Replacement, Reduction & Refinement Alternatives

Implementation of the 3 R Alternatives When Using Animals in Science

Colette Wheler, DVM, Consulting Veterinarian
President's Committee on Animal Care
University of Regina

Replacement ◆ Reduction ◆ Refinement
Good Animal Practice in Science

CCAC CCPA

University of Saskatchewan

Outline

- Historical Concerns About Animal Use 1700s and 1800s
- 1940s - Modern Era of Expanded Animal Use
- 1960s – Development of Laboratory Animal Care Guidelines
- Emergence of Animal Rights/Liberation
- The 3 R’s of Russell and Burch
- CCAC 3 R’s Microsite

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Concerns About Animal Use 1700s and 1800s

Marshall Hall, University of Edinburgh, Physiologist 1790-1857

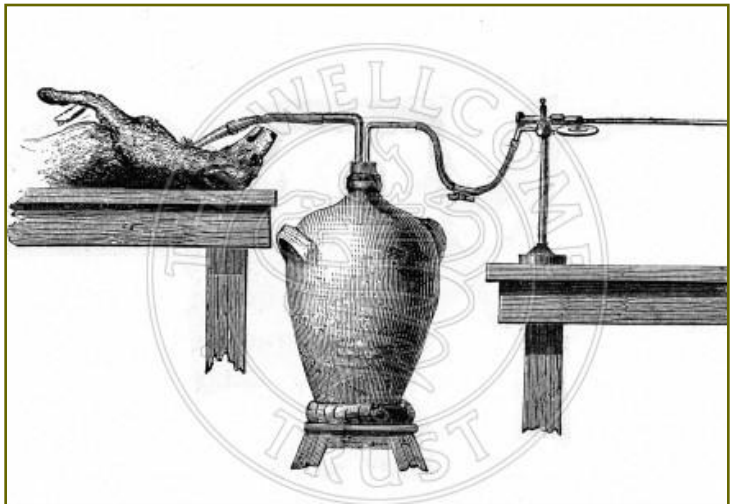
Marshall Hall

- He had been the focus of anti-vivisection concerns over his use of animals in physiological studies
- He felt that unless physiologists set some rules about their animal use, they would not be able to escape the charge that they were being cruel to the animals

Concerns About Animal Use 1700s and 1800s

“Unhappily for the physiologist, the subjects of … his science are sentient beings; and every new experiment, every new or unusual situation of such a being, is necessarily attended by pain or suffering of a bodily or mental kind.”

“Investigations in this science should therefore, being exposed to peculiar difficulties, be regulated by peculiar laws.”



UNIVERSITY OF SASKATCHEWAN

Concerns About Animal Use 1700s and 1800s

1837 Hall's Five Principles of physiological experimentatn

1) An experiment should never be resorted to if the necessary information could be gained by observation

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4) Any justifiable experiment should be carried out with the least possible infliction of suffering (and he recommended using lower, less sentient animals)

5) Every physiological experiment should be performed under such circumstances as will secure a due observation and attestation of its results…

Concerns About Animal Use 1700s and 1800s

Public Vivisection Demonstration Spurs First National Anti-Cruelty Law, in Britain

1874 - British Medical Association Congress

• physiologist Eugene Magnan conducted a public demonstration of the effects of injecting alcohol and absinthe into two dogs to produce epilepsy

Concerns About Animal Use 1700s and 1800s

Public Vivisection Demonstration Spurs First National Anti-Cruelty Law, in Britain

1874 - British Medical Association Congress

• physiologist Eugene Magnan conducted a public demonstration of the effects of injecting alcohol and absinthe into two dogs to produce epilepsy

• strong public protests; an observer (a surgeon) apparently cut the ties holding one of the dogs down and released it

Concerns About Animal Use 1700s and 1800s

Public Vivisection Demonstration Spurs First National Anti-Cruelty Law, in Britain

1874 - British Medical Association Congress

• prosecution under Martin's Act (anti-cruelty bill protecting cattle, horses and sheep) by the RSPCA failed

Concerns About Animal Use 1700s and 1800s

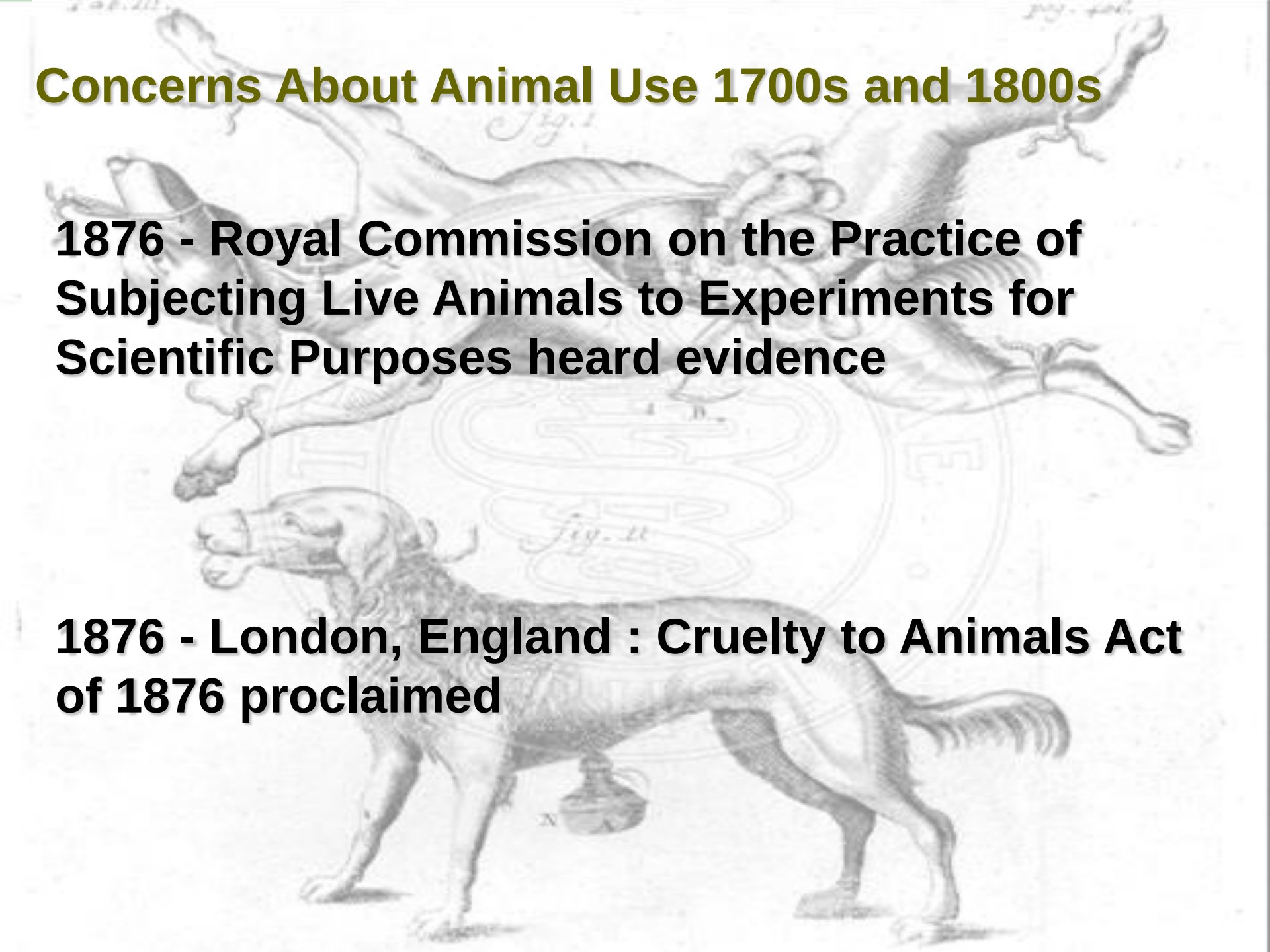
Public Vivisection Demonstration Spurs First National Anti-Cruelty Law, in Britain

