

Assessing and Managing Pain and Distress for Ethics Committees

Paul Flecknell¹ and Alicia Karas²

¹Comparative Biology Centre, Medical School, Newcastle upon Tyne, UK; ²Tufts Veterinary School, North Grafton, MA 01536, USA

Address for correspondence: P. Flecknell, Comparative Biology Centre, Medical School, Framlington Place, Newcastle upon Tyne NE2 4HH, UK.

The workshop was opened by Professor Paul Flecknell, who highlighted a number of issues:

In order to reduce pain and distress, it is necessary to assess the degree of pain or distress experienced by animals during particular procedures. Although considerable efforts have been made to refine procedures, these have often been carried out without attempting to assess pain objectively. The use of post-operative analgesics is a good example of this. Analgesic use in laboratory animals has increased dramatically in the last decade, but the dose rates used are often not based on any reliable measures of clinical efficacy. Despite this, many ethics committees have proceeded to mandate specific drug and dosing regimens after surgical procedures. Given the wide variation in analgesic requirements in people and animals after surgery, and the large differences in analgesic effects between strains of rodents, this is a policy that cannot provide appropriate pain relief. It may also have detrimental effects when unnecessarily high doses of analgesics are administered for prolonged periods.

Although analgesic use is becoming more widespread, ethics committees are often informed that pain-relieving drugs cannot be given because of interactions with the research protocol. This may be an issue in particular circumstances, but such objections should be placed in the overall context of the procedures being conducted. For example, the specific and non-specific effects of anaesthesia and the influence of surgical stress may far outweigh the potential interactions of analgesic administration. In some circumstances, the use of analgesics to reduce post-operative inappetence and inactivity can lead to a more rapid recovery following surgery.

In order to develop appropriate recommendations for analgesic use, and to make informed decisions concerning particular research protocols, it is important to attempt to assess pain. Relatively little work has been undertaken in laboratory species, but parallels can be drawn with studies in farm animals.

Professor David Mellor then presented data on pain assessment in farm animals, as an example of what had been achieved in developing objective assessment systems. The principles and caveats derived from this work, which must be met for particular physiological and behavioural parameters to be used as indices of the presence or absence of pain, are outlined below.

Dr Norman Peterson described a novel approach to evaluation of pain and distress by developing new bio-markers. His research goal is to correlate a procedure, such as the injection of complete Freund's adjuvant into the footpad, with indicators of physical appearance, corticosterone production, modification of urinary proteins and the modulation of gene expression in the thalamus. Gene expression is measured using micro-array techniques, which enable very large numbers of different genes to be evaluated simultaneously. Data collected from mice after the presumed painful procedures are compared with normal control animals to attempt to identify potential new markers for pain and distress.

Dr Alicia Karas then opened the discussion by emphasising a number of problems:

Elevations of cortisol levels and other stress markers, together with decreased normal behaviours and the occurrence of abnormal behaviours, all indicate the presence of pain in animals in some situations. This is supported by the response to analgesics in reducing or reversing these responses. However, these data are only available for a limited range of procedures and species.

This presents problems to ethics committees, as their members lack specialist expertise in evaluating pain and in pain therapy. The advice from a veterinarian might also be limited, particularly with less familiar models and species. In smaller establishments, veterinary input may be from a non-specialist, with limited involvement in the day-to-day work of the institution.

This raised the question of who should be targeted to inform ethics committees of new advances in pain recognition and alleviation. This could be indi-

vidual IACUC members, individual investigators, veterinary staff or animal care staff. Structured training of animal care staff might be most effective because of their close contact with the research animals.

At the conclusion of the invited contributions, a general discussion followed. Five main areas of concern were raised.

1. It was felt that animal care staff often had significant skills in the recognition of animal pain and distress, but that this expertise was frequently overlooked or ignored, as they had no formal role in the ethics committees of many establishments. Several participants highlighted the benefits of allowing animal care staff to be directly involved in the discussions of ethics committees. It was also recommended that direct reporting of concerns related to the welfare of experimental animals to the ethics committee should be encouraged. Although veterinary staff often had a mandatory involvement on ethics committees, their expertise in pain assessment and in pain management might not always be adequate. Providing appropriate training and education of both veterinary and animal care staff in this area was seen as an important method of supporting the decisions of the ethics committee.
2. Advances in genetic modification of mice, coupled with a better understanding of the fundamental mechanisms of pain perception, presented the possibility of developing laboratory mice with an increased ability to tolerate pain and distress. The implications of this suggestion were discussed, with several participants voicing concerns that this would lead to decreased attention being paid to issues of pain and distress. A further concern was that modification of pain systems could have extensive and unpredictable effects on other body systems.
3. The validity of different measures of pain and distress was discussed, and the consensus view was that an integrated approach, utilising all available indices, should be adopted.
4. It was suggested that the technical expertise of the surgeon was a major factor in determining the degree of pain experienced following surgery. It was apparent that a wide diversity of approaches were adopted. In some institutes, all major surgery was undertaken by experienced, appropriately qualified staff. In other institutes, surgery was carried out by research staff after they had received a minimum of training. Between these extremes, a number of methods of assessing competency of staff were outlined, including assessing new investigators when they first carried out a procedure, or refusing to certify as competent those staff who failed to reach an appropriate level of expertise during training.
5. The discussions had focused on post-surgical pain, since this was an area in which some progress in assessment and alleviation had been made. The potentially greater problem of animal distress was highlighted, and the need for considerably greater efforts in addressing this issue were emphasised.