

SECOND WORLD CONGRESS ON HUMANE ENDPOINTS

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Careful monitoring of animals for the determination of humane endpoints

Some comments on HEPs

HUMANE

- Derives from being human and so having moral choices, concerned with inhumanity (Montaigne 16C)
- Treatment of others e.g. slaves, women, children and animals - early humane societies in 18/19C was Property versus Persons (animals?) AND debate is still here today
- Our actions require some moral justification - motives and intentions - cruelty.

WHY BE HUMANE?

- ETHICAL
- LEGAL
- SCIENTIFIC
- ECONOMIC

OBLIGATIONS

OECD Guidance (2001, Monograph 19)

Humane Endpoint:

The earliest indicator in an animal experiment of severe pain, severe distress, suffering or impending death.

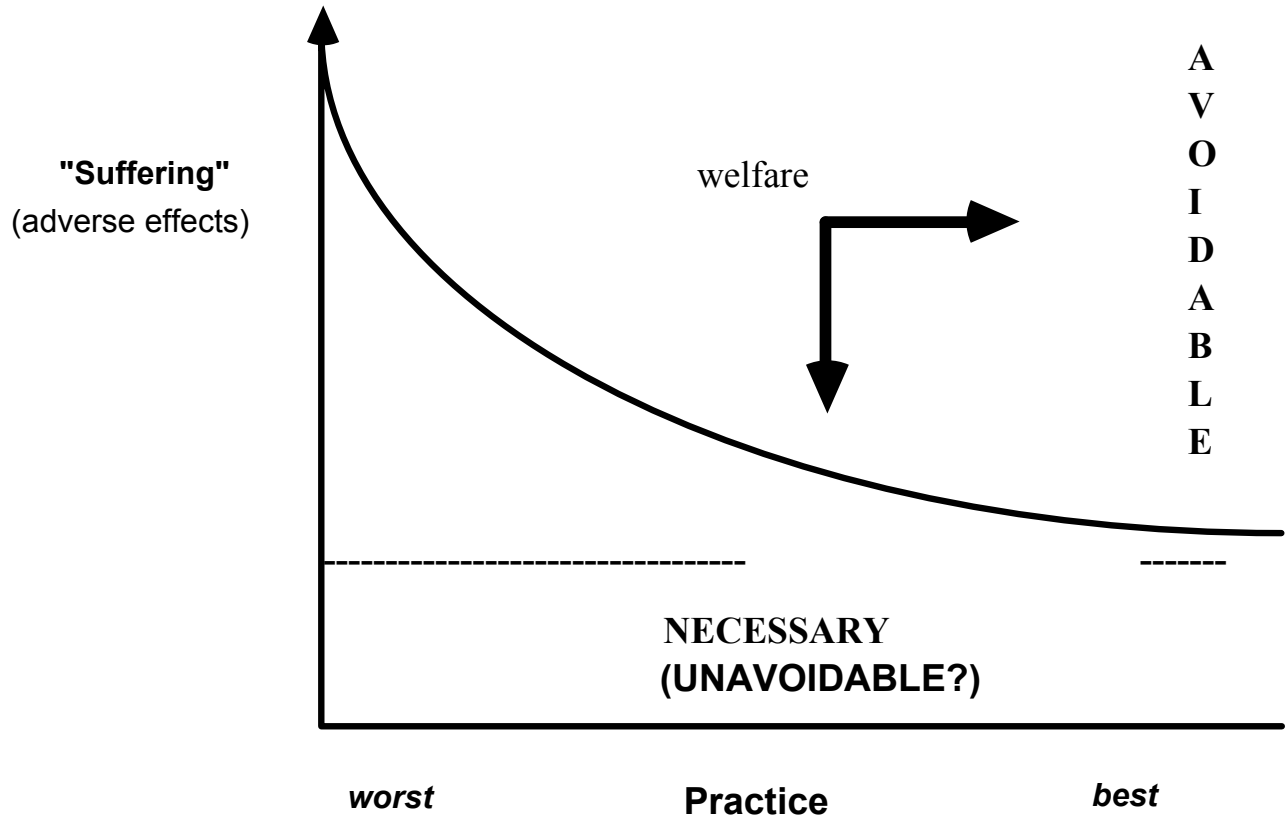
Extreme interpretation? Aimed at toxicity testing.

