

Animal **pain** ethics 360° tour

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What's the lecture about

A journey into animal pain

Welfare and ethics

Clinical pain as an animal welfare issue

(Animal) pain in research and as a research topic

Is animal pain ever justified? Back to welfare

Looking for a less painful future

360°....

> Animal species

- Vertebrate
- Invertebrate
- **Domestic**
- Wild

> Context

- **Pet**
- Production
- Research
- Wild

> Actors

- **Veterinarians**
- Legislators
- Owners
- Public



“the basic problem facing many ethicists has been the wide diversity of opinion on what constitutes ethical behavior toward animals in the broadest sense, let alone with regard to pain. Livingston 2002”

The plasticity of pain in animals

- > Clinical pain
 - Disease or injury

- > Pain as by-product
 - Animal care
 - Research

- > Pain as the focus of research
 - Translational
 - Species specific



A time journey through animal pain



A long way forwards

- > *Ethical issues regarding pain in animals JAVMA 2002*
 - Utilitarian approach
 - Understanding of animal pain
 - Memory of pain
 - Research in pain

Silent suffering

By R. Scott Nolen
Posted Dec. 1, 2001

AVMA ANIMAL WELFARE FORUM

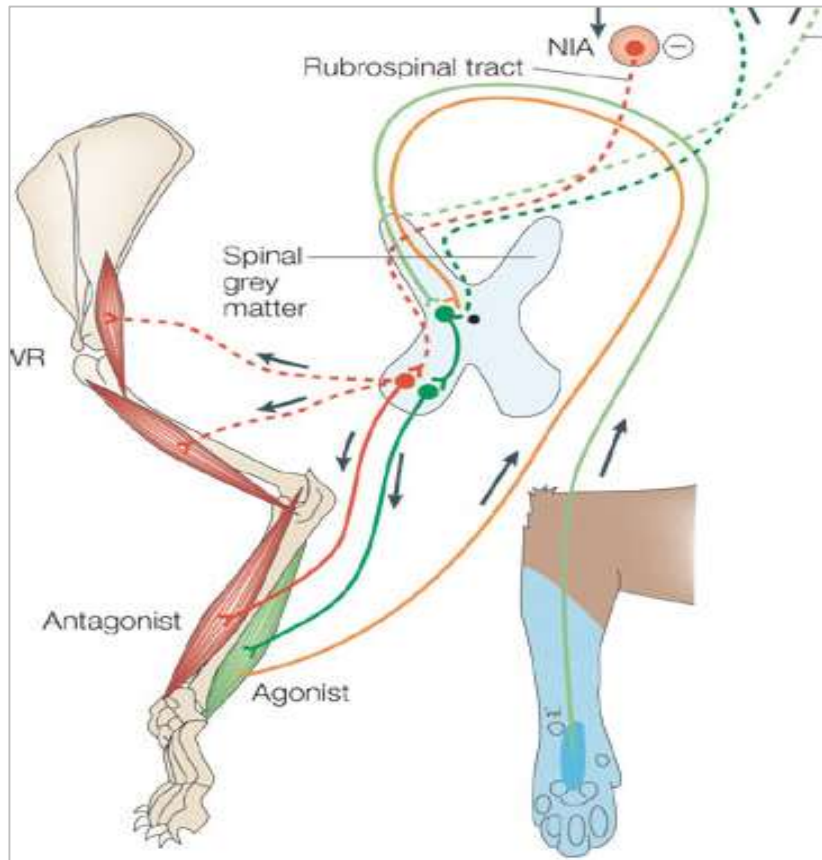
Silent suffering

AVMA Animal Welfare Forum addresses pain management in animals

A decade ago, an entire forum could be devoted to whether animals feel pain or not. Today, the question is no longer "Do they hurt" but "How can we best manage their pain?"

- > Graduated in 1990: only deontology
- > Now welfare and ethics is included in vet. Med. curricula
- > <http://onewelfare.cve.edu.au/animal-ethics>

Definitions: Nociception vs Pain



Definition :



u^b

b
UNIVERSITÄT
BERN

*“An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage. **Note:** The inability to communicate verbally does not negate the possibility that an individual is experiencing pain and is in need of appropriate pain-relieving treatment. Pain is always subjective.”*

Animal Welfare

- > Welfare = achieving a good life

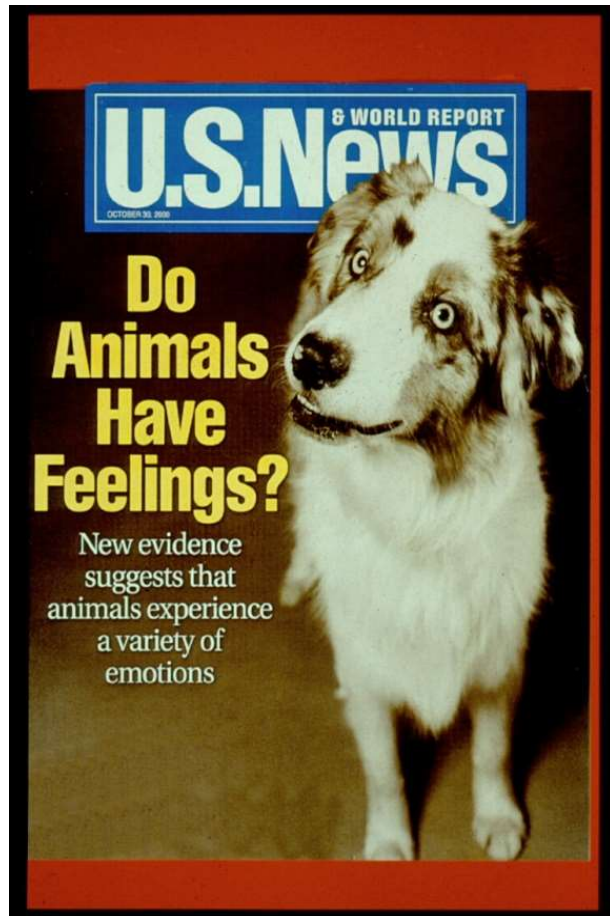
- > Hedonism (Bentham 1789) = have a happy life and minimise pain and suffering

- > Brambell report (1990)= widening of the concept of suffering
 - 5 freedoms
 - Free of hunger and thirst
 - Free of discomfort
 - Free of pain, injury and disease
 - Free to express normal behavior
 - Free of fear and distress

Interests = dignity

*The question is not can they reason? Nor can they talk?
But can they suffer?*

Jeremy Bentham: An Introduction to the Principles of Morals and Legislation. 1789



Animal ethics

- > Ethical theories provide a systematic way of **explaining** and **justifying moral** decisions. They can help work out what is the right thing to do and assist in understanding the ethical views and decisions of other people. No ethical theory is without shortcomings.

