Meeting the Information Requirements of the Animal Welfare Act

Presented by
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Animal Welfare Information Center (AWIC)
U.S. Department of Agriculture

Laboratory Animal Welfare Training Exchange
June 5, 2013
Objectives

• List the information requirements of the Animal Welfare Act.

• Define the 3 Rs of Alternatives.

• Become familiar with databases and other resources helpful in searching for alternatives.

• Design and run a search for alternatives.
August 24, 1966
Laboratory Animal Welfare Act signed into law


“…the farm bill contains legislation dealing with the humane treatment of animals. The main thrust of the bill is to minimize pain and distress suffered by animals used for experiments and tests. In so doing, biomedical research will gain in accuracy and humanity. We owe much to laboratory animals and that debt can best be repaid by good treatment and keeping painful experiments to a minimum.”

Sen. R. Dole
Congressional Record
Senate
17 December 1985
Food Security Act of 1985
Subtitle F, Animal Welfare, Public Law 99-198

Improved Standards for Laboratory Animals Act

- Clarifies humane care to include specific criteria such as sanitation, ventilation, and housing.
- Directs the Secretary of Agriculture to establish regulations for
  - exercise for dogs and
  - a physical environment adequate to promote the psychological well-being of primates.
- Specifies that animal pain and distress must be minimized (veterinary care, anesthesia, analgesia, tranquilizers, and euthanasia).
Food Security Act of 1985
Subtitle F, Animal Welfare, Public Law 99-198
*Improved Standards for Laboratory Animals Act*

- Specifies that principal investigators must consider alternatives to any procedure likely to cause pain or distress.
- Establishes the Institutional Animal Care and Use Committee (IACUC).
- Explains penalties for the release of trade secrets.
- Establishes an information service at the National Agricultural Library.
AWA Defines Service at NAL
(7 U.S.C. 2142, Sec. 13, Subsection e)

The Secretary shall establish an information service at the National Agricultural Library. Such service shall, in cooperation with the National Library of Medicine, provide information--

(1) pertinent to employee training;

(2) which could prevent unintended duplication of animal experimentation as determined by the needs of the research facility; and

(3) on improved methods of animal experimentation which could--
   (A) reduce or replace animal use; and
   (B) minimize pain and distress to animals, such as anesthetic and analgesic procedures.
Farm Security and Rural Investment Act of 2002 (Farm Bill)  
Public Law 107-101

“Approval of this amendment will make sure that none of the important work taking place in the medical research community will be... otherwise compromised by regulatory shenanigans on the part of the U.S. Department of Agriculture.” Sen. J. Helms

- Modifies the definition of animals to exclude rats, mice and birds bred for use in research.
- Makes it illegal to knowingly sponsor or exhibit an animal in a fighting venture, if any animal was moved in interstate or foreign commerce and increases fines.
Code of Federal Regulations
Title 9, Chapter I, Subchapter A,
Animal Welfare

Painful Procedure, Sec. 1.1

…as applied to any animal means any procedure that would reasonably be expected to cause more than slight or momentary pain or distress in a human being to which that procedure was applied, that is pain in excess of that caused by injections or other minor procedures.
Information Requirements of the AWA 9 CFR 2.31 (d)

[The] IACUC shall determine that...

(ii) The principal investigator has considered alternatives to procedures that may cause more than momentary or slight pain or distress to the animals, and has provided a written narrative description of the methods and sources, e.g., the Animal Welfare Information Center, used to determine that alternatives were not available;

(iii) The principal investigator has provided written assurance that the activities do not unnecessarily duplicate previous experiments.
Information Requirements of the AWA 9 CFR 2.31 (d)

[The] IACUC shall determine that…

(iv) Procedures that may cause more than momentary or slight pain or distress to the animals will:

(A) Be performed with appropriate sedatives, analgesics or anesthetics, unless withholding such agents is justified for scientific reason, in writing, by the principal investigator and will continue for only the necessary period;
Information Requirements of the AWA 9 CFR 2.31 (d)

[The] IACUC shall determine that…

(x) No animal will be used in more than one major operative procedure from which it is allowed to recover unless:

(A) Justified for scientific reasons by the principal investigator in writing.

(B) Required as routine veterinary procedure.