1874 - British Medical Association Congress

• prosecution under Martin's Act (anti-cruelty bill protecting cattle, horses and sheep) by the RSPCA failed

• publicity spurred the creation of the Victoria Street Society for the Protection of Animals from Vivisection (off-shoot from the RSPCA)

Concerns About Animal Use 1700s and 1800s



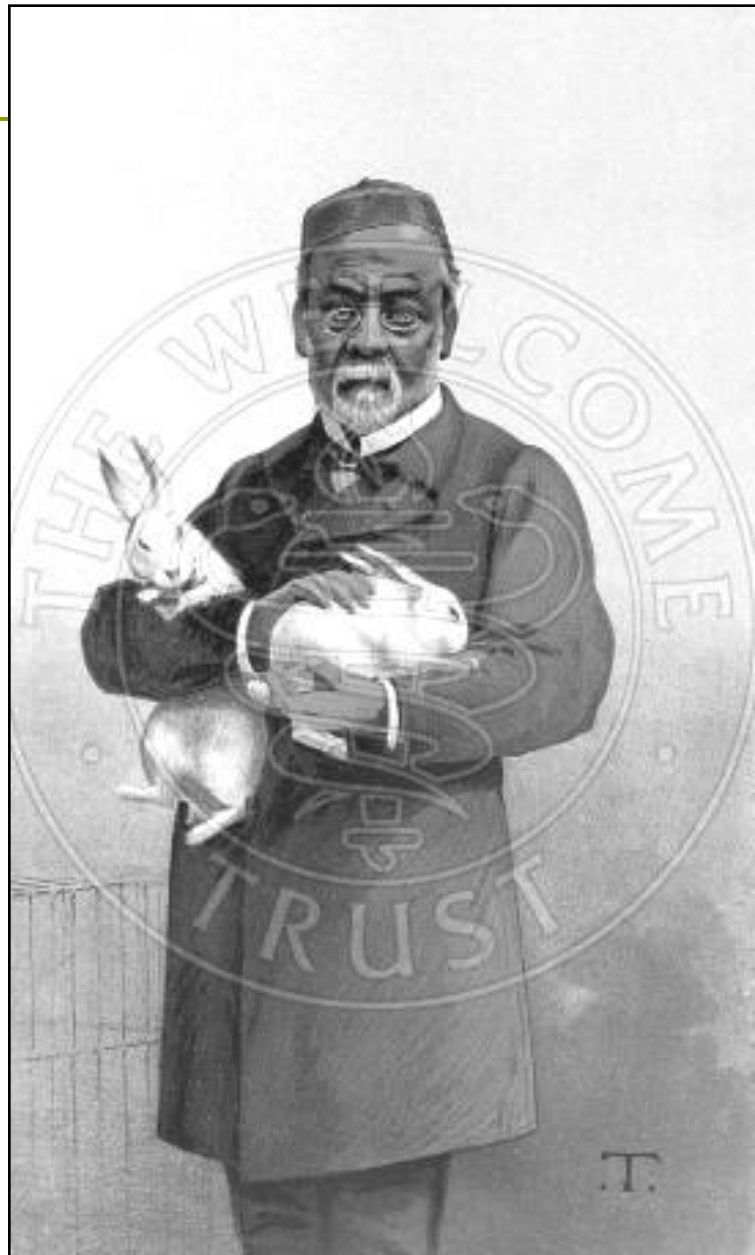
1876 - Royal Commission on the Practice of Subjecting Live Animals to Experiments for Scientific Purposes heard evidence