- > Classic normative theories
 - Deontology (animal rights)
 - Utilitarianism
 - Contractarianism
 - Relational theories

- > Midline principles: **Beauchamp & Childress (2013)**



Four Principles of Beauchamp and Childress

- > Autonomy – The right for an individual to make his/her own choice.
- > Beneficence – The principle of acting with the best interest of the other in mind.
- > Non-maleficence – The principle that “above all, do no harm,” as stated in the Hippocratic Oath.
- > Justice – A concept that emphasizes fairness and equality among individuals.

Human ethics and pain

Recognizing the intrinsic dignity of all persons and that withholding of pain treatment is profoundly wrong, leading to unnecessary suffering which is harmful; we declare that the following human rights must be recognized throughout the world:

- the right of all people to have access to pain management without discrimination
- the right of people in pain to acknowledgment of their pain and to be informed about how it can be assessed and managed
- the right of all people with pain to have access to appropriate assessment and treatment of the pain by adequately trained health care professionals

International Association for the Study of Pain,
"Declaration of Montreal: Declaration that Access to Pain Management Is a Fundamental Human Right,"
September 2010³

First, health care professionals have an ethical obligation to relieve pain.

Second, this obligation has been largely neglected.

Journal of Pain Research

Dovepress

open access to scientific and medical research

 Open Access Full Text Article

PERSPECTIVES

Ethical decision making in pain management:
a conceptual framework

Challenges in human pain txt

- > Various barriers to effective pain management (relief of pain and suffering as well as improvement in function and quality of life)
 - failure to identify pain as a priority in patient care
 - insufficient knowledge regarding pain management
 - fears associated with opioid prescription and utilization for pain relief
 - the “war on drugs and addiction”
 - cost constraints

Pain, welfare and ethics in veterinary medicine



GUIDELINES FOR RECOGNITION, ASSESSMENT
AND TREATMENT OF PAIN



WSAVA Animal Welfare Guidelines

for companion animal practitioners and veterinary teams

- > Huge progresses in
 - Knowledge in pain
 - Species specific pain detection
 - Species specific treatment
 - Attitude towards pain treatment

Clinical pain

- > Pain as a symptom, disease, and/or illness and phenomenon, ie, total pain
 - Disease or injury
 - Animal care: convenience procedures

- > Moral obligation to recognise, treat and prevent pain

- > Easy for acute or surgical pain

Ethical challenges in veterinary medicine?

- > Costs
- > Chronic pain
- > Oncological pain

- > Treatment in best interest of the animal ?
- > Non treatment in the best interest of the animal?

- > Where and when do we set the bar?

QOL

Gaia

Standard poodle apricot

- > 8 years old
- > Female, spayed
- > HD A



Gaia

1. History, Complaint
 2. Behavioural changes
 1. Pain score
 3. Physical examination
 1. Palpation
 2. Gait
 3. Rx, arthroscopy
 4. QST: pinprick
 4. Analgesic trial
- > Persistent lameness hind limb since 3 years
 - > Difficulty in standing
 - > Persistent lameness forelimbs since 2 years
 - > Decreased deambulation strength/resistance
 - Organization problem
 - > No jumping
-

Gaia

1. History, Complaint
 - > No playing and running
 2. Behavioural changes
 - 1. Pain score
 - > No jogging
 - Still wants to hike
 3. Physical examination
 - 1. Palpation
 - > Lays a lot
 - 2. Gait
 - > Sleeps a lot
 - 3. Rx, arthroscopy
 - 4. QST: pinprick
 4. Analgesic trial
-

Helsinki Chronic Pain Index

Sum of rating (0 to 4) of 11 questions

HELSINKI CHRONIC PAIN INDEX

Name of Dog _____ Owner _____ Diagnosis _____

Date _____ Questionnaire no. _____

Tick only one answer – the one that best describes your dog during the preceding week

					Points	
1. Rate your dog's mood:	Very alert	alert	neither alert, nor indifferent	indifferent	very indifferent	
	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<u>2</u>
2. Rate your dog's willingness to participate in play:	Very willingly	willingly	reluctantly	very reluctantly	does not at all	
	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<u>2</u>
3. Rate your dog's vocalization (audible complaining, such as whining or crying out):	Never	hardly ever	sometimes	often	very often	
	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<u>0</u>

Helsinki Chronic Pain Index (cont')