ENDPOINT

- DEATH - no more suffering
- MORIBUND - no more suffering
- CONSCIOUS - able to suffer
- SELF-CONSCIOUS - additional mental suffering?
- HUMANE ACTION is to end suffering as early as possible

HUMANE ENDPOINTS

- The earliest point at which an experiment can be stopped, or ought to be stopped
i.e. the least inhumane endpoint.
- Aim is not to cause avoidable suffering



SUFFERING

can be defined as

a negative emotional state which derives from adverse physical, physiological and psychological circumstances, in accordance with the cognitive capacity of the species and of the individual being, and its life's experience.

(Morton, 2000)

“We should concentrate on the individual because it is the individual - not the race, nation or the species - who actual suffers.

Inflicting 100 units of pain on one individual is far worse than one unit of pain on 1000, 1,000,000 others, even though the total is far greater.

(Ryder 2005)

CHOICE OF SPECIES

Sizeism

Polyism

HUMANE ENDPOINTS

- The experimental aim has been achieved
- The experimental aim cannot be achieved:
 - Animal not scientifically useful due to physiological perturbations: i.e. data will be skewed by adverse effects
 - Animal not scientifically useful due to psychological perturbations: i.e. data will be skewed by adverse effects
- Suffering higher than predicted – i.e. loss of proportionality
- Suffering too high - simply wrong
- Surrogate endpoints should be used to achieve the scientific objective as early as possible - death is unacceptable

ASSESSMENT often starts with a 'new' procedure to lab.

- Consult the literature (huh!)
- *Contact other groups using the 'model'
- Predict signs - use general sign and score sheet
- *Observe first group of animals individually i.e. pilot studies
- Verify the literature (huh!)
- *Re-draft signs and if possible: define care, set scores, set humane endpoints and actions, ensure adequate training and competence.

By how much has it deviated
from normality?

Is it possible to score/assess:
objectively
semi-objectively
subjectively

SIGNS vs SYMPTOMS

SIGNS: observable by the doctor

SYMPTOMS: reported by the patient

Classification of Signs

Metric Signs - a continuous variable quantity on a mathematical scale (linear or logarithmic)

- Body weight
- Body temperature
- Heart rate
- Respiratory
- Behaviour

Classification of Signs

Parametric signs can also be measured very accurately but often on the basis of whether they are present or absent.

They provide important information just as valid and objective as measurable signs

e.g. s

- Appearance - ruffled or starey coat, closed eyelids
- Response to given stimulus - withdrawal of a limb, induced aggressiveness or vocalization
- Posture: hunched, recumbent, boarded
- Clinical signs - diarrhoea, dyspnoea

Subjective

Interpretation of how an animal feels by:

**Visual observation - behavior
(Welmesfelder, 2000)**

Empathy (whisperers)

**If something is known to cause suffering
in humans, it should be assumed to
cause suffering in animals (OECD;
various)**

PAIN/WELLBEING ASSESSMENT IS SUBJECTIVE? IF SO -

IS IT:

- the clinical signs -
 - Measurable (metric)
 - Observable (parametric)

OR

- the INTERPRETATION of those clinical signs

AREAS OF RESEARCH AND PRACTICE

Absence of evidence is
not necessarily
evidence of absence

ASSESSING AN ANIMAL

- From a distance:
 - natural behavior,
 - appearance
 - new technologies?
- On handling:
 - bodyweight,
 - provoked behavior
 - red light response
 - handling
 - enrichments
 - clinical signs
 - new technologies?