1876 - London, England : Cruelty to Animals Act of 1876 proclaimed

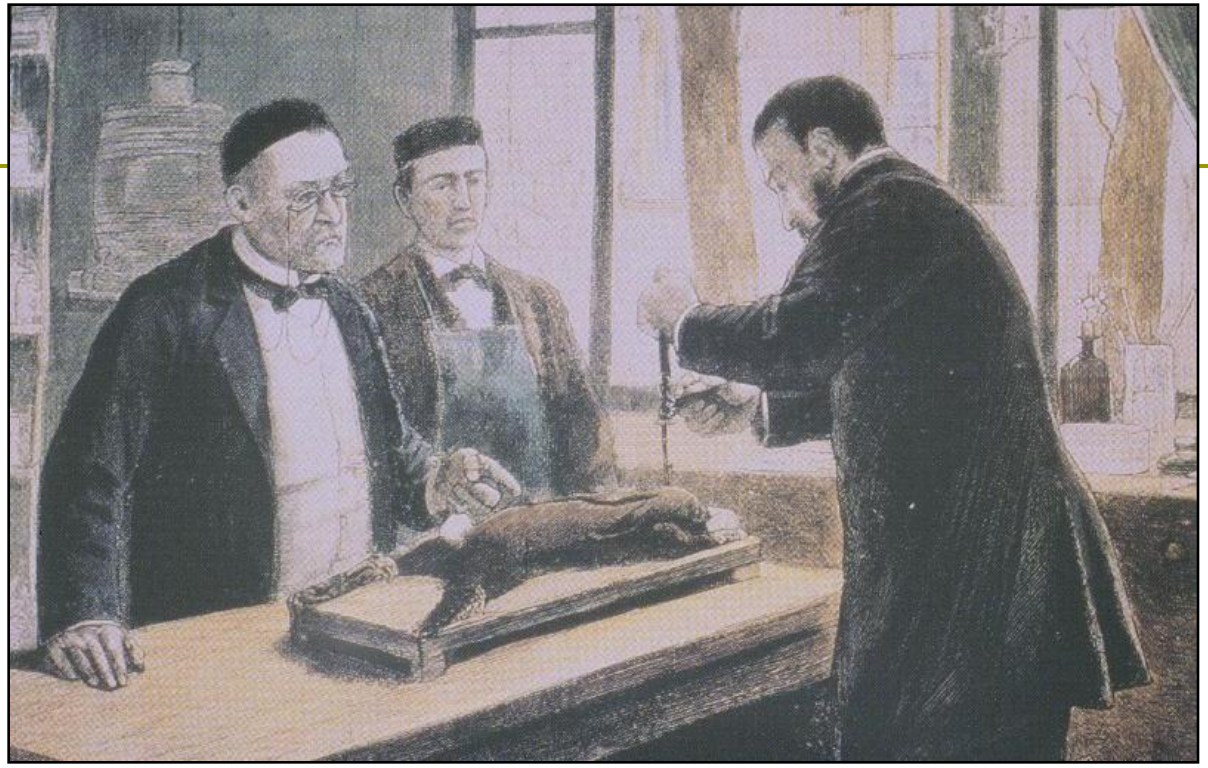
Concerns About Animal Use 1700s and 1800s

Dr Roux said of Pasteur (1880s):

"…Pasteur, who had been obliged to sacrifice so many animals in the course of his beneficent studies, felt a veritable repugnance toward vivisection.

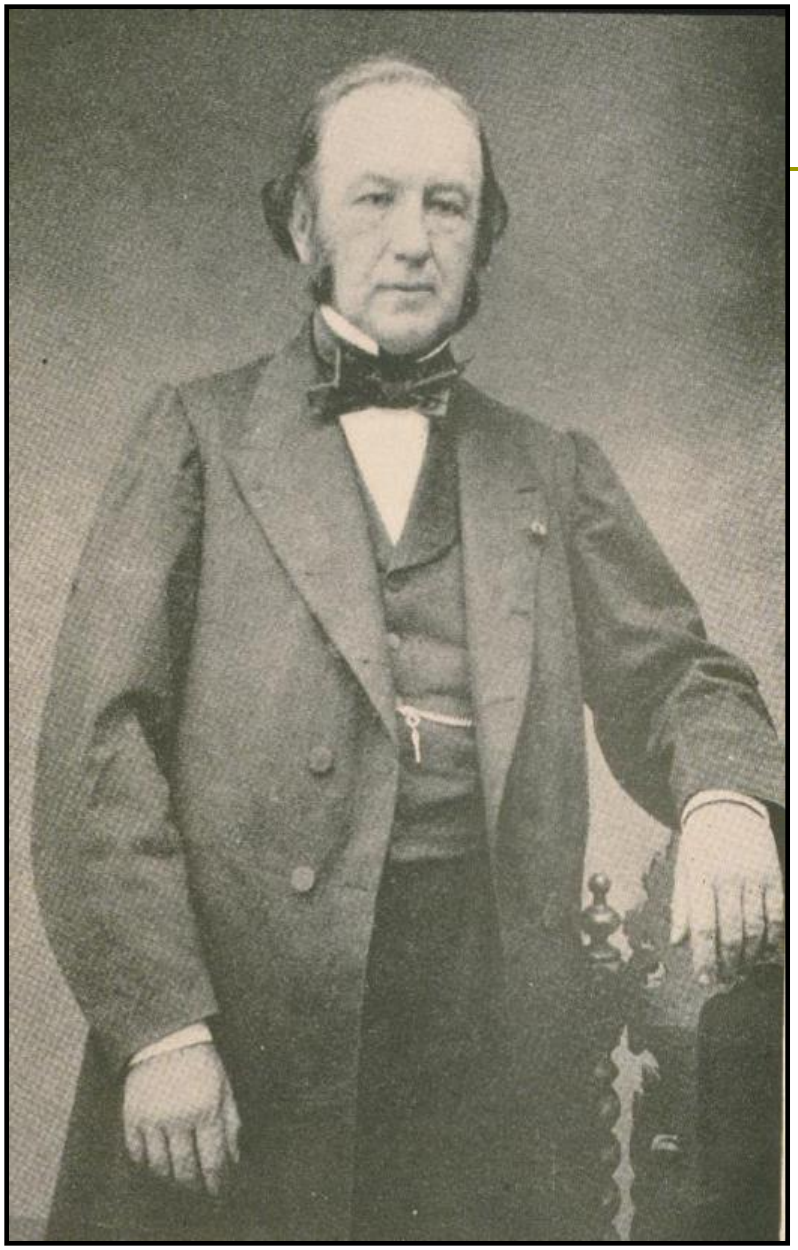


Concerns About Animal Use 1700s and 1800s



He was present without too much squeamishness at simple operations, such as subcutaneous inoculation, and yet, if the animal cried a little, Pasteur immediately felt pity and lavished on the victim consolation and encouragement …”