4. Rate your dog's willingness to walk:	Very willingly <input type="checkbox"/>	willingly <input checked="" type="checkbox"/>	reluctantly <input type="checkbox"/>	very reluctantly <input type="checkbox"/>	does not walk at all <input type="checkbox"/>	1
5. Rate your dog's willingness to trot:	Very willingly <input type="checkbox"/>	willingly <input type="checkbox"/>	reluctantly <input type="checkbox"/>	very reluctantly <input type="checkbox"/>	does not trot at all <input checked="" type="checkbox"/>	4
6. Rate your dog's willingness to gallop:	Very willingly <input type="checkbox"/>	willingly <input type="checkbox"/>	reluctantly <input checked="" type="checkbox"/>	very reluctantly <input type="checkbox"/>	does not gallop at all <input type="checkbox"/>	2
7. Rate your dog's willingness to jump (eg. into car, onto sofa...)	Very willingly <input type="checkbox"/>	willingly <input type="checkbox"/>	reluctantly <input type="checkbox"/>	very reluctantly <input type="checkbox"/>	does not jump at all <input checked="" type="checkbox"/>	4
8. Rate your dog's ease in lying down:	With great ease <input type="checkbox"/>	easily <input type="checkbox"/>	neither easily, nor difficultly <input type="checkbox"/>	with difficulty <input checked="" type="checkbox"/>	with great difficulty <input type="checkbox"/>	3
9. Rate your dog's ease in rising from a lying position:	With great ease <input type="checkbox"/>	easily <input type="checkbox"/>	neither easily, nor difficultly <input type="checkbox"/>	with difficulty <input checked="" type="checkbox"/>	with great difficulty <input type="checkbox"/>	3
10. Rate your dog's ease of movement after a long rest:	Never difficult <input type="checkbox"/>	hardly ever difficult <input type="checkbox"/>	sometimes difficult <input type="checkbox"/>	often difficult <input checked="" type="checkbox"/>	very often/always difficult <input type="checkbox"/>	3
11. Rate your dog's ease of movement after major activity or heavy exercise:	Never difficult <input type="checkbox"/>	hardly ever difficult <input type="checkbox"/>	sometimes difficult <input type="checkbox"/>	often difficult <input type="checkbox"/>	very often/always difficult <input checked="" type="checkbox"/>	4

Points 0 1 2 3 4

Total up the answers to all 11 questions. Total chronic pain index score:

28/44

Canine Brief Pain Inventory

Today's Date: / /
Month Day Year

Patient/Study ID# _____

Canine Brief Pain Inventory (CBPI)

Description of Pain:

Rate your dog's pain.

1. Fill in the oval next to the one number that best describes the pain at its **worst** in the last 7 days.

0 1 2 3 4 5 6 7 8 9 10
No Pain Extreme Pain

6

2. Fill in the oval next to the one number that best describes the pain at its **least** in the last 7 days.

0 1 2 3 4 5 6 7 8 9 10
No Pain Extreme Pain

3

3. Fill in the oval next to the one number that best describes the pain at its **average** in the last 7 days.

0 1 2 3 4 5 6 7 8 9 10
No Pain Extreme Pain

5

4. Fill in the oval next to the one number that best describes the pain as it is **right now**.

0 1 2 3 4 5 6 7 8 9 10
No Pain Extreme Pain

5

Canine Brief Pain Inventory (II)

Description of Function:

Fill in the oval next to the one number that describes how during the past 7 days pain has interfered with your dog's:

- | | | | | | | | | | | | | |
|---|-------------------------|-------------------------|-------------------------|-------------------------|------------------------------------|-------------------------|------------------------------------|------------------------------------|-------------------------|------------------------------------|--------------------------|---|
| 5. General Activity | <input type="radio"/> 0 | <input type="radio"/> 1 | <input type="radio"/> 2 | <input type="radio"/> 3 | <input type="radio"/> 4 | <input type="radio"/> 5 | <input checked="" type="radio"/> 6 | <input type="radio"/> 7 | <input type="radio"/> 8 | <input type="radio"/> 9 | <input type="radio"/> 10 | 6 |
| Does not Interfere | | | | | | | | | | | Completely Interferes | |
| 6. Enjoyment of Life | <input type="radio"/> 0 | <input type="radio"/> 1 | <input type="radio"/> 2 | <input type="radio"/> 3 | <input type="radio"/> 4 | <input type="radio"/> 5 | <input checked="" type="radio"/> 6 | <input type="radio"/> 7 | <input type="radio"/> 8 | <input type="radio"/> 9 | <input type="radio"/> 10 | 6 |
| Does not Interfere | | | | | | | | | | | Completely Interferes | |
| 7. Ability to Rise to Standing From Lying Down | <input type="radio"/> 0 | <input type="radio"/> 1 | <input type="radio"/> 2 | <input type="radio"/> 3 | <input type="radio"/> 4 | <input type="radio"/> 5 | <input type="radio"/> 6 | <input checked="" type="radio"/> 7 | <input type="radio"/> 8 | <input type="radio"/> 9 | <input type="radio"/> 10 | 7 |
| Does not Interfere | | | | | | | | | | | Completely Interferes | |
| 8. Ability to Walk | <input type="radio"/> 0 | <input type="radio"/> 1 | <input type="radio"/> 2 | <input type="radio"/> 3 | <input checked="" type="radio"/> 4 | <input type="radio"/> 5 | <input type="radio"/> 6 | <input type="radio"/> 7 | <input type="radio"/> 8 | <input type="radio"/> 9 | <input type="radio"/> 10 | 4 |
| Does not Interfere | | | | | | | | | | | Completely Interferes | |
| 9. Ability to Run | <input type="radio"/> 0 | <input type="radio"/> 1 | <input type="radio"/> 2 | <input type="radio"/> 3 | <input type="radio"/> 4 | <input type="radio"/> 5 | <input type="radio"/> 6 | <input type="radio"/> 7 | <input type="radio"/> 8 | <input checked="" type="radio"/> 9 | <input type="radio"/> 10 | 9 |
| Does not Interfere | | | | | | | | | | | Completely Interferes | |
| 10. Ability to Climb Up (for example Stairs or Curbs) | <input type="radio"/> 0 | <input type="radio"/> 1 | <input type="radio"/> 2 | <input type="radio"/> 3 | <input checked="" type="radio"/> 4 | <input type="radio"/> 5 | <input type="radio"/> 6 | <input type="radio"/> 7 | <input type="radio"/> 8 | <input type="radio"/> 9 | <input type="radio"/> 10 | 4 |
| Does not Interfere | | | | | | | | | | | Completely Interferes | |

Canine Brief Pain Inventory

Overall Impression:

11. Fill in the oval next to the one response best describes your dog's overall quality of life over the last 7 days?

- Poor Fair Good Very Good Excellent

Severity: ≈ 5

Interference: 6

QOL: 2

Gaia

1. History, Complaint
 1. Pain score
2. Behavioural changes
3. Physical examination
 1. Palpation
 2. Gait
 3. Rx, arthroscopy
 4. QST: pin prick
4. Analgesic trial



