An applied approach to the assessment of severity

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Summary

The assessment of humane endpoints can be one of the most difficult tasks facing scientists and animal care staff alike. In this paper we outline the use of guidance tables as one layer of a multilayered approach to the assessment and minimization of severity, during both the planning and the undertaking of scientific procedures using animals.

The assessment of humane endpoints both when designing and undertaking animal studies can be one of the most difficult tasks facing experimenters and animal care staff alike. While, occasionally, a single parameter can be predictive for significant morbidity or even mortality, rarely does it provide the whole picture of pain, suffering or distress in an animal. Even when a number of findings are obtained they may differ considerably between species, strains and even individual animals. More effective in practice is the assessment of a range of objective and semi-objective parameters in combination, as exemplified in the scoring scheme of Morton and Griffiths (1985) which uses five independent variables: body weight, appearance, clinical signs, unprovoked behaviour and response to an appropriate stimulus.

In the UK, the Animals (Scientific Procedures) Act 1986 requires that all regulated procedures have a severity limit. This is the upper limit of pain, suffering, distress or other lasting harm that any one animal may be permitted to experience and should be approached only when absolutely necessary. It is also incumbent on experimenters to limit any suffering to the minimum consistent with attaining the objectives of the procedure. For experiments involving conscious animals the categories of severity are mild, moderate and substantial (Home Office 1990). While in theory these categories are strictly demarcated, in reality they tend to form a spectrum where mild merges into moderate, and moderate into substantial. Severity can actually be quite a powerful tool to limit the suffering of experimental animals and can also be used as a baseline from which to further refine procedures and minimize pain, suffering, distress or lasting harm. But in order to achieve this we must be able to assess severity accurately and effectively.

Much time has been spent looking, not always very successfully, for novel and effective ways to help researchers and animal care staff gain a real ability to assess severity effectively. However people's efforts and initiatives often have a tendency to become more and more complex and less and less accessible. It was only when we returned to a very simple approach that we found something that our researchers and animal carers almost universally found useful and applicable to their everyday situation. We provide them with practical guidance by means of a series of tables covering a range of observations and measurements in 6 of the more commonly used laboratory animal species i.e. mouse, rat, guineapig, hamster, rabbit, beagle (see Tables 1–6). They have all been based on the cumulative experience of the authors, plus much existing published and unpublished data (see Morton & Griffiths 1985, LASA 1990, Buckwell 1992, FELASA 1994, Townsend 1995, Olfert 1996). This is not a novel approach and the tables do not contain any radically new information, but they have been well accepted and have proved useful as one layer of a multilayered

Table 1 Guidance on severity limits: Beagle dog

		Mild	Moderate	Substantial
Body weight	• Body weight	• Up to 10% weight loss over a 7-day period	• 10–25% weight loss over a 7-day period	• > 25% weight loss over a 7-day period
	• Food/water consumption	• 40–75% for 72 h	• < 40% for 72 h	• < 40% for 7 days or anorexia > 72 h
Appearance	• Coat condition	• Normal	• Dull coat, reduced grooming	• Very poor coat condition, absence of grooming, plus additional signs, e.g. 'hang dog' expression, unresponsive behaviour
	• Posture	• Normal	• Intermittent 'hang dog' posture	• Persistent 'hang dog' posture
Clinical signs	• Respiration	• Normal	• Intermittent abnormal pattern	• Persistently laboured
	• Tremors	• Transient	• Intermittent	• Continuous
	• Convulsions	• None	• Intermittent (but < 10 min duration)	• Continuous (euthanize if > 10 min duration)
	• Prostration	• None	• Transient < 1 h	• Persistent > 1 h (euthanize if > 2 h duration)
Unprovoked behaviour	• Socialization	• Peer interaction	• Little peer interaction	• No peer interaction
Response to stimulus	• Provoked behaviour	• Subdued but normal when stimulated	• Subdued even when stimulated	• Unresponsive to extraneous activity or stimulation