ASSESSING AN ANIMAL

The use of new technologies

- **Non-invasive** (other than some restraint!)
 - Cell tagging
 - NMR
 - Urine
 - Activity monitor
 - Body temperature(?)
- **Invasive**
 - Blood
 - Telemetry
 - Laparoscopy
 - Body temperature(?)

ASSESSING AN ANIMAL

Is it 'normal' for:

- the individual**
- the strain**
- the species**

In that environment

barren vs enriched

isolated vs grouped

CLINICAL OBSERVATION/SCORE SHEETS

To be effective often have to be:

- Specific for each species
- Specific for each experimental protocol

- Signs are scored as present or absent
- They list the common and the cardinal signs
- They detail various actions

RE-ASSESSMENT

Constantly:

- re-evaluate care, signs, scores, endpoints etc
- develop new signs e.g. red light response, weight bearing, enrichment interaction
- develop score sheet with cardinal signs and actions
- Evaluate the need for contemporaneous controls

Use personnel unfamiliar with the work e.g.

new technical staff

‘outside’ animal welfare workers

lay members of the ERP

ADVANTAGES OF 'SCORE' SHEETS

- **CAREFUL, CLOSE, METICULOUS** observation of animals by all staff as score sheets have indicated those times that are critical for the animal and for the experiment

ADVANTAGES OF 'SCORE' SHEETS

- Subjective assessments of suffering by animal care staff and scientists are avoided.**
- Promotes more fruitful dialogue, as evidence-based opinion becomes possible based on the clinical signs.**
- Helps experienced persons illustrate to less experienced persons why an animal is 'not right'.**

ADVANTAGES OF 'SCORE' SHEETS

- **Consistency of scoring is increased as the guidance is clear and the scoring options are limited.**
- **Single signs or combination of signs can be used to indicate overall severity of the procedure.**

ADVANTAGES OF 'SCORE' SHEETS

- **Helps to measure the impact of scientific procedures and aids comparing various alternative models**
- **Helps to indicate set points in a scientific procedure for intervention (e.g. blood sampling, analgesia).**

ADVANTAGES OF 'SCORE' SHEETS

- **The sheets help to determine the effectiveness of any therapy intended to relieve adverse effects**

COMPETENCE of the 'TEAM'

- Animal care staff
- PIs, veterinary technicians, and all who carry out scientific procedures on animals
- Project leaders and experimental design
- Statisticians
- Veterinarians (do they need more training?)
- Ethics committee members
- Enforcers
- Regulators
- Duty of care - culture of care - standards of care

Mice isolated, starey coat, hunched, immobile, ears down, eyes closed, pinched abdomen, pinched face

QuickTime™ and a
Photo - JPEG decompressor
are needed to see this picture.

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MOUSE ACTIVITY

- ALWAYS COMPARE WITH NORMAL ANIMALS NOT “CONTROLS”

SHOW VIDEO CLIP

Temporal occurrence of clinical signs during a pertussis potency test

(with Coenraad Hendricksen)

- 1.Reduced activity, Lack of grooming**
- 2.Ruffled fur over body, Crouching**
- 3.Loss of appetite, Bodyweight loss**
- 4.Dehydration, Sunken eyes, Apathy,
Loss of motor control**
- 5.Convulsions, Death**

FALSE POSITIVES - too early an endpoint (N = 46)

BOD YTEMP.

(DEGREES C)

35.5

<35

<34.5

<34.0

FALSE

(%)

19.5

4.3

0

0

FALSE POSITIVES - too early an endpoint (N = 46)

BOD YWEIGHT

(%)

<20

<30

<40

<50

FALSE

(%)

45.6

21.7

2.2

0

FALSE POSITIVES - too early an endpoint (N = 46)

CLINICAL SCORE

FALSE

(%)

1

47.8

2

23.9

3

2.17