Quantitative sensory testing

- > Thresholds
 - Mechanical
 - Electrical stimul
 - Thermal i
 - > Endpoint
 - Behavioural
 - Neurophysiological
 - > Single stimulus
 - > Repeated stimulus:
temporal summation
- > What do we expect?
 - Decreased thresholds
 - Shorter latencies
 - Lower intensities
 - > **NO NORMATIVE VALUES!**
-

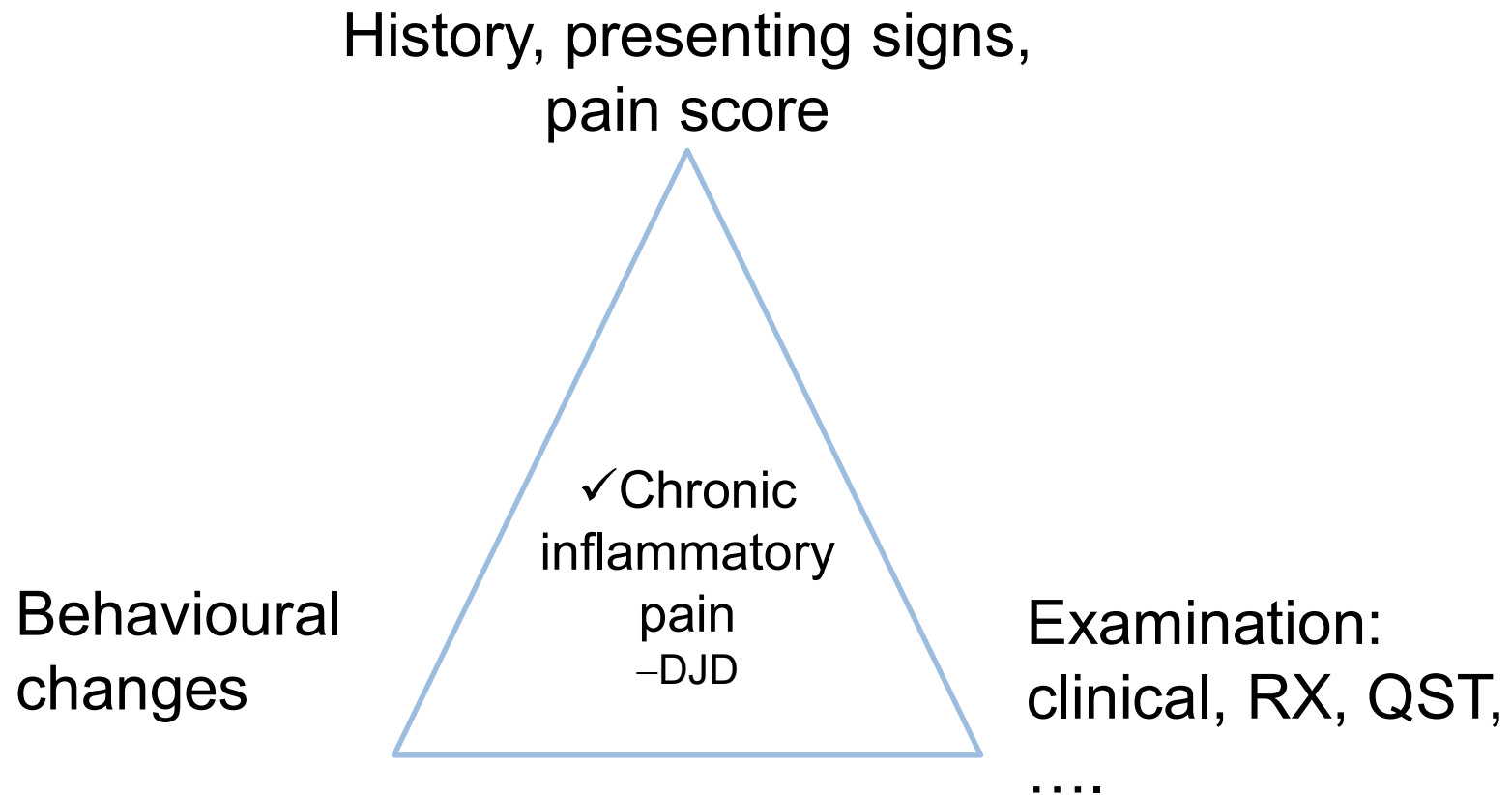


Gaia

1. History, Complaint
 1. Pain score
2. Behavioural changes
3. Physical examination
 1. Palpation
 2. Gait
 3. Rx, arthroscopy
 4. QST: von Freys
4. Analgesic trial



The triangulation technique for Gaia



Just because you can, doesn't mean you should

- The status of animals in (Western) societies has changed
- Harming animals always needs justification (including clinical cases)
- Professional codes, owner expectation, technology, money, technical skill, ambition: promotes maximum intervention
- Where do we draw the line as professionals?
- providing an ethical framework and methods to inform guidance

Drawing the line in clinical treatment of companion animals: recommendations from an ethics working party

Herwig Grimm,^{1,2,3} Alessandra Bergadano,⁴ Gabrielle C Musk,⁵ Klaus Otto,⁶ Polly M Taylor,⁷ Juliet Clare Duncan⁸



Triad veterinarian-animal-owner

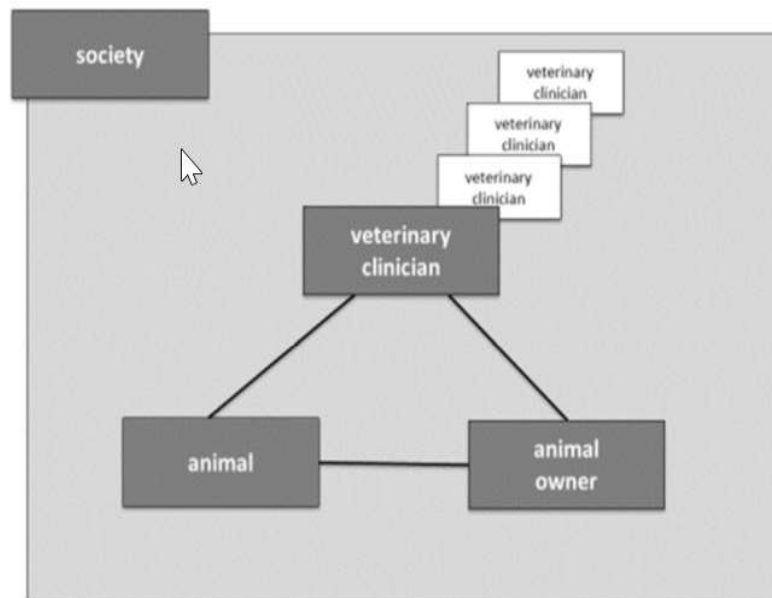


TABLE 3: Relationships and corresponding factors to consider in ethical clinical decision-making