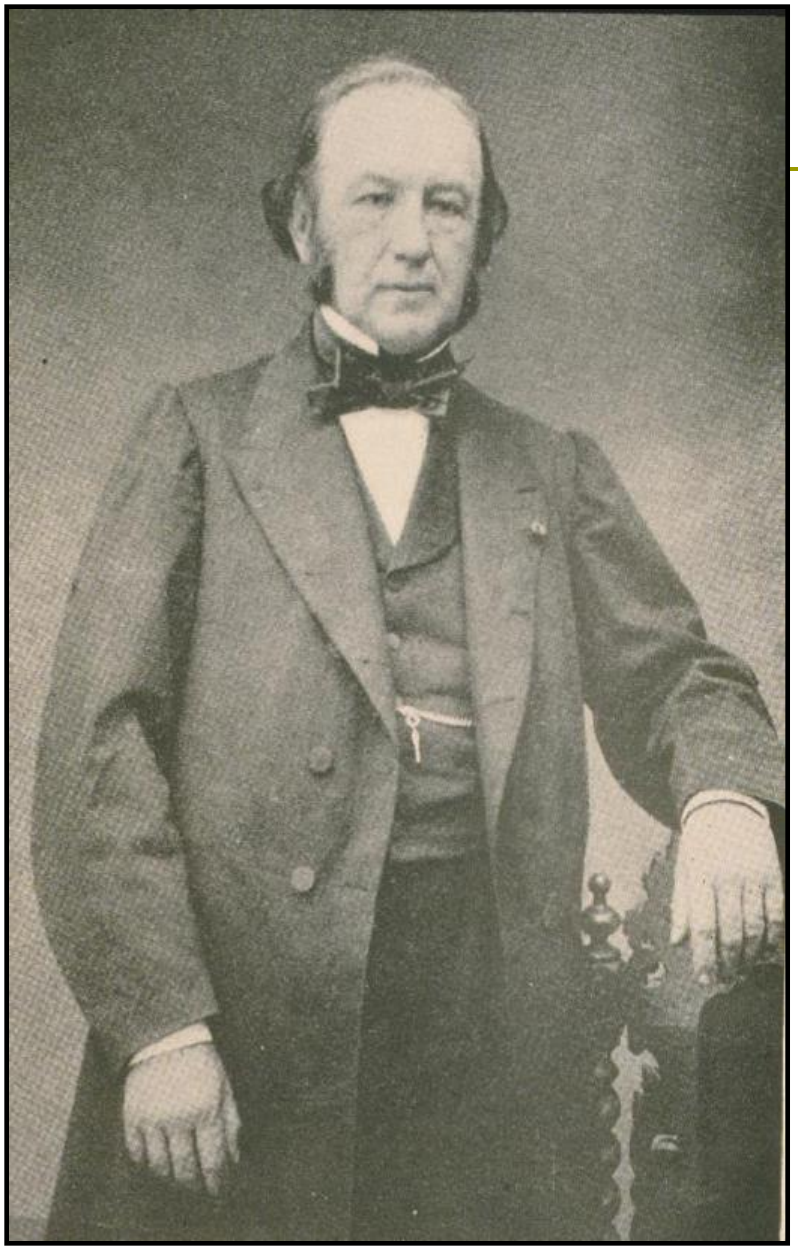
Concerns About Animal Use 1700s and 1800s



Claude Bernard, late 1800s
- founded scientific physiology
- father of modern experimental medicine

"The physiologist is not an ordinary man. He's an intellectual. He is a man who is possessed and absorbed by the scientific idea he pursues.

Concerns About Animal Use 1700s and 1800s



Claude Bernard, late 1800s
- founded scientific physiology
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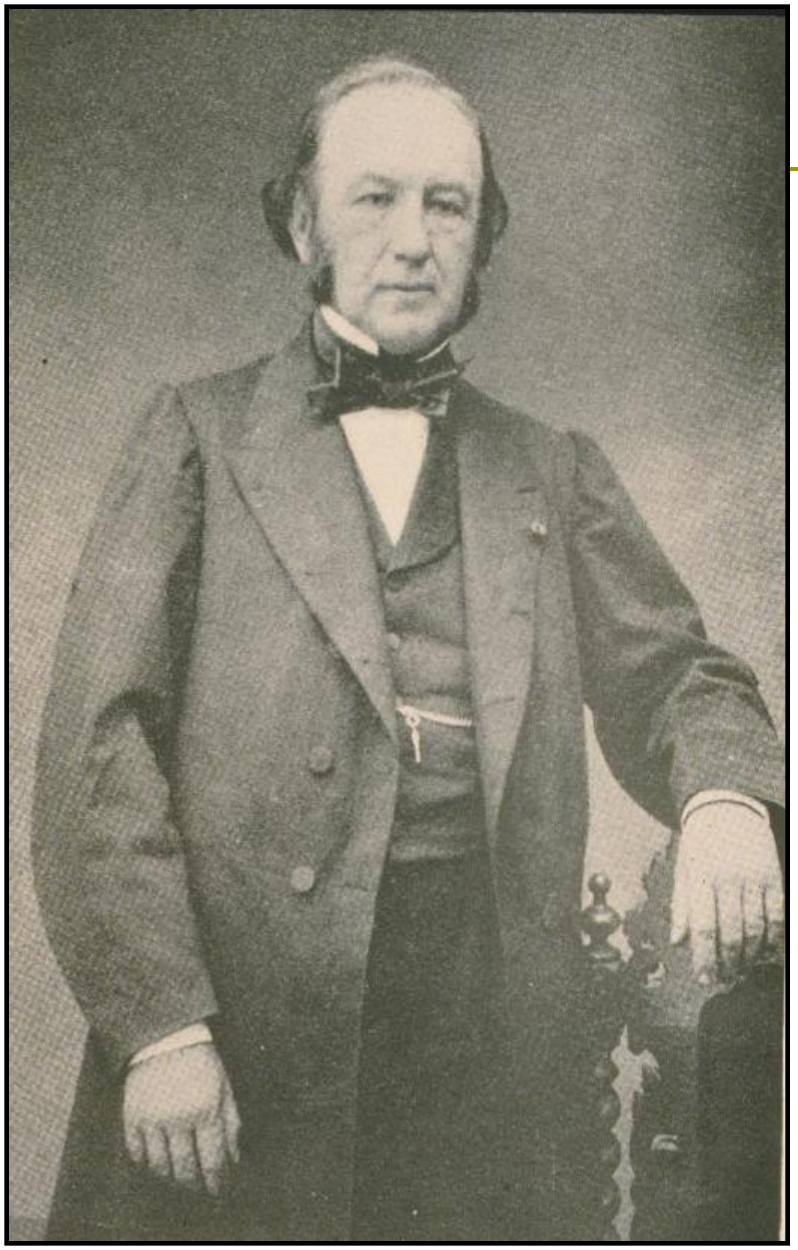
"He doesn't hear the cry of the animals or see the blood that is shed. He only sees his ideas, he sees nothing but the organism that hides the mysteries that he wants to uncover…

Concerns About Animal Use 1700s and 1800s



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"...He searches with exhilaration through pieces of pale, rotten flesh, something that for others would be the object of disgust and horror."

