Refinement of humane endpoints for rodents used in cancer research
Dr. Rafael Frias               Oulu, 28.1.2015

OUTLINE

KEY MESSAGES

IDEAS

RESOURCES

Refinement of humane endpoints for rodents used in cancer research
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Euthanasia
= humane killing

Humane killing
= without (with minimal) pain/distress

Animals are beasts and cannot feel pain
René Descartes
1596-1650

Animals also feel pain

Clinical observations

Scientific evidence

Animals also feel pain

Unpleasant sensory and emotional experience associated with tissue damage
-- IASP
In animals used in cancer research, pain is a significant factor that can affect the quality of data and increase variance. Ethical, legal, and scientific responsibilities must be considered when research involves animals and pain/distress.

Pain can lead to suffering, anorexia, self-mutilation, prolonged recovery, disease, shock, death, and slow healing. More pain results in less gain.

Significant pain - a bias factor in research leads to worse quality of data, more variance.
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Humane endpoints
Criteria that allows EARLY termination of experiment BEFORE animals experience SIGNIFICANT harm while meeting SCIENTIFIC OBJECTIVES

AIM
To implement MORE EFFORTS in order TO REDUCE SIGNIFICANT harm in animals used in cancer research

WHO WILL BENEFIT
Animals & Science
improved welfare  better data

Humane endpoints
DO NOT REPLACE the use of analgesics

3 R’s
Replacement  Reduction  Refinement
non-sentient alternatives  fewer animals  minimize pain & distress

W Russell & R Burch 1959

Humane endpoints

ANIMALS USED IN CANCER RESEARCH

Opioids

Local anesthetics

Non-steroidal anti-inflammatory drugs

Refinement

Humane endpoints

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Refinement
Humane endpoints
4P's

Pilot studies
To assess morbidity – behavior, clinical, physiological
To assess time course of effects
To estimate type/frequency of observations
Necropsy (full extent of tumor growth)

Responsible person/s involved in studies
Must be competent (well trained, experienced)
Must be involved with animal work/study protocols (expected morbidity, critical points in experiment, keeping records)
Effort for CPD

CPD
GROUP – Courses, seminars
INDIVIDUAL - textbooks, websites (videos), guidelines, recommendations, reports, articles

Textbooks
Euthanasia & Humane Endpoints Chapters 14 & 15
Welfare Assessment & Humane Endpoints Chapter 18

Websites
nc3rs.org.uk
For the welfare and use of animals in cancer research
Workman P et al. 2010

For the recognition, assessment, and use of clinical signs as humane endpoints (safety evaluation)
OECD, 2000

For better recognition and classification of pain & distress in rodents & rabbits
Baumans et al. 1994

Pulse oximetry accurately predicts lung pathology in mice
Verhoeven D et al. 2009

Body temperature, food and water consumption as biomarkers of disease progression in mice
Hunter JE et al. 2014
To monitor for morbidity/disease progression

- Stary coat
- Weight gain/loss
- Altered breathing
- Lack of grooming
- Body Isolation
- Body mass: Tumor masses
- Body condition: Temperature, posture
- No eating or drinking
- Frank bleeding
- Altered consistency, amount, color of feces

**DEVELOPMENT OF SCORE SHEET** should include:

<table>
<thead>
<tr>
<th>CLINICAL SIGNS / CONDITIONS</th>
<th>EXTENT OF PAIN/DISTRESS</th>
</tr>
</thead>
<tbody>
<tr>
<td>MILD</td>
<td>MODERATE</td>
</tr>
</tbody>
</table>

**EXAMPLE**

*Animals with total score > 5 will be euthanized*

<table>
<thead>
<tr>
<th>SCORE</th>
<th>BODY WEIGHT</th>
<th>Fecal consistency</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>1</td>
<td>&lt; 10% loss</td>
<td>Poor consistency</td>
</tr>
<tr>
<td>2</td>
<td>10-15% loss</td>
<td>Very moist/pasty</td>
</tr>
<tr>
<td>3</td>
<td>&gt; 20% loss</td>
<td>Watery</td>
</tr>
</tbody>
</table>

**SUMMARY**

Avoidable pain is detrimental for animals (reduced welfare) and science (bias factor)

More efforts could be implemented to refine humane endpoints

**IMPORTANT**

- Pilot studies
- Competent personnel
- Score sheets
- Report it!