



Welfare assessment and severity classification

1

Why is good welfare important?

- Poor welfare produces undesirable physiological effects – on science and welfare
- Scientific procedures are regulated if they have the potential to cause harm
- **Direct** suffering – from the procedure. Must be minimised.
 - anaesthesia or analgesia must be used unless more traumatic than the procedure
 - most refined research techniques possible
 - animals in severe pain must be killed
 - physiological and behavioural needs must be catered for
- **Contingent** suffering – from housing and husbandry
- Failure to provide for the animal's needs can result in abnormal animal, and abnormal experimental results.

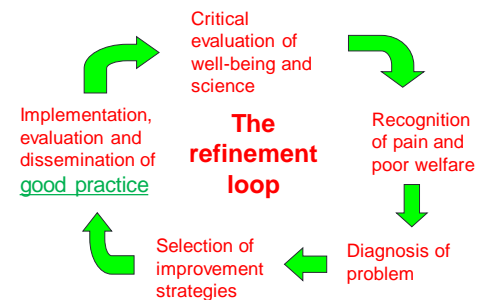
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Why do we need to assess welfare?

- To determine if adverse effects have been minimised
- To facilitate harm:benefit analysis
- To aid decision making - responses to treatment, decisions about euthanasia
- Implementation of ongoing refinement – refinement loop
- Keeping to project licence protocol severity category
- Retrospective assessment of actual severity

3

Implementation of ongoing refinement



4

The Status Quo



5

What is good welfare?

- Need to understand what can lead to poor welfare.
- Five welfare needs of the AWA 2006
 - the need for a suitable environment
 - the need for a suitable diet
 - the need to be able to exhibit normal behaviour patterns
 - the need to be housed with, or apart from, other animals
 - the need to be protected from pain, suffering, injury and disease.
- If these are met, welfare is probably not compromised.
- Scientific procedures can impact negatively on all these.

6

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7

Impact of research on welfare needs

- Suitable environment
- Suitable diet
- Normal behaviour patterns
- Housed with, or apart from, other animals
- Pain, suffering, injury and disease
- Metal cages, grid floors
- Food/fluid regulation paradigms
- Single housing, restricted space, little or no enrichment
- Surgery, chronic implants, handling methods, procedures

7

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8

What adverse effects may be caused?

- **Stress**
 - Induced alteration in biological equilibrium caused by internal or external factors, physiological or psychological.
 - Animals encounter stressors all the time
 - Behavioural and physiological mechanisms activate to counter the perturbation and return to normality
 - Physiological stress – mild, animal unconscious of it
 - Overstress – starts to be detrimental



8

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9

What adverse effects may be caused?

- **Distress**
 - Aversive, negative state
 - coping and adaptation processes fail to return an organism to physiological and/or psychological homeostasis
 - occurs if animal cannot escape from or adapt to the stressors or conditions that it is experiencing
 - results in negative effects on well-being
- Leads to abnormal, maladaptive behaviours

9

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10

Stress vs distress

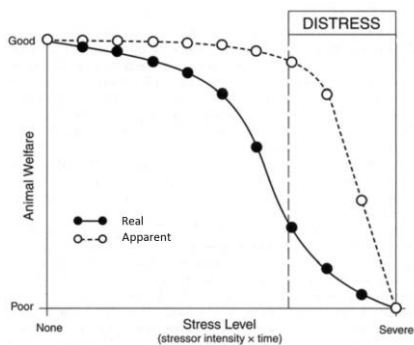
- When **stress** becomes **distress** depends on several factors:
 - the type, duration and intensity of stress
 - species
 - capacity of an animal to respond
- Animal may deteriorate whilst apparently coping with a stressor
- At some unknown moment, the animal rapidly deteriorates into a sick or debilitated animal



10

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11



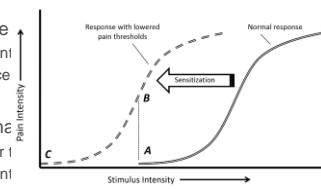
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12

What adverse effects may be caused?