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1940 - Start of Modern Era of Expanded Animal Use

In 1933 at least 17 women in the USA were blinded and one eventually died of complications resulting from the use of a new mascara called *Lash Lure*

At that time there were no laws or regulations governing the safety of consumer products

UNIVERSITY OF SASKATCHEWAN

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1940 - Start of Modern Era of Expanded Animal Use

The Lash Lure incident is credited with spurring development of the regulatory requirement that products destined for human use be proven safe

US Congress passed the Federal Food, Drug and Cosmetic Act of 1938, requiring food, drugs and cosmetics be safe for human use before they could be sold

1940 - Start of Modern Era of Expanded Animal Use

PENICILLIN - THE FIRST MIRACLE DRUG

1929 - Alexander Fleming discovers "penicillin" from mold growing on bacterial culture plate

1935 - Howard Florey & Ernest Chain purify the compound

1940 - Start of Modern Era of Expanded Animal Use

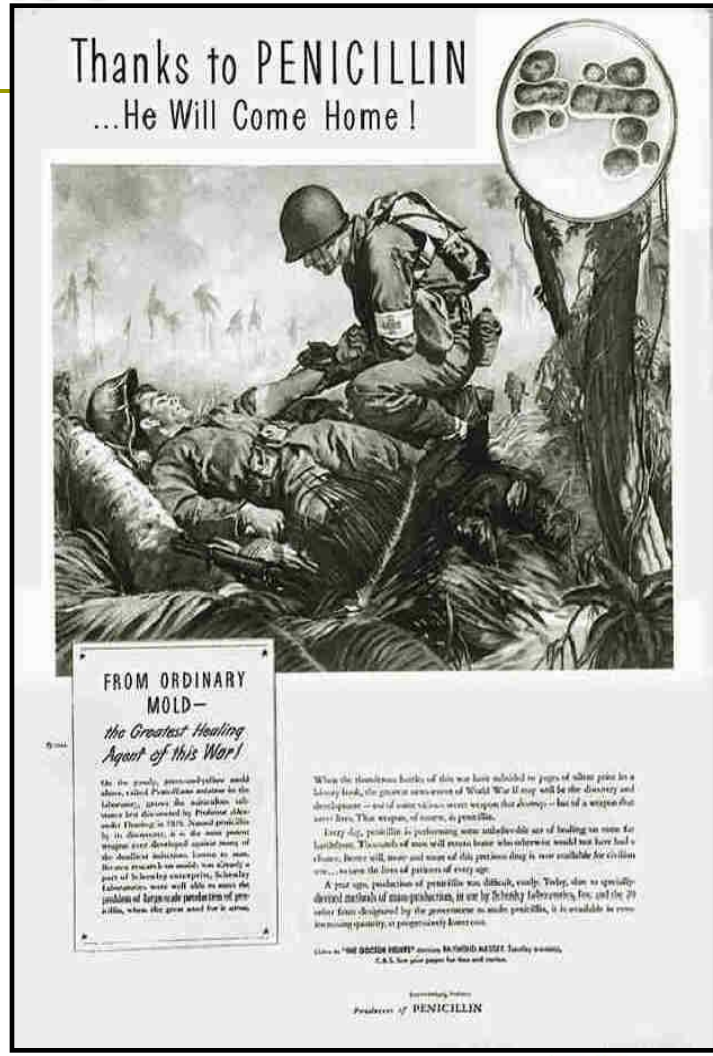
PENICILLIN - THE FIRST MIRACLE DRUG

1938-39 (onset of World War II)
- **mice with bacterial infections "cured"**
- **human trials with amazing results**

1943- mass production in USA

1945 - Nobel Prize in Medicine award

1950s - companies devoted to finding better treatments for diseases



****start of the biopharmaceutical industry****

1940 - Start of Modern Era of Expanded Animal Use

Range of Animal Use in Research, Education, Testing Today

Biomedical Research and Education
Medical and Veterinary Research
- **Basic**
- **Applied**

Nonmedical Research and Education
- **Biological**
- **Psychological**

Agricultural
Drug Testing (Safety / Efficacy)
Regulatory Toxicology / Safety
Biologicals Production
- **Vaccines**
- **Tissue Culture**

Government Non-Medical

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England

1959 - England

The Principles of Humane Experimental Technique, WMS Russell and RL Burch, London, Methuen, 238pp (subsequently reprinted by UFAW); electronic copy also available: **http://altweb.jhsph.edu/publications/humane_exp/het-toc.htm**

Development of Standards for Experimental Animal Care and Use in Canada

- research/teaching in biomedical sciences increased greatly in the 1950s and 1960s
- public concern over the use of animals in research also increased, as did the sensitivity of the scientific community to this issue

Development of Standards for Experimental Animal Care and Use in Canada

- **1961:** Canadian Federation of Biological Societies drafted "*Guiding Principles on the Care of Experimental Animals"*, a one page document

- **1964/66:** Medical Research Council (MRC) and National Research Council (NRC) reviewed the need for a national program of standards for experimental animals in Canada

Development of Standards for Experimental Animal Care and Use in Canada

- **1968:** Canadian Council on Animal Care (CCAC) created, based on recommendations from the MRC/NRC review

- **1968:** First "*Guide to the Care and use of Experimental Animals*" in Canada published by Canadian Council on Animal Care (CCAC)

USA: Animal Welfare Act
passed by US Congress 1966

Dogs, cats, and other animals intended for research or experimental use.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled. That, in order to protect the owners of dogs and cats from theft of such pets, to prevent the sale or use of dogs and cats which have been stolen, and to insure that certain animals intended for use in research facilities are provided humane care and treatment,

Animal Welfare Act
passed by US Congress 1966

it is essential to regulate the transportation, purchase, sale, housing, care, handling, and treatment of such animals by persons or organizations engaged in using them for research or experimental purposes or in transporting, buying, or selling them for such use.