Table 2 Guidance on severity limits: Guineapig

		Mild	Moderate	Substantial
Body weight	• Body weight • Food/water consumption	• Up to 10% weight loss • 40–75% of normal for 72 h	• 10–25% weight loss • < 40% of normal for 72 h	• > 25% weight loss • < 40% of normal for 7 days or anorexia > 72 h
Appearance	• Coat condition	• Partial hair loss	• Marked staring coat, hair loss	• Marked staring coat, plus additional signs, e.g. hunched posture, unresponsive behaviour
	• Posture	• Transiently hunched—especially after dosing	• Intermittently hunched	• Persistently hunched
Clinical signs	• Respiration	• Normal	• Intermittent abnormal pattern	• Persistently laboured
	• Salivation	• Transient	• Intermittent with wetting of fur under chin	• Persistent, permanently wet fur
	• Tremors	• Transient especially during handling	• Intermittent	• Continuous
	• Convulsions	• None	• Intermittent (but < 10 min duration)	• Continuous (euthanize if > 10 min duration)
	• Prostration	• None	• Transient < 1 h	• Persistent > 1 h (euthanize if > 3 h duration)
Unprovoked behaviour	• Socialization • Vocalization	• Peer interaction • Has normal range of vocal sounds	• Little peer interaction • Intermittent, distressed vocal sounds and when stimulated	• No peer interaction • Distressed, unprovoked vocalization. May be absence of vocalization
Response to stimulus	• Provoked behaviour	• Subdued but normal when stimulated	• Subdued even when stimulated	• Unresponsive to extraneous activity or stimulation

Table 3 Guidance on severity limits: Hamster

		Mild	Moderate	Substantial
Body weight	• Body weight • Food/water consumption	• Up to 10% weight loss • 40–75% of normal for 72 h	• 10–25% weight loss • < 40% of normal for 72 h	• > 25% weight loss • < 40% of normal for 7 days or anorexia > 72 h
Appearance	• Coat condition	• Normal	• Poor coat condition, reduced grooming	• Very poor coat condition, absence of grooming, plus additional signs, e.g hunched posture, unresponsive behaviour
	• Posture	• Transiently hunched—especially after dosing	• Intermittently hunched	• Persistently hunched
Clinical signs	• Tremors	• Transient	• Intermittent	• Continuous
	• Convulsions	• None	• Intermittent (but < 10 min duration)	• Continuous (euthanize if > 10 min duration)
	• Prostration	• None	• Transient < 1 h	• Persistent > 1 h (euthanize if > 3 h duration)
Unprovoked behaviour	• Vocalization	• Has normal range of vocal sounds	• Intermittent distressed vocal sounds	• Distressed, unprovoked persistent or no vocalization. May be absence of vocalization
Response to stimulus	• Provoked behaviour	• Minimal changes	• Subdued–responds when stimulated	• Unresponsive to extraneous activity or stimulation

Table 4 Guidance on severity limits: Mouse

		Mild	Moderate	Substantial
Body weight	• Body weight	• Up to 10% weight loss	• 10–20% weight loss	• > 20% weight loss
Appearance	• Posture	• Transiently hunched—especially after dosing	• Intermittently hunched	• Persistently hunched
	• Piloerection	• Partial	• Marked staring coat	• Marked staring coat plus additional signs of hunched posture, unresponsive behaviour
Clinical signs	• Respiration	• Normal	• Intermittent abnormal pattern	• Persistently laboured
	• Salivation	• Transient	• Intermittent with wetting of fur under chin	• Persistent, permanently wet fur
	• Tremors	• Transient	• Intermittent	• Continuous
	• Convulsions	• None	• Intermittent (but < 10 min duration)	• Continuous (euthanize if > 10 min duration)
	• Prostration	• None	• Transient < 1 h	• Persistent > 1 h (euthanize if > 3 h duration)
Unprovoked behaviour	• Socialization	• Peer interaction	• Little peer interaction	• No peer interaction
Response to stimulus	• Provoked behaviour	• Minimal changes	• Subdued—responds when stimulated (e.g. handling)	• Unresponsive to extraneous activity or provocation