- **Pain**
 - Unpleasant sensory and emotional experience associated with actual or potential tissue damage
- Normal/protective
 - Intended to prevent
 - Learned avoidance
- Non-protective/maladaptive
 - Pain persists after injury
 - peripheral and central sensitization
 - pain experienced is out of proportion to the injury



12

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13

What adverse effects may be caused?

- **Suffering**
- A negative avoidable state derived from adverse physical, physiological and psychological circumstances in accordance with the cognitive ability of the species and the life experiences of the individual.
 - Conscious experience
 - Induced by pain, distress, malaise, boredom, frustration, grief etc
- Direct suffering
 - From the procedure
- Contingent suffering
 - From other aspects: transport, housing, injury etc

13

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14

How do animals respond to pain and distress?

- Biological and behavioural responses
- Physiological/biochemical
 - HR, BP, hormonal, immunological
- Behavioural
 - Automatic
 - Population – animals communicate with each other
- These changes can be monitored to identify when animals are experiencing distress

14

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15

Welfare assessment is not straightforward

- Responses vary between species and among individuals.
- No universally agreed criteria
- Several methods described, each has merits
- Most include assessment of behaviour



15

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16

How do we recognise these responses?

- First become familiar with what is normal
 - for the species
 - for the physiological state
 - for the individual
 - normal behavioural repertoire
- **'Normal' behaviour may be different from behaviour observed in the laboratory**
- Contrast 'normal' with what is normally seen.
- Observe animals and consulting experts
- Once familiar with normal, can identify abnormal.
- Abnormalities evaluated and quantified

16

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17

What factors should I evaluate when assessing welfare?

- Individual: Species, age, and origin.
- Husbandry and history: Environment and procedures? Disease problems? Transport?
- Current condition: Clinical examination? Depends on species.
- Mental status: Dull, depressed, aggressive, hyperexcitable?
- Activity: Changes in gait, posture, facial expression
- Vocalisation: Depends on the species. Sound may be outside human auditory range

17

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18

How do I use this to carry out quantitative welfare assessment (distress scoring)?

- Evaluation of abnormalities allows semi-quantitative assessments of pain and distress. Requires detailed species knowledge and understanding of baseline.
- Distress scoring systems have to be easy to use, consistent, specific and sensitive
- Select parameters indicative of well being
- Assign score with the aid of descriptors – normal or abnormal, degree of abnormality

18

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19

Scoring systems - benefits

- Scoring systems encourage regular close observation of the animal
- If animal is deteriorating, then corrective action can be taken in a timely manner
- NB if analgesics are given, remember to re-score the animal **after** treatment to ensure that they have worked and the animal has improved



19

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20

Scoring systems - limitations

- Lack of universal criteria
 - Changes may be due to non-pain related causes
 - Behaviour improves effectiveness
- Inter-observer variation
 - Different interpretation of same signs
 - Needs proactive approach to develop consistency
- Lack of sensitivity
 - 'General' score sheets not sensitive enough to pick up specific effects, specific systems needed for each model.
- Time consuming - impractical on large scale



20

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21

Distress scoring 1

- Morton and Griffiths (1985) (Veterinary Record 116, 431-36)
- Parameters:
 - Appearance
 - Food and water intake
 - Clinical signs
 - Natural behaviour
 - Provoked behaviour

21

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22

ANIMAL IDENTIFICATION	SCORE	DEFINITION
APPEARANCE – Normal	0	
- General lack of grooming	1	
- Coat staring, ocular/nasal discharge	2	
- Piloerection, hunched up	3	
FOOD AND WATER INTAKE – Normal	0	
- Uncertain, body weight ↓ <5%	1	
- ↓ intake, body weight ↓ 10-15%	2	
- No food or water intake	3	
CLINICAL SIGNS – Normal T, cardiac and resp. rates	0	
- Slight changes	1	
- T ± 1°C, C/R rates ± 30%	2	
- T ± 2°C, C/R rates ↓ 50% or very ↓	3	
NATURAL BEHAVIOUR – Normal	0	
- Minor changes	1	
- Less mobile and alert, isolated	2	
- Vocalisation, self mutilation, restless or very still	3	
PROVOKED BEHAVIOUR – Normal	0	
- minor depression or exaggerated response	1	
- moderate changes in expected behaviour	2	
- Reacts violently, or very weak/comatose	3	
SCORE ADJUSTMENT - If 3 scored more than once, score extra point for each 3	2-5	
TOTAL	0-20	