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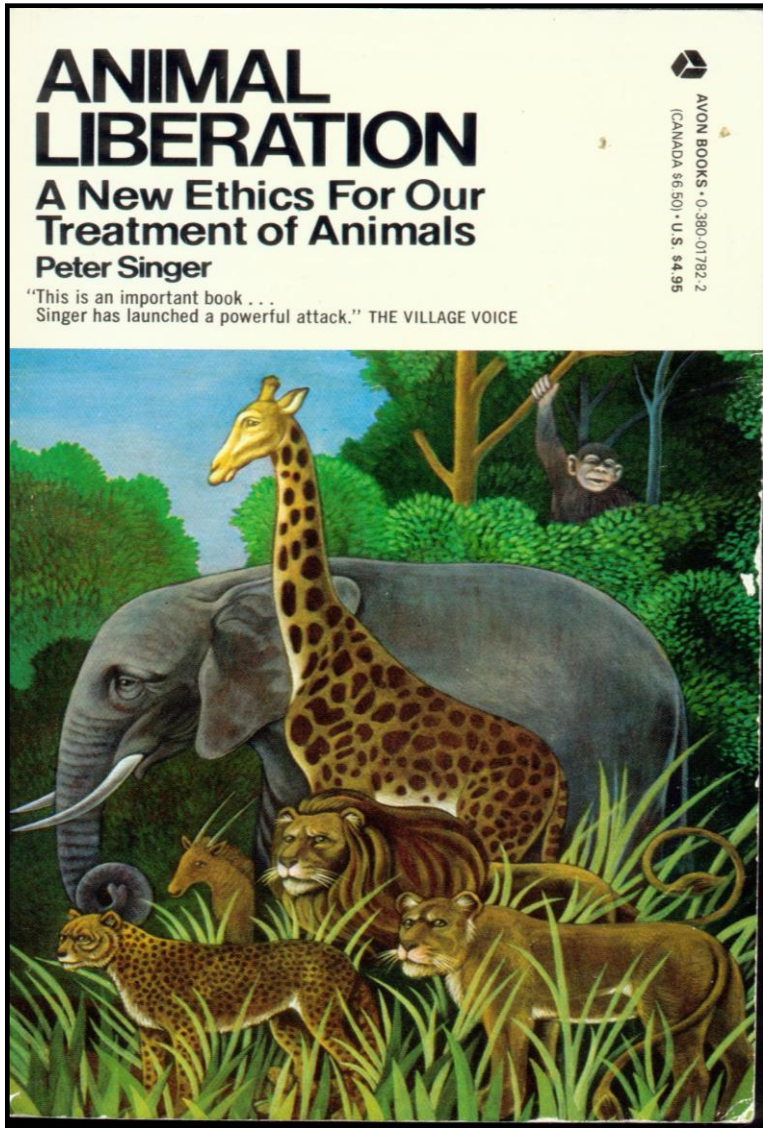
1975 - Emergence of Animal Rights/Liberation

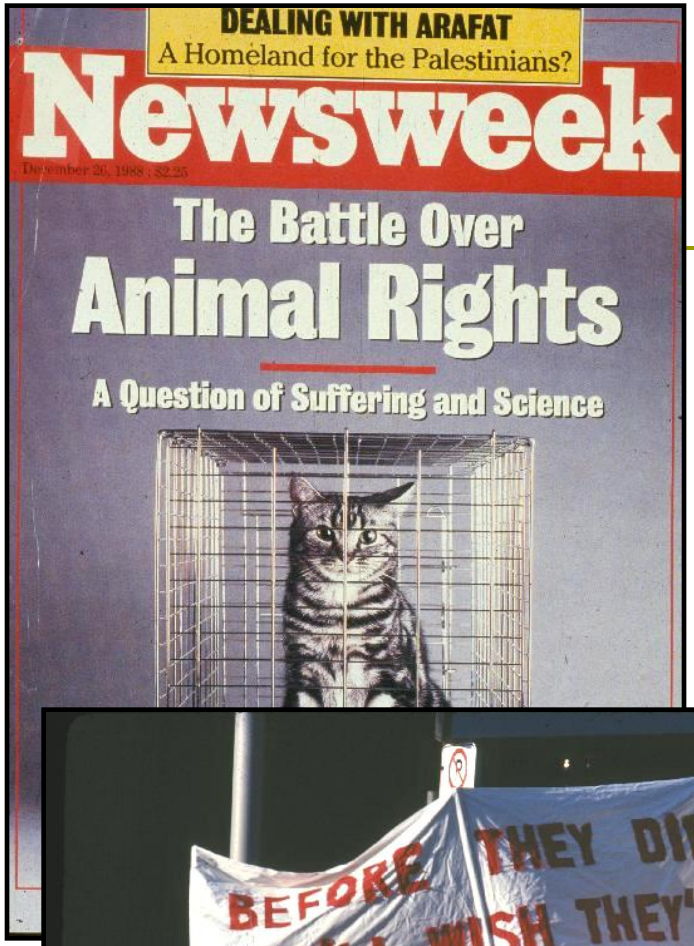
1975

Publication of Animal Liberation - A New Ethics for Our Treatment of Animals, by Australian philosopher Peter Singer

- often credited with providing basis for today's animal rights movement

- many other philosophical positions and publications since 1975

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The Battle Over
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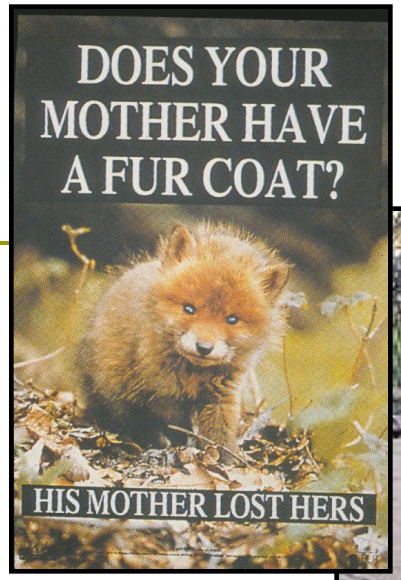
A Question of Suffering and Science


DOES YOUR MOTHER HAVE A FUR COAT?
HIS MOTHER LOST HERS


WE'D RATHER NAKED THA WEAR FUR
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BEFORE THEY DIE
THEY'LL WISH THEY'D
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« "Greening" the Dining Halls at ECC! Creating PETA Ads in Production Class at Parsons! »

Hosting an Animal Rights Event at the University of Saskatchewan!

Written by Amanda Griffiths, a student at the University of Saskatchewan in Saskatoon.

The Carnival of Solidarity was meant to raise awareness about groups at the University working against oppression. There were many booths set up about **human rights issues**, **the environment**, and other great causes, as well as some rockin' local bands and beer!

Currently, there is no animal rights **student group** at the U of S (yet), but I really thought it was an important issue to cover, group or no group. Our campus is quite well known for its large Agriculture sector. I took an Animal Science class the previous term, not knowing what I was getting myself into, and was shocked at how one sided the attitudes were in the college regarding animal rights. We were taught how to feed a veal calf an iron deficient diet, and taught that debeaking and other **inhumane practices** were needed for the animal's own well being. I think that class inspired me more than anything to get the word out to our campus that animals are not just a means for economic gain. They are not meant to be exploited and used. So when I heard about the Carnival of Solidarity, I decided to **set up a booth** to raise awareness about the oppression of animals.

in this section

- College Home Page
- Student Spotlight
- Hot Off the Student Press
- Build Your Résumé
- Activism Ideas
- Campaigns
- Start a Group
- Campus Living
- Star College Activists
- Contact Ryan, peta2's College Activist Liaison

campaigns

Thanks to animal research, they'll be able to protest 20.8 years longer.