Table 5 Guidance on severity limits: Rabbit

		Mild	Moderate	Substantial
Body weight	• Body weight • Food/water intake	• Up to 10% weight loss • 40–75% of normal for 72 h	• 10–25% weight loss • < 40% of normal for 72 h or anorexia > 48 h	• > 25% weight loss • < 40% of normal for 7 days or anorexia > 72 h
Appearance	• Coat condition	• Normal	• Poor coat condition, reduced grooming	• Very poor coat condition, absence of grooming, plus additional signs, e.g. hunched posture, unresponsive behaviour
	• Posture	• Transiently hunched—especially after dosing	• Intermittently hunched	• Persistently hunched
Clinical signs	• Respiration • Salivation	• Normal • Transient	• Intermittent abnormal pattern • Intermittent with wetting of fur under chin	• Persistently laboured • Persistent, permanently wet fur
	• Tremors • Convulsions	• Transient • None	• Intermittent • Intermittent (but < 10 min duration)	• Continuous • Continuous (euthanize if > 10 min duration)
	• Prostration	• None	• Transient < 30 min	• Persistent > 30 min (euthanize if > 1 h duration)
Unprovoked behaviour	• Socialization • Vocalization	• Peer interaction	• Little peer interaction	• No peer interaction • Unprovoked vocalization likely to be indicative of distress
Response to stimulus	• Provoked behaviour	• Subdued but normal when stimulated	• Subdued even when stimulated	• Unresponsive to extraneous activity or stimulation

Table 6 Guidance on severity limits: Rat

		Mild	Moderate	Substantial
Body weight (excluding transient weight loss)	• Body weight • Food/water consumption	• Up to 10% weight loss • 40–75% for 72 h	• 10–25% weight loss • < 40% for 72 h	• > 25% weight loss • < 40% for 7 days or anorexia > 72 h
Appearance	• Posture	• Transiently hunched—especially after dosing	• Intermittently hunched	• Persistently hunched
	• Piloerection	• Partial	• Marked staring coat	• Marked staring coat plus additional signs of hunched posture, unresponsive behaviour
Clinical signs	• Respiration	• Normal	• Intermittent abnormal pattern	• Persistently laboured
	• Salivation	• Transient	• Intermittent with wetting of fur under chin	• Persistent, permanently wet fur
	• Tremors	• Transient	• Intermittent	• Continuous
	• Convulsions	• None	• Intermittent (but < 10 min duration)	• Continuous (euthanize if > 10 min duration)
	• Prostration	• None	• Transient < 1 h	• Persistent > 1 h (euthanize if > 3 h duration)
Unprovoked behaviour	• Socialization	• Peer interaction	• Little peer interaction	• No peer interaction
Response to stimulus	• Provoked behaviour	• Minimal changes	• Subdued–responds when stimulated (e.g. handling)	• Unresponsive to extraneous activity or provocation

approach to assessing and minimizing pain, suffering, distress and other lasting harm.

One of the key factors in their success is in being used as guidance and not as something that should be followed too prescriptively or slavishly. The tables cover more frequently recorded clinical observations rather than specific adverse effects resulting from a particular agent or procedure, and thus are not intended to be comprehensive, nor are the values likely to be absolutely correct in every situation. However, they are an attempt to provide assistance for anyone required to establish and assess humane endpoints, whether during experimental procedures, or even at other times such as during breeding and maintenance. Moreover, the terms used in the tables are deliberately imprecise. They are intended to cover the more general aspects of severity and are not intended to replace or conflict with the very specific adverse effects that may be expected and that are required to be set out in detail in every project licence in the UK.

We find these tables provide assistance with severity assessment and that they help provide a framework within which consultations between researchers, veterinarians and animal care and welfare officers can be encouraged and enhanced. This can occur while undertaking scientific procedures but particularly to establish realistic humane endpoints during the experimental design phase. In addition they aid a consistency of approach and understanding of the issues under discussion.

In the future we hope to be able to use more objective endpoints as well as increased accuracy and predictability of the endpoints we currently use. A measure of our success in the future might be minimizing the need for 'substantial' procedures. David Morton said some time ago that society's view on what is acceptable in experiments changes over time, some of what was perfectly routine 20 years ago in many cases is no longer allowed (e.g. the classical LD_{50} and Draize tests). How will our attitudes to severity and endpoint selection change in the next decade or so? Will what is currently moderate become mild, and substantial eventually become moderate? Will we be put under pressure not to carry out substantial procedures at all? Obviously we would all be happier if substantial procedures were able to be reduced through our own efforts by using better predictors of severity, refinement of methodology and environment, and by effective ethical review. Surely, this approach is preferable to legislation being imposed by a society which does not feel we are moving forward fast enough?

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