22

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23

Disadvantages

- General system - not sensitive in all situations
- It must be developed to fit the model
- Pilot studies are important
- Modify the system as the experiment progresses, to include more specific parameters

23

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Distress scoring 2: Pain assessment in the rat

- Rats were scored post laparotomy for specific pain related behaviours: twitching, back arching, and falling.
- Quantifying these behaviours allows for reasonably reliable assessment of pain and response to analgesics in this model
- J Roughan and P Flecknell, University of Newcastle
- <http://www.digires.co.uk/>

24

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25

Distress scoring 3: Mouse Grimace Scale

- Facial expression is used to measure pain in children
- Recent research shows mice show pain through facial expression
- Langford, D.J., Bailey, A.L., Chanda, M.L., Clarke, S.E., Drummond, T.E., Echols, S., Glick, S., Ingraio, J., Klassen-Ross, T., LaCroix-Fralish, M.L., Matsumiya, L., Sorge, R.E., Sotocinal, S.G., Tabaka, J.M., Wong, D., van den Maagdenberg, A.M.J.M., Ferrari, M.D., Craig, K.D., and Mogil, J.S. Coding of facial expressions of pain in the laboratory mouse. *Nature Methods*, 7:447-449, 2010.

25

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26

Lamb grimace scale

- Five facial action units:
 - Orbital Tightening
 - Mouth Features
 - Nose Features
 - Cheek Flattening
 - Ear Posture
- E.g. Still images of the faces of restrained lambs before and after injury. Score by naïve human observers.
- LGS scores significantly increase after injury
- Mouth Features and Orbital Tightening, showed significant quantitative changes after docking

26

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27

Pain faces in other animals

- Rat grimace scale
 - Sotocinal et al. *Molecular Pain* 2011, 7:55
 - <http://www.molecularpain.com/content/7/1/55>
- Rabbit grimace scale
 - Keating et al 2012. Evaluation of EMLA Cream for Preventing Pain during Tattooing of Rabbits: Changes in Physiological, Behavioural and Facial Expression Responses.
 - PLoS ONE 7(9):e44437.doi:10.1371/journal.pone.0044437
- Mouse Grimace Scale.
 - Langford, D.J., Bailey, A.L., Chanda, M.L., Clarke, S.E., Drummond, T.E., Echols, S., Glick, S., Ingraio, J., Klassen-Ross, T., LaCroix-Fralish, M.L., Matsumiya, L., Sorge, R.E., Sotocinal, S.G., Tabaka, J.M., Wong, D., van den Maagdenberg, A.M.J.M., Ferrari, M.D., Craig, K.D., and Mogil, J.S. Coding of facial expressions of pain in the laboratory mouse. *Nature Methods*, 7:447-449, 2010.

27

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28



- Bloom T and Friedman H (2013). Classifying dogs' (*Canis familiaris*) facial expressions from photographs. *Behavioural Processes*, 96: 1-10.

28

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29

What are end points and how do I set them?

- Welfare assessment must be accompanied by a plan of action - monitoring without intervention does NOTHING
- Predetermined intervention points (end points) should be defined:
 - Scientific end point – when all required data has been collected.
 - Error end point – experiment has gone wrong
 - Humane end point – animal has suffered enough
- Welfare assessment can be used to define **humane end point - predetermined limit of acceptable suffering**.
- Identify clear, predictable and irreversible criteria to determine when the degree of suffering experienced reaches agreed limit.
- Action taken to minimise pain or distress.
- Criteria: body temperature, body weight, behaviour, pathology, PO₂
See <https://www.nc3rs.org.uk/humane-endpoints>