According to the U.S. Department of Health and Human Services, animal research has helped extend our life expectancy by 20.8 years. Of course, how you choose to spend those extra years is up to you.

Foundation for Biomedical Research

To demonstrate your support, write the Foundation for Biomedical Research, 818 Connecticut Ave. NW Suite 303, Washington, DC 20006. Or call (202) 857-0666

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What are the Three Rs?

1959 - England

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THE PRINCIPLES OF HUMANE EXPERIMENTAL TECHNIQUE

W.M.S. Russell and R.L. Burch

CHAPTER 4

THE SOURCES, INCIDENCE, AND REMOVAL OF INHUMANITY

The three chief principles stated...

The Removal of Inhumanity: The Three R's

We turn now to consideration of the ways in which inhumanity can be and is being diminished or removed. These ways can be discussed under the three broad headings of Replacement, Reduction, and Refinement (Russell, 1957a; cf. also Hume, 1957; Medawar, 1957). An earlier attempt to classify the subject (Russell, 1955) dispensed, like the Mock Turtle, with the advantages of alliteration; but the three modes now considered have conveniently been referred to as the three R's of humane technique (Russell, 1957a).

Replacement means the substitution for conscious living higher animals of insentient material. Reduction means reduction in the numbers of animals used to obtain information of a given amount and precision. Refinement means any decrease in the incidence or severity of inhumane procedures applied to those animals which still have to be used.

There are clearly areas of overlap between these categories. Consider the use of animal tissue cultures in virology (Sanders, 1957). In a fundamental sense, we are here replacing animals by insentient material, and the method has been classified as replacement for the present purpose. But since one animal may be used to provide many cultures, each providing more information than a single whole animal used directly, we might legitimately speak of reduction. Finally, the

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From: The Principles of Humane Experimental Technique; WMS Russell and RL Burch, 1959

"**Replacement** means the substitution for conscious living higher animals of insentient material. **Reduction** means reduction in the numbers of animals used to obtain information of a given amount and precision. **Refinement** means any decrease in the incidence or severity of inhumane procedures applied to those animals which still have to be used."

The Three Rs of Russell and Burch

Over the past 40 years the Three Rs of Russell and Burch have become widely accepted ethical principles, and are now embedded in the conduct of animal-based science in Canada and throughout many countries in the world.

National Centre for the Replacement, Refinement and Reduction of Animals in Research

NC3Rs 3Rs Prize

The NC3Rs awards an annual prize for an original contribution to scientific and technological advances in the 3Rs in medical, biological or veterinary sciences published within the last two years. Sponsored by GSK, the prize consists of a prize grant of £10k, plus a personal award of £1k, and is part of the Centre's commitment to recognise and reward high quality research which has an impact on the use of animals in the life sciences.

The **2008 prize went to Dr Keith Martin and Mr Thomas Johnson** for replacing the use of animals in their research that explores the use of stem cells to treat sight-threatening conditions such as glaucoma.

The 2009 3Rs prize, which is awarded to the first author(s) on the paper, will be presented at the launch of the NC3Rs annual report.

The deadline for submission for the 2009 prize has now passed.

Nomination process

The online application process for the prize comprises two stages; a nomination by a proposer and a short statement by the candidate of how the prize grant will be used. Candidates are also able to self-nominate.

Selection panel

A **prestigious panel** has been appointed to assess nominations and to select the winner. Selection is based on the quality of the published research and its impact on the 3Rs.

Eligibility

The 2009 prize is for a piece of primary research published in a peer-reviewed journal in the last two years and is open to any researcher, in academia or industry, based in the UK. The prize is awarded to the first author(s).

For further information on the 3Rs Prize please contact **tim.watson@nc3rs.org.uk**

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THE HUMANE SOCIETY OF THE UNITED STATES

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Russell and Burch Award

Details

The Humane Society of the United States presents the Russell and Burch Award to scientists who have made outstanding contributions toward the advancement of alternative methods in the areas of biomedical research, testing or higher education. Alternative methods are those that can replace or reduce the use of animals in specific procedures, or refine procedures so that animals experience less pain or suffering.

The award is a means of recognizing the important role that individual scientists can and do play in limiting the use and suffering of animals in laboratories. The HSUS presents the award at the World Congresses on Alternatives and Animal Use in the Life Sciences, which is held every two to three years. The Seventh World Congress will be held Aug-Sept 2009 in Rome, Italy.

The award, which carries a $5,000 prize, is named in honor of William M. Russell and Rex L. Burch, the scientists who formulated the Three R's approach of replacement, reduction, and refinement.

Nominations

The Russell and Burch Award is intended for scientists who have made outstanding contributions toward the advancement of alternative methods in the areas of biomedical research, testing, or higher education. Preference is given to scientists who are still living.

No special forms are necessary. Persons nominating themselves should submit a cover letter explaining their suitability for the award (see above), a

Alternatives

The term "alternatives" was coined by the distinguished physiologist David Smyth in his 1978 book Alternatives to Animal Experiments. It is used to describe any change to established scientific procedures that will result in the **replacement** of animals, a **reduction** in the numbers used or a **refinement** of techniques that may minimize harms to the animals.

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The 3 R's and Alternatives

The CCAC has combined the Three Rs of Russell and Burch with David Smyth's "Alternatives", to come up with the terms:

- **Replacement alternatives**
- **Reduction alternatives**
- **Refinement alternatives**

and has developed the **CCAC Three Rs Microsite** to assist animal users with their implementation

Welcome to the CCAC

The CCAC is the national organization responsible for setting and maintaining standards for the care and use of animals in science in Canada.

- **Assessment Program**
- Animal Care Committee Resources
- **Guidelines Program**
- **Education, Training and Communications Program**
- **CCAC Three Rs Microsite:** Replacement, Reduction and Refinement alternatives:

Replacement Reduction Refinement

- Good Animal Practice Certificate
- **Reporting of Animal Use Statistics**
- CCAC Annual Reports
- Portal
- WebMail

Subscribe to our

NEW DOCUMENTS

The CCAC is pleased to announce that the **CCAC guidelines on: the care and use of farm animals in research, teaching and testing** is now available.

Click here to download the guidelines.

Please also see details on the implementation of the guidelines.

Report: CCAC Forum 2008 – Building on Strength

CCAC Survey of Animal Use – 2007

The CCAC is pleased to announce the release of the Annual Survey of Animal Use for scientific purposes in Canada between January and December 2007.

