the response to pain in fish. Although they may exhibit a pronounced response to acute injuries or to contact with irritants, their response to chronic stimuli may be small or absent. For example, fish with severe wounds, which would cause immobility in a mammal, may often appear to behave normally and even resume feeding.

Fish may react to noxious stimuli such as a hypodermic needle by strong muscular movements. When exposed to a noxious environment such as a strong acid, they may show abnormal swimming behaviour with attempts to jump from the water, their colouring may darken and their opercular movements may become more rapid. Such effects are indicative of some degree of distress.

6. Guinea pig

Pain and distress in this species may result in usually quiet behaviour or abnormal vocalisation (urgent, repetitive squealing). They may appear terrified or agitated. Lack of spillage of food or water in the cage may be noticed. Other signs may include cyanosis, congestion or jaundice of mucous membranes, and dragging of the back legs.

7. Marsupial

The general signs of stress in marsupials include escape behaviour, decreased feed intake and body weight, failure to thrive, listlessness and decreased activity, and increased incidence of disease and parasitism. With hand-raised animals, inappropriate husbandry can result in symmetrical alopecia ("stress alopecia"). In addition to these signs, species specific signs of stress include the following.

Platypus: Acute stress may cause males to growl and to attempt to stab with their spurs. Escape behaviour may result in abrasions on the bill. Acute pain may cause flinching eg. during blood sampling. A reduction of the amount of tail fat may be observed in a animal exposed to chronic stress.

Koala: Assessment of the demeanour of the koala is important when evaluating its well-being. The normal animal appears relaxed and sleepy. This behaviour may be altered in response to stress. Acute stress, or

anticipation of an adverse event, may result in vocalisation and aggressive behaviour. Head shaking and ear flicking may be seen, with shaking of the whole body being observed in juveniles. Chronic stress may cause diarrhoea or a reduction in the number of faecal pellets passed, conjunctivitis, and perianal moist dermatitis ("wet bum").

Possum: Loud vocalisation, aggression, urination and defecation are signs of acute stress in possums. Some animals may exhibit sluggishness or torpor. Exposure to chronic stress may result in the development of symmetrical alopecia.

Macropod: Acute stress may produce vocalisation, flinching, attempts to escape, thumping of the ground, body trembling, teeth grinding, head shaking and ear flicking. Animals may lick excessively at their forearms and flanks, resulting in wetting of these areas with saliva. If stress is associated with muscular exertion, the animal may become recumbent and be unable to move or lift its head. This condition, known as capture myopathy, can be fatal. Chronic stress may cause thinning of the hair and symmetrical alopecia.

8. Pig

Vocalisation and the lack of normal social behaviour may be helpful indicators of a pig in pain. Changes in gait and posture may be obvious. Pigs normally squeal and attempt to escape when handled. These reactions may be accentuated when the animal is in pain. Adults may become aggressive. Pigs may also show unwillingness to move and, if possible, may hide in bedding.

9. Rabbit

Rabbits in pain or distress may appear anxious, apprehensive, dull, or inactive. They may assume a "hunched" appearance and may face towards the back of their cage. They sometimes, however, show aggressive behaviour, increased activity, and excessive scratching and licking. Reactions to handling may be exaggerated. Acute pain may result in vocalisation. Breathing frequency may be increased and there may be inappetence.

10. Rat, mouse

Pain or distress in rats and mice usually results in decreased activity, piloerection, and an ungroomed appearance. Red staining around the eyes and nose may be apparent. There may also be excessive licking and scratching. They may adopt a "doormouse" posture, and may become unusually docile or aggressive when handled. Acute pain may cause vocalisation. Inappetence or a change in feeding activity may be observed and, if housed with others, a change in the normal group behaviour may be noted. Pain and distress in rodents may also result in the eating of bedding or neonates.

11. Reptile

Acute pain in reptiles may be characterised by flinching and muscle contractions. There may be aversive movements away from the unpleasant stimulus and attempts to bite. More chronic and persistent pain may be associated with anorexia, lethargy and weight loss. However it is difficult to associate any of these signs of lack of well-being specifically with pain.

12. Sheep and goat

Pain in these species usually causes dullness and depression with the animal showing little interest in its surroundings. Changes in posture and facial expression may be apparent. There may be inappetence, weight loss and a general reluctance to move. Severe pain may result in rapid, shallow breathing. Grinding of the teeth and grunting may be heard. Goats may vocalise in response to pain. It is important to note that sheep, in particular, tolerate severe injury without overt signs of pain or distress.

D. SCORING SYSTEM

A scoring system for the quantification of pain, distress and suffering in laboratory animals was first proposed by Morton and Griffiths (1985). In their publication, they presented a set of criteria for assessment of the animal's condition based on the evaluation of five independent variables: a) changes in body weight; b) external appearance; c) measurable clinical signs (eg. changes in heart rate, breathing frequency and nature); d) unprovoked behaviour; e) behavioural responses to external stimuli. In each of these categories, a rating of 0

(normal to mild) to 3 (severe changes from normal) is assigned. The cumulative rating is then interpreted as an indication of increasing pain, distress and suffering. Table 1 presents this proposed scoring system in a "check-list" format.

The development and use of observational "check-lists" for scoring of the animal's condition provide an objective basis upon which decisions can be made e.g. if treatment is required, to evaluate the effectiveness of any treatment given or any experimental variable, to reach an agreed score at which an experiment is to be terminated. While it has been claimed that such a system may result in complacency on the part of the observer, the advantage of a check-list is that nothing is overlooked or taken for granted. The use of this system may result in the improvement of the observational capabilities of the researcher, particularly with the smaller laboratory animals where some of the conventional clinical observations made on larger animals are not as useful (e.g. temperature, heart rate, breathing frequency).

CONCLUSION

At present, the judgement of the severity of pain and distress should be based on the recognition and assessment of a wide range of parameters by trained and experienced observers. Guidelines outlined in this document may indicate, to the less experienced observer, the need to seek further advice from more experienced colleagues. It must be emphasised that none of these signs, singly or together, gives definite evidence of pain. However, at the current level of understanding, it must be assumed that pain may be present and that appropriate action should be taken to prevent or relieve it.

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TABLE 1. QUANTIFYING PAIN, DISTRESS AND SUFFERING

VARIABLE	SCORE
<u>Body Weight Changes</u> 0 Normal 1 < 10 % Weight loss 2 10 - 15 % Weight loss 3 > 20 % Weight loss	
<u>Physical appearance</u> 0 Normal 1 Lack of grooming 2 Rough coat, nasal/ocular discharge 3 Very rough coat, abnormal posture, enlarged pupils	
<u>Measurable clinical signs</u> 0 Normal 1 Small changes of potential significance 2 Temperature changes of 1-2 ⁰ C, cardiac and respiratory rates increased up to 30% 3 Temperature changes of > 2 ⁰ C, cardiac and respiratory rates increased up to 50%, or markedly reduced	
<u>Unprovoked behaviour</u> 0 Normal 1 Minor changes 2 Abnormal; reduced mobility, decreased alertness, inactive 3 Unsolicited vocalisations, self mutilation, restlessness, immobility	
<u>Behavioural responses to external stimuli</u> 0 Normal 1 Minor depression/exaggeration of responses 2 Moderately abnormal responses 3 Violent reactions, comatose	
TOTAL SCORE	

Adapted from : Morton, D.B. and Griffiths, P.M.H. (1985)