Clinician-patient (clinical responsibility)	<p>A. Legitimate aim: Is the clinical intervention in the best interest of the animal? A1. Will the proposed treatment improve the patient's health? A2. Will the proposed treatment improve the patient's quality of life (immediately/long term)?</p> <p>B. Alternative measures: Is the proposed treatment the one with the least potential to cause harm and suffering while still achieving the intended clinical goal?</p> <p>C. Reducing harm and suffering: Have measures been taken to minimise the potential for harm and suffering?</p> <p>D. Proportionality test: Do the expected benefits outweigh the potential harm and suffering inflicted on the animal or are they at least in balance?</p>
Clinician-profession (professional responsibility)	<p>E. Clinician experience: Does the primary clinician/team have experience in carrying out the proposed treatment and/or is it a well-documented recognised treatment?</p> <p>F. Ethical decision-making: Is this case an example of good ethical decision-making for students/trainees/colleagues?</p> <p>G. Professional justification: Would you feel comfortable justifying the proposed treatment to professional colleagues?</p>
Client-patient	<p>H. Treatment impact: Would proceeding with the proposed treatment have a positive impact on the owner-animal relationship?</p> <p>I. Benefit to client: Would proceeding with the proposed treatment have a positive impact on the client's quality of life and/or financial benefits (eg, the proposed treatment will allow breeding from a valuable animal)?</p>
Clinician-client	<p>J. Cost: Is the proposed treatment financially viable for the client?</p> <p>K. Recovery: Is the client capable of providing a suitable home environment and/or administering medication during the recovery period?</p>
Priority of justification (moral v non-moral)	<p>L. Moral proportionality test: Are answers to E-K more influential in your clinical decision than the A-D?</p>

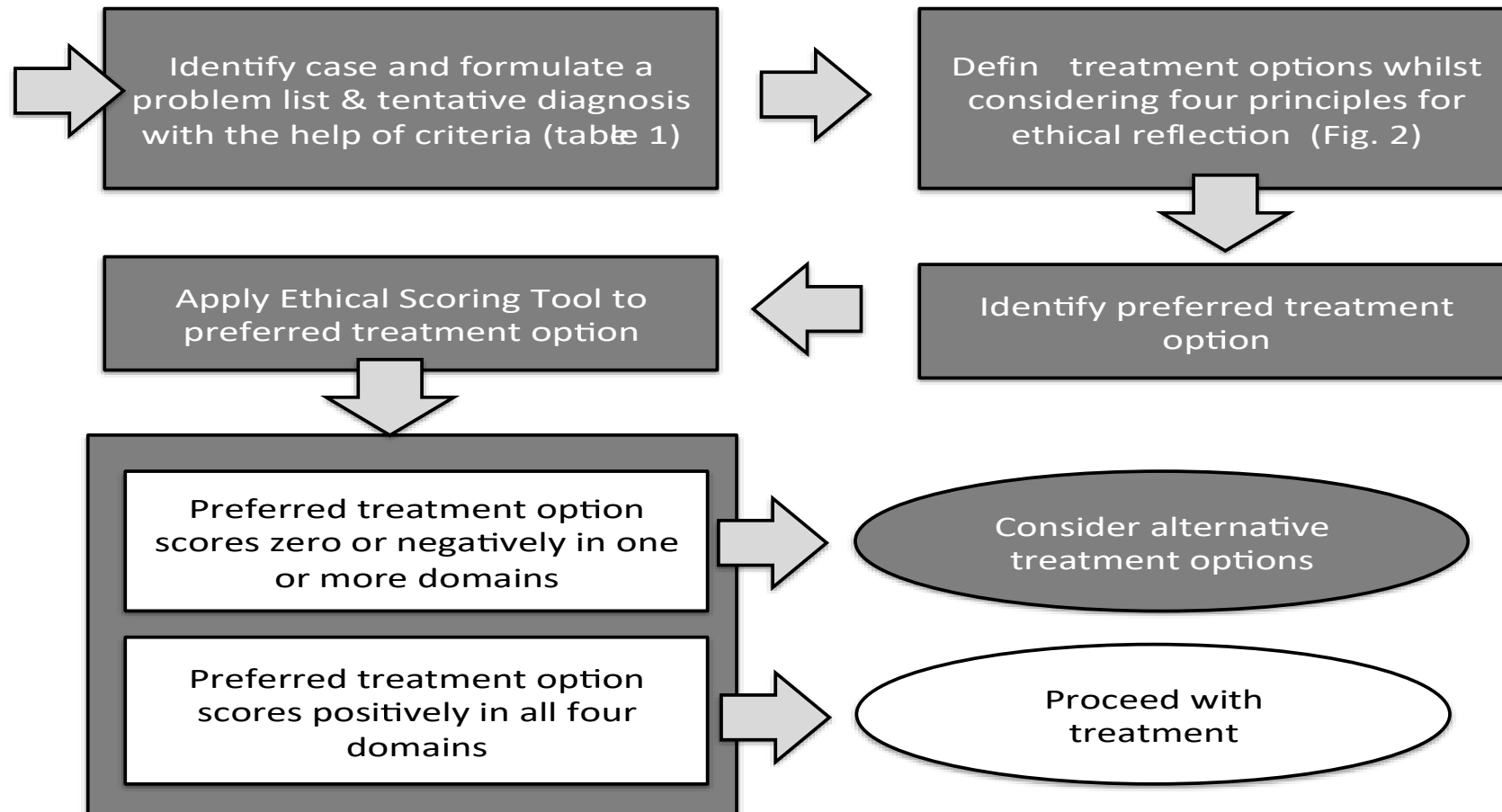
Scoring tool

TABLE 4: Prototype of a veterinary ethics tool (VET) to facilitate decision-making in clinical veterinary medicine