(C) Approved by the Administrator of APHIS.
Animal Care Policy #11
Painful and Distressful Procedures: March 25, 2011

Examples of procedures that may cause more than momentary or slight pain include, but are not limited to, the following:

– **Surgery (survival or terminal)**: considered a painful procedure in which pain is alleviated by anesthesia. Survival surgery may also require the use of peri-operative analgesia.
– **Freund’s Complete Adjuvant**: may cause a severe inflammatory reaction depending on the species and route of administration.
– **Ocular or Dermal Toxicity Testing**: the dosing procedure itself is generally not painful but the reaction caused by the product being tested may cause pain.

Examples of procedures that may cause more than momentary or slight distress include, but are not limited to, the following:

– **Food and/or water deprivation or restriction** beyond that necessary for normal presurgical preparation.
– **Noxious electrical shock or thermal stress** that is not immediately escapable.
– **Paralysis or immobility** in a conscious animal.
– **Forced exercise** (e.g., swimming or treadmill protocols).
– **Infectious and inflammatory disease models**.

Examples of procedures that may cause more than momentary or slight pain as well as distress would include:

– **studies involving extensive irradiation**
– **inhalation toxicity studies**
– **tumor growth**

Animal Care Policy #12
Written Narrative for Alternatives to Painful/Distressful Procedures: March 25, 2011

• “..APHIS continues to recommend a database search as the most effective and efficient method for demonstrating compliance with the requirement to consider alternatives to painful/distressful procedures.”

• The database search narrative must, at a minimum, include
  – Names of the databases searched (“one database is seldom adequate”)
  – Date the search was performed
  – Time period covered by the search
  – The search strategy (including scientifically relevant terminology) used.

Alternatives should be considered in the planning phase of the animal use proposal. …

“If a database search or other source identifies a bona fide alternative method (one that could be used to accomplish the goals of the animal use protocol), the IACUC may and should ask the PI to explain why an alternative that had been found was not used”.
Alternatives - The 3Rs
Definition of Alternatives

• Russell and Burch (1959) – *The Principles of Humane Experimental Technique*

  – Full text available online at AltWeb: http://altweb.jhsph.edu/pubs/books/humane_exp/het-toc

• Development of the concept of the 3Rs:
  – Reduction
  – Refinement
  – Replacement
Alternatives
The 3Rs of Russell and Burch

**Reduction** - Minimize the number of animals used.

**Refinement** - Employ techniques that reduce pain and distress.

**Replacement** - Substitute animal with nonanimal methods or lower organisms.
Alternatives: Reduction

*The Principles of Humane Experimental Technique (1959)*

- Quality literature search
- Appropriate statistical design
- Pilot studies
- Sharing animals, tissues, or organs
- New methods in testing
  (e.g. limit test, local lymph node assay, etc.)
3Rs—Reduction/Refinement

- **Emerging Technologies**
  - Imaging Devices for Use in Small Animals
    - positron emission tomography
    - single-photon emission computed tomography
    - computed tomography
    - magnetic resonance imaging
    - ultrasound
    - optical imaging with fluorescent and bioluminescent tracer technology

In vivo imaging modalities, within the context of animal welfare concerns, are seen as **technical refinements** in that they are much less invasive than older diagnostic and monitoring techniques. In addition, animal imaging devices now offer the possibility of **reduction of animal sacrifice** through longitudinal study that uses animals as their own controls, thereby also **simultaneously improving science** by the use of the improved statistics of paired observations. Wade Koba, et al. (2011). Imaging Devices for Use in Small Animals. Seminars in Nuclear Medicine Volume 41, Issue 3, May 2011, Pages 151–165
Imaging

PET system for small animals
http://zmbe.uni-muenster.de/institutes/izb/stemres_de.htm
New animal models


- One problem limiting development of therapeutic interventions is that the relevance of rodent models to human spinal cord injury is not clear. Progress in developing therapies would be better facilitated by a valid, humane non-human primate model that would allow testing of potentially efficacious pharmacological treatments. This brief report addresses the feasibility of this concept. In human spinal cord injury, the primary impairment is the inability to control the limb to perform functional tasks such as walking, grooming, feeding, etc. However, to propose a primate model of acute spinal cord injury that induce significant hind limb and/or forelimb limb paralysis would be unacceptable. As well, extensive lesions of the spinal cord could result in bowel and bladder dysfunction. To appropriately address the animal welfare issues, this spinal cord injury model is predicated on a monkey’s tail being the ‘fifth limb’. As such, this model focuses on creating a selective, small lesion on one side of the sacral spinal cord that partially impairs movement of the tail.
3Rs—Reduction/Refinement