29

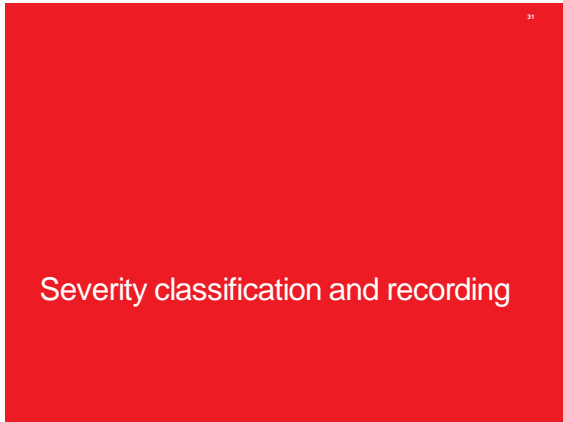
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30

Setting endpoints

- Understand desired scientific outcomes
 - criteria to determine when these have been met
- Identify potential adverse effects - what and when
- Place adverse effects in the context of scientific outputs
- Pilot studies helpful
- Validate and monitor end points
 - sufficiently sensitive to minimise suffering without interference with the scientific objectives?
- Monitor frequently enough to detect signs of distress at an early stage. Take ACTION to reduce potential suffering.

30



31

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What are the project licence severity categories?

- Protocols assigned to one of four **severity categories**
 - **Non-recovery, mild, moderate, or severe.**
 - Maximum degree of permitted severity in pursuit of the scientific goal.
 - Reflects the single worst case scenario
- If this severity is exceeded, PPLh must inform Home Office

32

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What is retrospective recording of actual severity?

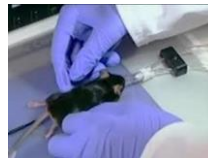
- PPLh must record maximum level of **actual severity** caused by procedures.
- Procedural harms only
 - Non-recovery
 - Mild
 - Moderate
 - Severe
 - **Sub-threshold**
- PILh may be asked to help with classification of procedures.
- Good, accurate, contemporaneous records are required.

33

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1) Non-recovery

- Procedures performed entirely under general anaesthesia from which the animal does not recover consciousness.
- E.g. exsanguination, perfusion fixation



34

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2) Mild

- Procedures causing short-term mild pain, suffering or distress, and no significant impairment of the well-being or general condition.
- E.g. Single blood sample, breeding GA animals.



35

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3) Moderate

- Procedures causing short-term moderate pain, suffering or distress, or long-lasting mild pain, suffering or distress. Procedures causing moderate impairment of the well-being or general condition.
- E.g. most surgical techniques.



36

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37

4) Severe



- Procedures causing severe pain, suffering or distress, or long-lasting moderate effects.
- Severe impairment of well-being or general condition.
- E.g. epilepsy, EAE, death.
- Animals found dead are classified as **severe** unless:
 - cause of death is not procedure related; or
 - animal did not experience severe suffering prior to death

37

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39

What factors should I consider when determining the severity of a procedure?

- **Factors include:**
 - Procedure related factors
 - Husbandry related factors
 - Animal related factors
 - Refinements applied

39

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41

What about cumulative severity?

- In some cases, it is necessary to assess total lifetime severity an animal may have experienced
- E.g. if animal is to be re-used or re-homed
- This judgment may include consideration of intercurrent problems such as illness, injury, or contingent suffering due to transport, restrictive housing etc.
- Veterinary assessment may be needed

41

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38

Sub-threshold

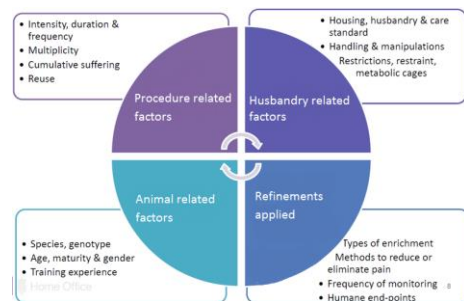
- If an animal or animals has experienced actual severity which is below the lower threshold for regulation.
- i.e. The level of pain, suffering, distress or lasting harm equivalent to, or higher than, that caused by the introduction of a needle in accordance with good veterinary practice

38

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40

Severity Classification criteria



40

Summary

- Understand the species
- Know the individual
- Observe carefully: appearance, behaviour, physiology
- Keep monitoring – keep records
- Take ACTION to REFINE procedures

42



43