	Relationship	Questions to facilitate ethical deliberation	No	I don't know	Possibly	Definitely
Animal-centred factors (justificatory reasons)	Clinician-patient (clinical responsibility)	A. Do you perceive the proposed treatment to be in the best interests of the patient?	Red	Orange	Green	Green
		A1. Will the proposed treatment improve the patient's health?	Red	Orange	Green	Green
		A2. Will the proposed treatment improve the patient's quality of life: (a) immediately (b) long term	Red	Orange	Green	Green
		B. Is the proposed treatment option the one with the least potential to cause harm and suffering while still achieving the intended clinical goal?	Orange	Orange	Green	Green
	C. Have measures been taken to minimise the potential for harm and suffering?	Orange	Orange	Green	Green	
		D. Do the expected benefits outweigh the potential harm and suffering inflicted on the animal or are they at least in balance?	Red	Orange	Green	Green
Secondary factors (explanatory reasons)	Clinician-profession (professional responsibility)	E. Does the primary clinician/team have experience in carrying out the proposed treatment and/or is it a well-documented recognised treatment?	Orange	Orange	Green	Green
		F. Is this case an example of good ethical decision-making for students/trainees/colleagues?	Orange	Orange	Green	Green
		G. Would you feel comfortable justifying the proposed treatment to professional colleagues?	Orange	Orange	Green	Green
	Client-patient	H. Would proceeding with the proposed treatment have a positive impact on the owner-animal relationship?	Orange	Orange	Green	Green
		I. Would proceeding with the proposed treatment have a positive impact on the client's quality of life and/or financial benefits (eg, the proposed treatment will allow breeding from a valuable animal)?	Orange	Orange	Green	Green
	Clinician-client	J. Is the proposed treatment financially viable for the client?	Red	Orange	Green	Green
K. Is the client capable of providing a suitable home environment and/or administering medication during the recovery period?		Red	Orange	Green	Green	
Priority check	Professional responsibility	L. Are the secondary factors E–K (explanatory reasons) more influential in your clinical decision than the animal-centred factors A–D (justificatory reasons)?	Green	Orange	Red	Red

■ Consider alternative treatment options.
■ Reconsider procedure and the clinician's responsibility.
■ Valid reasons for clinical procedure.

How to draw the line...



Animal pain in research

- > Well regulated

 - > Pain in research animals **must** be relieved for a series of interlinked reasons:
 - Ethical must and honor an ideal
 - In compliance to law
 - Scientifically sound
 - Addresses public concern
-

In compliance to law & regulations

> **TschG, TschV**

> **Eu 63 /2010**

- *The choice of methods should therefore ensure the selection of the method that is able to provide the most satisfactory results and is likely to cause the minimum pain, suffering or distress.*
- *From an ethical standpoint, there should be an upper limit of pain, suffering and distress above which animals should not be subjected in scientific procedures. To that end, the performance of procedures that result in severe pain, suffering or distress, which is likely to be long-lasting and cannot be ameliorated, should be prohibited*

> **Principle 4, US Government**, Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Teaching, IRAC 1985

> **Position Statements**

- *“Procedures expected to cause more than slight or momentary pain (e.g needle prick or injection) require the appropriate use of pain-relieving measures unless scientifically justified in an approved animal care and use protocol” ACLAM Position Statement 2001*
 - *“institutions are expected to provide oversight of all research animals and ensure that pain and distress are minimized” The Guide 2011*
-

In compliance to law & regulations

- > **ARRIVE guidelines:** *details of anesthesia and analgesia to be published*
- > **Ethical Guidelines for Investigations of Experimental Pain in Conscious Animals IASP 1985**
 - *Investigators of animals models for chronic pain, as well as those applying acute painful stimuli to animals, should be aware of the problems pertinent to such studies and should make every effort to minimize pain*
- > **<http://www.veteditors.org/consensus-author-guidelines-on-animal-ethics-and-welfare-for-editors/>**

International Association of Veterinary Editors

Consensus Author Guidelines on Animal Ethics and Welfare for Veterinary Journals

All material published in [journal name] must adhere to high ethical standards concerning animal

Animal ethics-based criteria for manuscript rejection

- 1) Manuscripts and authors that fail to meet the aforementioned requirements;
- 2) Studies that involve unnecessary pain, distress, suffering, or lasting harm to animals;
- 3) The Editor retains the right to reject manuscripts on the basis of ethical or welfare concerns.

Scientifically sound

- > Clinical effects of pain
 - Maladaptive physiological and behavioural reactions
 - Activation of neuroendocrine system
 - Respiratory and CV impairment
 - Decreased myocardial and intestinal perfusion
 - Decreased wound healing
 - Increased morbidity and mortality

 - > Scientific bias
 - Greater data variability
 - Non reproducible data
 - Missing data points
 - Non publishable data
-