• Telemetry
  – Affect welfare in several ways
  • Can be used to reduce stress by capturing data without increased handling
  • Can be used to capture data to determine if experimental methods are stressful
Searching Pubmed - Telemetry

- **Useful Terms**
  - telemetry
  - species
  - data to be collected

- **Example**
  - telemetry and mice

  - Sample citation—shows both reduction of numbers/ refined procedure that minimizes stress


  - Reactogenicity often represents a major hurdle to the clinical use of new substances. Yet, irrespective of its importance, this parameter has remained difficult to screen for, owing to a lack of sensitive small animal models with a capacity for high throughput testing. Here we report that continuous telemetric measurements of heart rate, heart rate variability, body core temperature and locomotor activity in laboratory mice readily unmasked systemic side-effects of vaccination, which went undetected by conventional observational assessment and clinical scoring. Using only limited numbers of mice, this method allows for their automated evaluation, differentiation and selection without sizeable risk for investigator-related bias.
Alternatives: **Refinement**

*The Principles of Humane Experimental Technique* (1959)

- Knowledge of species physiology and normal and abnormal behavior
- Proper use of anesthetics and analgesics
- Modifications in restraint, handling, blood collection
- Increased sensitivity of monitoring devices and chemical assays
- Proper training of personnel
Social Housing

Cage Design
Handling and Training

Environmental Enrichment
Alternatives: **Replacement**
The Principles of Humane Experimental Technique (1959)

• **Relative replacement** - some animal involvement
  – Isolated cell and nerve preparations
  – Use of tissues from slaughter house or grocer
  – Computer simulations based on in vivo data
Virtual Alternatives

Non-animal Models Used in Teaching
Alternatives: **Replacement**

*The Principles of Humane Experimental Technique* (1959)

- Absolute replacement – no animal involvement
  - Endoparasites, plants, microorganisms
  - Computer automated structure evaluation systems
  - Human tissue culture
3Rs - Replacement

• Emerging Technologies
  – Artificial Organs/Tissue Engineering
    • Liver on a chip
    • Organ/tissue printing technology

Where Can I Find the Information?
Databases

Biomedical and Biological

- CAB Abstracts file 50
- EMBASE file 73
- BIOSIS file 5
- Scopus and ScienceDirect
- Web of Science
Pharmacokinetics
pharmacokinetics and pain

BIOSIS

1464

35

551

119

MEDLINE

449

332

EMBASE

989

Total: 3,939

Without BIOSIS Previews, you would be missing 1,464 unique citations.

In addition to hundreds of journal article records, BIOSIS Unique records contain 415 Meeting records.
Additional Databases

Available on the Web

- DTIC Online
  
  http://multisearch.deepwebaccess.com/multisearch/search.html?searchMode=advancedDoD

- NC3Rs Blood Sampling Microsite
  
  http://www.nc3rs.org.uk/bloodsamplingmicrosite/

- Best Practices for Common Procedures
  
  http://www.procedureswithcare.org.uk/

- Altweb
  
  http://altweb.jhsph.edu/

- AltBib: Bibliography on Alternatives to Animal Testing
  

- Norecopa – Norwegian consensus platform for replacement, reduction and refinement of animal experiments
  - http://oslovet.norecopa.no
  - Film and Slide Shows: http://film.oslovet.norecopa.no/
Searching for Alternatives
AWIC’s Approach

- Approach the search in two phases.
- Analyze the protocol to determine where alternatives might be used and for terminology.
- Decide where to go for the information.
  - Databases
  - Websites
- Link terminology appropriately for best search results.
- Evaluate the search results.
Searching for Alternatives
Search Strategy

Two Phases

• *Phase I*: Reduction and refinement- citations pertinent to PI’s field of study.

• *Phase II*: Replacement- use of nonanimal or alternative animal models.
Searching for Alternatives

• Consists of three types of terms:
  – Scientific terms related to the research protocol;
  – Alternative (3Rs) terminology; and
  – Search terminology: Boolean operators, limits, truncations, years, types of materials…
Searching for Alternatives

Tips

• Description of protocol and area of study
• Species being used
• Organ systems involved
• Acronyms (CNS, BSE, MAb)
• Spelling (behavior, behaviour)
• Names of hormones, enzymes, CAS#, trade names (xylazine = rompun)
• Authors in the field including the PI
• Is the PI aware of any possible alternatives?
• Previous searches with keywords, years and databases searched
Alternatives Search Example
Objective/Hypothesis

The environment of an open fracture can be manipulated in both a salutary and degratory fashion with respect to the establishment of acute osteomyelitis. L-fucose should decrease and arachidonic acid should increase the propensity toward infection in comparison with controls.
Materials and Methods

• Animals: Albino Sprague-Dawley rats will be used.

