

Impediments to Humane Endpoints in Infectious Disease Research

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Barriers to Refinement of Animal Models

- US perspective
- Focus on infectious disease research but application to other areas of study
- Perspectives of a laboratory animal veterinarian and a veterinary anesthesiologist
(Clinicians, Scientists, IACUC members)

Barriers to Refinement of Animal Models

- **Misunderstanding the Alternatives Philosophy**
- Resistance to alternatives concept
 - Link to animal protection/rights movement
 - Interference with science
 - Refinements developed by animal welfare scientists rather than research scientists
 - Refinements=better science

Barriers to Refinement of Animal Models

- **Misunderstanding the Alternatives Philosophy**
- Focus on Refinement
 - Species/strain selection
 - Susceptible/resistant
 - Enrichment
 - Housing
 - Psychological
 - Handling/training

Barriers to Refinement of Animal Models

- **Misunderstanding the Alternatives Philosophy**
- Focus on Refinement
 - Supportive care
 - Analgesics
 - Fluid support
 - Humane Endpoints
 - Monitoring/assessment
 - Validation

Barriers to Refinement of Animal Models

- **Misunderstanding Animal Biology/Physiology**
- Paradox: requirement for a “complex biological system”
 - whole animal testing without knowledge of whole animal biology/physiology
- Psychological distancing-scientists do not see the whole animal just the effects they want or expect to see

Barriers to Refinement of Animal Models

- **Misunderstanding Animal Biology/Physiology**
- Pathophysiological mechanisms of disease
 - Graded responses versus all or nothing approach (live/dead)
 - “gold standard” assays
- “Proximate cause of death” concept
 - sequellae to infection or dehydration?

Barriers to Refinement of Animal Models

- **Misunderstanding Animal Biology/Physiology**
- Training in monitoring and assessment
 - Behavioral-activity levels, food/water consumption
 - Physiological-body weight, body temperature
- Graduate programs-PhD, MD, DVM
- IACUC
- AALAS, FELASA, ICLAS

Barriers to Refinement of Animal Models

- Lack of Motivation for the Use of Alternatives
- Time/effort
 - Allocation of resources (staff, equipment)
 - Analogy: watch gel=watch animal

Barriers to Refinement of Animal Models

- Lack of Motivation for the Use of Alternatives
- Regulations
 - USDA AWA
 - Inspect/review protocols
 - PHS NIH-PHS Policy
 - Disconnect with NIH study sections reviewing grant submissions
 - Pitting IACUCs against PIs
 - AAALAC

Barriers to Refinement of Animal Models

- Lack of Motivation for the Use of Alternatives
- Dissemination of alternatives information
 - Databases: ALTWEB, AWIC
 - Conferences
 - Publications
 - Editors/reviewers
 - Guidelines for alternatives consideration and use
 - Published in journals not read by scientists

Barriers to Refinement of Animal Models

- Lack of Motivation for the Use of Alternatives
- Sources of funding for alternatives
 - Government
 - NIH
 - USDA
 - FDA/EPA
 - Foundations
 - Private institutions
 - Academic
 - Industry

Barriers to Refinement of Animal Models

- **Proposals for Overcoming these Barriers:**
- Enhanced training on the alternatives concept reaching scientists
- Enhanced access to alternatives information through publications, conferences, databases
- Enhanced regulatory requirement for implementation of alternatives
- Enhanced funding for alternatives development and implementation