Ethical must

Using animals is a PRIVILEGE, not a right

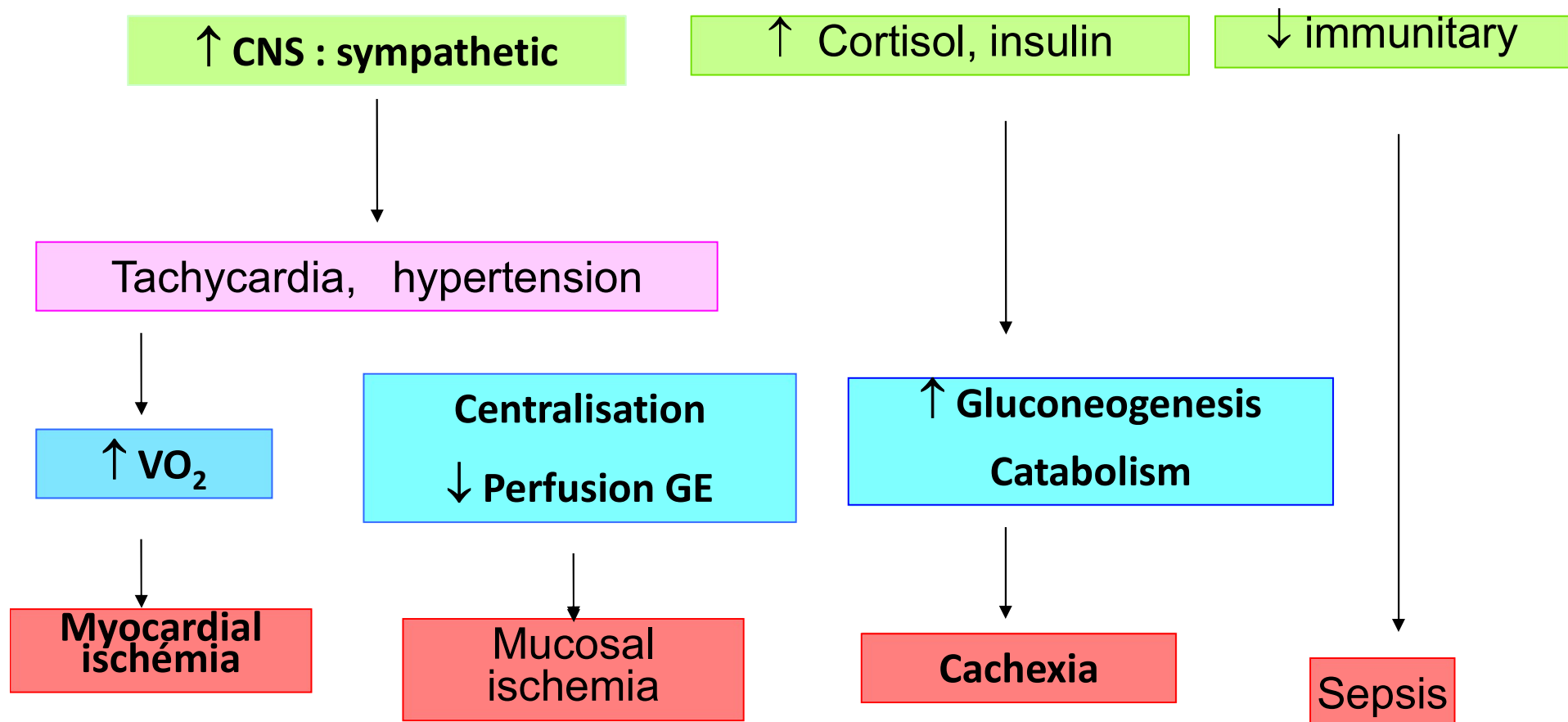
- > The 5 freedoms... *Free of pain, injury & disease*
 - Analgesia
 - Shortest duration
 - Humane euthanasia
 - Upper limit for pain

- > Ethical analysis = harm benefit analysis



Systemic effects of nociception

Activation of neuro-endocrine system



(Animal) Pain as a research topic

- Phasic /acute nociception
 - Thermal
 - Chemical
 - Mechanical
 - Electrical
 - Somatic
 - Tonic /chronic pain
 - Inflammatory pain
 - Somatic
 - Visceral
 - Neuropathic pain
 - Ligated sciatic nerve
 - Spare nerve model
 - Cancer pain
-
- > Veterinary or translational
 - > Age: neonatal, pediatric, adult or aged
 - > Basic and applied research (analgesics & treatments)
-

(Animal) Pain as a research topic

- Do animal models tell us about human pain?
 - Difficult to translate results of experimental rat models to clinically relevant human (animal) pain with therapeutic failures and side effects

- Do not represent population...
- Receptor differences
- Excessive simplification of models
- Environmental bias
- Do not reflect clinical pain

- Critics & frustration

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Painful dilemmas: the ethics of animal-based pain research

M Magalhães-Sant'Ana*†‡ P Sandae§ and IAS Olsson¶§

Is research in (animal) pain or pain in animal research ever justifiable? Back to welfare

- > Actually... causing pain is not categorically prohibited -> Needs justification -> Outstanding scientific advance

 - > Models of acute nociception vs models of chronic pain
 - purposefully elicit pain of longer duration as hyperalgesia and allodynia that can be distressing and often induce irreversible changes.
 - For these models the administration of analgesics is contraindicated and the definition of **adequate endpoints** is essential to avoid unnecessary suffering

 - > (No) Animal pain, no pain in research and research in animal pain... a sustainable paradox
-

Looking to a less painful future

Pain and distress must be minimized!

- Refine: diagnosis & treatment, endpoints. models, studies,
 - Reduce: animal numbers
 - Replace: animal studies, natural models of disease
-

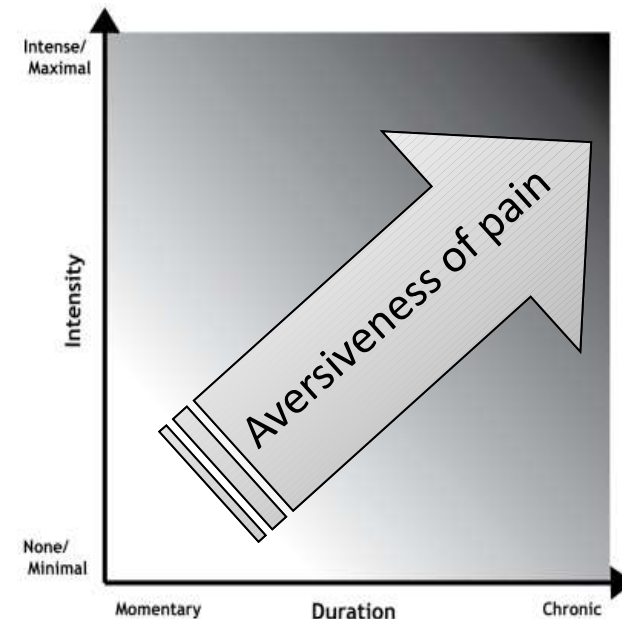
Refine: Evidence based diagnosis

- > Is possible to treat pain only when it is recognized and quantified
 - Subjective vs objective