• Bacteria: Strain SMH of *Staphylococcus aureus*. 
Technical Methods

Pain Alleviation:
The rats will be anesthetized with a cocktail of 1.5 ml ketamine and 1.5 ml xylazine and 0.5 ml acepromazine given at a dosage of 0.5 to 0.7 ml/kg. If the plane of anesthesia is too light as determined by a positive toe pinch reflex, one half the original cocktail dose or isoflurane may be given. Buprenorphine will be given up to 3x/day if the animal shows signs of pain.
Establishment of infection

Tibia exposed and wound created in the bone with dental burr. Wound inoculated with *S. aureus* or *S. aureus* with L-fucose or arachidonic acid, allowed to incubate and rinsed with sterile saline. Wound is closed and animals sampled at various times to track development of osteomyelitic lesions.
Searching for Alternatives
Osteomyelitis Search Information

The search will be developed to find answers to questions such as:

• Are there other animal models that may be more suitable for testing potential therapeutics or that more closely resemble the human condition?

• Is there useful information on the proposed model that might allow the use of fewer animals or might reduce the pain suffered by the animals?

• Are there any in vitro methods that might allow for early screening of potential therapeutics?

• Do the proposed anesthetics, analgesics, or α2-adrenergic antagonist (yohimbine) pose a confounding influence on the outcome?

• Are there methods available to track the infection that don’t require sequential killing of the animals?
## Searching for Alternatives

### Osteomyelitis Search Strategy

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**Japanese Science and Technology**
# Searching for Alternatives

## Osteomyelitis Search Strategy

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<td>S4</td>
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Synergy of HBO2 and a local antibiotic carrier for experimental osteomyelitis due to Staphylococcus aureus in rats.
Mendel V; Simanowski H J; Scholz H Ch
Undersea & hyperbaric medicine - journal of the Undersea and Hyperbaric Medical Society, Inc Winter 2004, 31 (4) p407-16

A standard rat model of Staphylococcus aureus-induced osteomyelitis was used to compare the effect of HBO2, a local antibiotic carrier (gentamicin-containing collagen sponge) and the combination of HBO2 with a local antibiotic carrier. For the induction of osteomyelitis, a defined Staphylococcus aureus suspension was inoculated into the medullary cavity. Arachidonic acid was used as sclerosing agent. With that procedure an infection rate of more than 95 percent was attained.
Arachidonic acid facilitates experimental chronic osteomyelitis in rats.
Rissing JP; Buxton TB; Fisher J; Harris R; Shockley RK
Infect Immun (UNITED STATES) Jul 1985, 49 (1) p141-4

Arachidonic acid was used as a facilitating agent in experimental rat Staphylococcus aureus osteomyelitis and compared with the more commonly used agent, sodium morrhuate. The injection of arachidonic acid or sodium morrhuate and S. aureus into rat tibiae caused increased quantitative bacterial bone counts, gross bone pathology, roentgenographic changes, and weight loss. The doses required to produce these changes appeared to be lower for arachidonic acid.
Binding of a Staphylococcus aureus bone pathogen to type I collagen.
Buxton T B; Rissing J P; Horner J A; Plowman K M; Scott D F; Sprinkle TJ; Best G K
Microbial pathogenesis  Jun 1990 ,  8 (6) p441-8.

We contrasted the collagen-binding potential of the experimental osteomyelitis pathogen, Staphylococcus aureus strain SMH, to several other strains. These included Cowan 1 (binder), Wood 46 (non-binder) and six capsular variants. These measurements were made using an 125I-collagen binding assay. These data suggest that the prototype bone pathogen binds to the major protein component of bone's extracellular matrix. Collagen-binding is promoted by protein adhesin(s), not capsule. The latter, in fact, appeared to interfere with this interaction. **Binding was inhibited by solutions containing the simple monosaccharide, L-fucose.**
# Searching for Alternatives

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<td>S9</td>
<td>S7 AND S8</td>
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An Acute Osteomyelitis Model in Traumatized Rat Tibiae Involving Sand as a Foreign Body, Thermal Injury, and Bimicrobial Contamination

McPherson, James C. III  Runner, Royce R.; Shapiro, Brian; Walsh, Douglas S.; et al

Comparative medicine. 2008 Aug., v. 58, no. 4  p. 369-374.