 - > Validated species-specific pain assessment tools
 - Rats *Roughan 2001*
 - Mice *Arras 2007*
 - Dogs *Holton 2001*
 - Lambs after castration *Molony 2006*
 - Pigs after castration *Jaegglin 2004*
-

Refine: Evidence based treatment

- > The aversiveness of pain is primarily determined by duration and intensity
 - Duration and intensity interact to affect aversiveness, although not in a simple additive way.
 - In humans, the aversiveness of pain is also affected by psychological factors, such as how controllable or predictable the pain is, and its context or consequences.
 - There is little information about the influence of such effects in animals
- **The alleviation of pain in research animals typically means reducing its duration and/or its intensity, and both are refinements to be made whenever possible**



State-of-the-art concepts for analgesia

« *Pharmacological treatment is the base of pain treatment* » American Pain Society

1. Timing

- Preventive
- Sufficient duration

2. Multimodal

- Different mechanisms of action/targets
- Combination of drugs → synergic analgesia
- ↓ dose and ↓ side effects = **Balance**

3. Individualized

- Strain
- Model
- Experimental read out

4. Monitored

- Pain evaluation or scoring

1. Peripheral modulation

1. Nav channels
2. TRPV Vanilloid receptors
3. Cold receptors
4. Alfa receptors

2. Central modulation

1. Na channels
2. TRPV Vanilloid receptors
3. Alfa receptors
4. Ca channels
5. NMDA receptors

3. Central perception

1. GABA receptors

4. Descending inhibition

1. Opioiergic
2. Noradrenergic

Holistic measures

- > Appropriate animal handling
 - > Appropriate restraint
 - > Training “*gentling*” -> influencing the psychological modulation
 - > Minimization of tissue trauma during surgery
 - Minimally invasive surgery
 - Skills
 - Asepsis
 - > Appropriate nursing & post op care
 - > Sedation and neuroleptanalgesia
 - > Adjunctive drugs
 - > Acupuncture
 - > Medical massage
 - > Nursing
 - > Physiotherapy
 - > Diets & supplements
 - > Salvage surgery
-

Refine animal models, generate better data

- > Humane action and endpoints: balance between research results and animal welfare
 - Preemptive reflection and planning, validated, based on sound science
 - Highly relevant in chronic pain models, where pain-relieving drugs cannot be used
 - Humane action points
 - Preventive measures, therapeutic measures (Analgesia \pm Adjunctive txt) or a combination of the two
 - Humane endpoints
 - Early cut offs
 - Euthanasia as pain killer
 - Upper limits for pain
-

Refine animal models, generate better data

- > Include more complex outcome measures
 - Multi-model approach: i.e. nociceptive and behavioural test
 - Multi-outcome approach: i.e. facial pain scales and burrowing and clinical signs
 - Move to non-reflexive (operant) read outs
 - Positive controls: baseline with use of analgesia

 - > Evidence based
 - Thorough literature searches for alternatives
 - Species specific efficacy of analgesic & anesthetics
 - Influence of analgesics and anesthetics on research models
-

Reduce

- > Sharing data and resources
 - Publication of research results and best practices
 - Publication of negative results
 - Interaction and communication among actors: vets, researchers, IACUCs, welfare, societies...

- > Control for variability
 - Influence of background strains
 - Diet and environment

- > Improved experimental design & statistical analysis
 - SOPs
 - Reproducibility: GLP/GCP
 - Power : less is not always better
 - Gender differences

□ Kathryn Sandberg, Jason G. Umans,
and the Georgetown Consensus Conference Work Group
**Recommendations concerning the new U.S. National Institutes of Health
initiative to balance the sex of cells and animals in preclinical research**
FASEB J May 2015 29:1646–1652; published ahead of print February 20,
2015, doi:10.1096/fj.14-269548

Replace

- > Computer modeling
 - Educational purposes
 - > Animal cells, tissues and organs
 - Pain pathways on a chip???
 - > Naturally occurring diseases in animals
 - Osteoarthritis in dogs
 - DJD in cats
 - Muscular disease in horses
 - Cancer in dogs
-

Actions

- > Pain assessment should accompany every patient assessment
- > We can't always know that our patient does hurt, but we can do our best to ensure that it doesn't hurt
- > Include an ethical evaluation of complex clinical cases
 - Creating a culture of collaborative and transparent professional responsibility in the clinic
- > Have a Multidisciplinary Clinical Ethical Committees in place
- > Provide continuing education of the teams

What is a Culture of Care

- > The culture of care is an important principle that indicates a commitment to **improve animal welfare**, **scientific quality**, **care of the staff** and **transparency** for the stakeholders.

- > Science-based performance standards
 - Provide criteria for assessment of a desired outcome
 - Dynamic: evolve as new information becomes available, thereby allowing new discoveries to be implemented in a timely manner and in a way that more effectively benefits the animals and the science.

- > Beyond legal standards

And the journey continues...

- > Pain as achieving successful strategies for its treatment is an overarching experience which can benefit from the continuing collegial discussion and sharing of the different stakeholders.

 - > Pain vs suffering
 - > Ethical analysis = harm/benefit = Where to draw the line
 - > Compassion and empathy
 - > All animal species
-

A time journey through welfare in animal research



Sir Charles Sherrington
1857-1952

PROCEEDINGS
OF THE
ROYAL SOCIETY OF LONDON.

Cataleptoid Reflexes in the Monkey." By C. S. SHERRINGTON,
M.A., M.D., F.R.S., Holt Professor of Physiology, University
College, Liverpool. Received December 29, 1896,—Read
January 21, 1897.



1959

The ethic



2010

The dignity



Creating a Culture of Care

2020

The compassion

LYON
27 / 11
2019



CAPdoulleur
CHANGE ANIMAL PAIN

1^{ère} JOURNÉE DOULEUR
Boehringer-Ingelheim Bat. Boréal

La Confluence des douleurs
de l'homme à l'animal :
l'intelligence des regards croisés
la rencontre scientifique
la volonté de l'échange



Musée des Confluences



ALCYON
VOS ÉTATS DANS L'ÉCLAIR DE NOS CÉLÉSTES



miKan
PROTEIN. FOR. BALANCE.