The multifactorial nature of bone injuries in modern warfare and emergency trauma patients warrants enhancement of existing models. To develop a more appropriate model, rat tibiae (n = 195) were mechanically injured, divided into 2 groups (with or without thermal injury), and contaminated with a range of Staphylococcus aureus (Cowan 1) inocula. In some experiments, S. aureus inocula also contained Escherichia coli or foreign bodies (sand or soil). The primary outcome measure was the amount of S. aureus remaining in the tibia (tibial bacterial load) 24 h after contamination, reported as log(10) cfu/g bone. S. aureus showed ID50 and ID95 values of 72 and 977 cfu, respectively. Sand, added as a foreign body, increased tibial bacterial load. Combined mechanical and thermal trauma of the tibia is associated with increased S. aureus tibial bacterial loads, increasing the risk of acute osteomyelitis. Understanding the interplay of mechanical and thermal injuries, bimicrobial contamination, and foreign bodies may improve our understanding of traumatic bone injuries and the pathogenesis of osteomyelitis.
Subasi M; Kapukaya A; Kesemenli C; Kaya H; Sari I
Archives of orthopaedic and trauma surgery *(Germany)* 2001, 121(3) p170-3.

Granulocyte-macrophage colony-stimulating factor (GM-CSF) is a cytokine that affects the various developmental steps of hematopoietic cells and enhances the phagocytic activity of these cells. The effect of GM-CSF on acute osteomyelitis, developed in rats, was investigated. For this purpose, osteomyelitis was firstly developed through the direct inoculation of Staphylococcus aureus into rat tibial metaphysis. Twenty-four rats in which diagnosis of osteomyelitis was histopathologically established were divided into two groups. Antibiotic only was given to the first group, and antibiotic as well as GM-CSF to the second group. Rats were followed up for 3 months with plain radiographs and scintigraphic methods using 67Ga-citrate.
The effect of wound environment on the incidence of acute osteomyelitis.
Evans RP; Nelson CL; Harrison BH

A model was developed to identify and compare the local wound factors that induce acute osteomyelitis in a prospective, controlled investigation. When compared with wounds containing either virulent bacteria or dead bone, statistical analysis disclosed a significant increase in the incidence of osteomyelitis when virulent bacteria and dead bone were combined. The incidence of osteomyelitis in wounds containing an inoculated, hematoma-filled dead space was significantly less when compared with wounds containing dead bone and virulent bacteria. The incidence of osteomyelitis is significantly less when a nonvirulent strain of bacteria is substituted for a virulent strain. Although rigid internal fixation increased the incidence of osteomyelitis to 100% and long-term antibiotic therapy decreased the incidence, these changes were not statistically significant. These data allow the authors to predict the relative risk of osteomyelitis when these wound factors are present. The prevention of osteomyelitis depends on the clinical identification and modification of these local wound factors.
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Biosis

Daptomycin and Gentamicin Show Limited Activity in a Novel In Vitro Model of Osteomyelitis
Sweeney E (Reprint); Nelson S; Lovering A; Bowker K; Macgowan A
Washington, DC, USA 20081025,
*Sponsor: * Infect Dis Soc Amer
*ISSN: *0733-6373
*Document Type: * Meeting; Meeting Poster
*Record Type: * Citation
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EmBase, Medline

**Establishment of a real-time, quantitative, and reproducible mouse model of Staphylococcus osteomyelitis using bioluminescence imaging.**

Funao, H., et al. Department of Orthopaedic Surgery, School of Medicine, Keio University, Shinjuku, Tokyo, Japan.

**Abstract**

Osteomyelitis remains a serious problem in the orthopedic field. There are only a few animal models in which the quantity and distribution of bacteria can be reproducibly traced. Here, we established a **real-time quantitative mouse model of osteomyelitis using bioluminescence imaging (BLI) without sacrificing the animals.** A bioluminescent strain of Staphylococcus aureus was inoculated into the femurs of mice. The bacterial photon intensity (PI) was then sequentially measured by BLI. Serological and histological analyses of the mice were performed. The mean PI peaked at 3 days, and stable signals were maintained for over 3 months after inoculation. The serum levels of interleukin-6, interleukin-1β, and C-reactive protein were significantly higher in the infected mice than in the control mice on day 7. The serum monocyte chemotactic protein 1 level was also significantly higher in the infected group at 12 h than in the control group. A significantly higher proportion of granulocytes was detected in the peripheral blood of the infected group after day 7. Additionally, both acute and chronic histological manifestations were observed in the infected group. **This model is useful for elucidating the pathophysiology of both acute and chronic osteomyelitis and to assess the effects of novel antibiotics or antibacterial implants.**
(68)Ga-DOTAVAP-P1 PET imaging capable of demonstrating the phase of inflammation in healing bones and the progress of infection in osteomyelitic bones.

Differentiation between bacterial infection and nonbacterial inflammation remains a diagnostic challenge. Vascular adhesion protein 1 (VAP-1) is a human endothelial protein whose cell surface expression is induced under inflammatory conditions, thus making it a highly promising target molecule for studying inflammatory processes in vivo. We hypothesized that positron emission tomography (PET) with gallium-68-labeled 1,4,7,10-tetraazacyclododecane-N',N'',N''',N''''-tetraacetic acid-peptide targeted to VAP-1 ((68)Ga-DOTAVAP-P1) could be feasible for imaging the early inflammatory and infectious processes in healing bones.

MATERIALS AND METHODS:
Thirty-four Sprague-Dawley rats with diffuse Staphylococcus aureus tibial osteomyelitis and 34 rats with healing cortical bone defects (representing the inflammation stage of healing) were PET imaged using (68)Ga-DOTAVAP-P1 as a tracer. In addition, peripheral quantitative computed tomography and conventional radiography were performed. Bone samples for quantitative bacteriology and specimens were also processed for histomorphometry of inflammatory and infectious reactions. Quantitative bacteriology confirmed infection in all osteomyelitic animals in our study. Induced infection is primarily localized in the medullary area and its adjacent bone, thus minimizing the impact on the affect for the general well-being of the animal.

CONCLUSIONS:
The current study showed that PET imaging with the new (68)Ga-DOTAVAP-P1 is capable of accurately demonstrating the phase of inflammation in healing bones and the progress of bacterial infection in osteomyelitic bones. Consequently, this novel imaging agent allowed for the differentiation of bone infection due to S. aureus and normal bone healing as soon as 7 days after onset.
A different perspective for radiological evaluation of experimental osteomyelitis.
Aktekin Cem Nuri; Ozturk Akif Muhtar; Tabak Abdullah Yalcin; Altay Murat; Korkusuz Feza

INTRODUCTION: Radiological scoring systems used in experimental osteomyelitis combine several factors into a single score. Because response of bone tissue to infection is a dynamic process, such systems have limited ability to differentiate between treatment groups. The analyzing of radiological criteria separately at different stages of the disease may be superior to a general score. METHODS AND METHODS: Osteomyelitis was induced with Staphylococcus aureus in the left tibiae of 72 adult Wistar albino rats. The rats were assigned to one of six different treatment groups. Their radiographs were graded (1) by the use of previously published general scoring systems and (2) by the evaluation of periosteal reaction, bone deformation, diaphyseal widening, osteolysis, soft tissue swelling, bone mineral content (BMC) and bone mineral density (BMD), separately. The assessments were performed 3 weeks after induction as well as 3 weeks and 6 weeks after treatment. RESULTS: Periosteal reaction and diaphyseal widening demonstrated significant differences within 3 weeks of treatment, contrary to the general scores. After 6 weeks of treatment, individual criteria, including diaphyseal widening, osteolysis and BMC but only one of the general grading scores, were able to differentiate between treatment groups. CONCLUSIONS: For differentiation of treatments in experimental osteomyelitis individual assessment of radiological criteria is superior to previously published general scoring systems.
Search Evaluation
The PI Role

• Check terminology, strategy, sources, and dates of search.
• Review the search **before** completing the protocol.
• Assess and evaluate the alternative possibilities.
• Be prepared to support the use or non-use of any alternatives in writing.
• Keep a copy of strategy, databases searched, and years of search for future use.
Search Evaluation
The IACUC Role

- Review the protocol form. Are the questions asked in a clear way to gather the information needed?
- Review the
  - Databases searched,
  - Terminology used *and*
  - Years of coverage.
- Review the search strategy.
- Ask about the order of search and protocol writing.
- Have an information provider on the committee as a resource.
Search Evaluation
Red Flags

- Search completed at the last minute.
- Only 1 database searched.
- Terms only for painful aspects.
- The term “alternative” used alone with no other alternative terms.
- Keywords listed not relevant to protocol.
- Keywords and concepts linked in an incorrect manner (e.g. wrong Boolean operators).
- Search doesn’t cover adequate time period (5-10 years).
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