UPCOMING EVENTS

8th World Congress on Alternatives & Animal Use in the Life Sciences

The **CCAC** will host the **8th World Congress on Alternatives & Animal Use in the Life Sciences** on August 21-25, 2011 in Montréal (Canada). Click here (all browsers except Firefox) to watch the promotional video.

For more information on the city of *Montréal*, please click here.

For more information on the province of *Québec*, please click here

More information to come.

CCAC Three Rs Microsite

Welcome to the Canadian Council on Animal Care (CCAC) Three Rs Microsite.

The use of animals in research, teaching, and testing is acceptable ONLY if it promises to contribute to understanding of fundamental biological principles, or to the development of knowledge that can reasonably be expected to benefit humans or animals. Therefore, in Canada people involved with the use of animals in science (such as investigators, technicians, veterinary personnel and animal care committee members) must prepare and review scientific protocols with a view to replace, reduce, and refine animal use whenever possible. This is the concept of "The Three Rs" (replacement, reduction, refinement) which provides a set of guiding ethical principles that help to minimize harms to animals used in science.

To support implementation of the Three Rs in Canada this microsite aims to provide easily accessible, useful, and relevant information and resources related to Replacement, Reduction and Refinement.

Replacement alternatives refers to methods which avoid or replace the use of animals in an area where animals would otherwise have been used. This includes both absolute replacements (i.e. replacing animals with inanimate systems, such as computer programs) and relative replacements (i.e. replacing more sentient animals, such as vertebrates, with animals that current scientific evidence indicates have a significantly lower potential for pain perception, such as some invertebrates).

Reduction alternatives refers to any strategy that will result in fewer animals being used to obtain sufficient data to answer the research question, or in maximizing the information obtained per animal and thus potentially limiting or avoiding the subsequent use of additional animals, without compromising animal welfare.

CCAC Definitions:

Replacement alternatives refers to methods which avoid or replace the use of animals in an area where animals would otherwise have been used. This includes both absolute replacements (i.e. replacing animals with inanimate systems, such as computer programs, models) and relative replacements (i.e. replacing more sentient animals, such as vertebrates, with animals that current scientific evidence indicates have a significantly lower potential for pain perception, such as some invertebrates).

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Top of the line cat CPR mannikin!

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K9 BreathSound and HeartSound Simulator

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Guidelines
Links
Health monitoring
TML(S)
Legislation
Applications
FDU
Statistics
News
Coming events
Newsletter

Vascular Access Training Model: Canine Foreleg

Record number: 5056

Category: Anatomy, Handling and Medicine

Type: Model

Description: The Canine Foreleg is constructed in the same way as the Canine Head model (record number 5055) and contains a simulated cephalic vein. It can be used to teach students blood collection, fluid and drug administration, and the fundamentals of catheterization using the butterfly and over-the-needle catheter. Includes an instructional video film. This is one of two Vascular Access Training Models (VATMs). Please see record number 5055 for the Canine Head model. VATMs are designed to provide students with the correct "look" and "feel" while learning to give injections, place catheters or draw blood. Special features of the VATMs include identifiable and palpable structural landmarks, replaceable vessels (tubing), flashback response, and a moveable, replaceable latex skin and components to provide longevity for the model.

Comments & References: Canine Foreleg: item number DOGL1, Replacement Foreleg Skin: item number 4113-1, and Replacement Foreleg Tubing: item number 4113-3. This model was developed by Dr. Jan Ilkiw with funds provided by a gift from the Bosack Kruger Foundation of Redmond, Washington. It is manufactured exclusively for the School of Veterinary Medicine at University of California, Davis. This model may be ordered online here. International orders must be paid in advance in U.S. dollars and drafted through a U.S. bank or paid by credit card. An

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Vascular Access Training Model: Canine Head

Record number: 5055

Category: Anatomy, Handling and Medicine

Type: Model

Description: The head and neck model consists of a sculpted mandrel containing channels for a simulated jugular vein covered with a moveable latex "skin". This model can be used to teach advanced techniques such as placement of through-the-needle catheters, special procedures like the Seldinger (guide wire) Technique for placement of multi-lumen and pulmonary artery catheters, and blood collection techniques with a syringe and needle, or through an existing catheter. Includes an instructional video film. This is one of two Vascular Access Training Models (VATMs). Please see record number 5056 for the Canine Foreleg model. VATMs are designed to provide students with the correct "look" and "feel" while learning to give injections, place catheters or draw blood. Special features of the VATMs include identifiable and palpable structural landmarks, replaceable vessels (tubing), flashback response, and a moveable, replaceable latex skin and components to provide longevity for the model.

Comments & References: Item number DOGH1. This model was developed by Dr. Jan Ilkiw with funds provided by a gift from the Bosack Kruger Foundation of Redmond, Washington. This model is manufactured exclusively for the School of Veterinary Medicine at University of California, Davis. This model may be ordered online here. International orders must be paid in advance in U.S. dollars and drafted through a U.S.

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Alpaca Venipuncture/Catheterization Model

Medium:	model
Discipline:	catheterization, venipuncture
Species:	Camelid, Nonhuman animal
Educational Level:	veterinary medical continuing education, veterinary medical residency, veterinary medical school
Cost:	
Source / Company:	Dr. Ben Kitchen, Alternavitae, alternavitae@wowway.com
Catalog / Production Information:	

The alpaca venipuncture / catheterization model is a rigid plastic model demonstrating the topography of the head and neck with a procedure window in the neck modeled in soft materials at the level of the preferred site for venopuncture. Palpable fluid filled vessel targets are affixed in anatomically correct positions within the model. Jugular and carotid vessels are supplied with variable pressure fluid reservoirs such that the flashback achieved upon vessel penetration corresponds to the pressure variance between the arterial and venous systems. Palpable osseous structures are embedded within the procedure

Star Phoenix
August 28, 2009

Trauma training on pigs criticized

❑ Sask. course plans switch to mannequins instead of live animals

By Janet French
of The StarPhoenix

A Saskatchewan medical training course is under fire for its practise of using live pigs to teach residents and doctors how to do trauma procedures.

American non-profit group Physicians Committee for Responsible Medicine (PCRM) says not only is the use of the pigs unethical, but students learn procedures such as tracheotomies and inserting chest tubes more effectively by using cadavers or simulators than by practising on animals.

But Dr. Paul Hayes, the Saskatoon surgeon who chairs the training program in Saskatchewan, says he already plans to stop using pigs for training starting later this fall.

A course running during the first week of September will still use four pigs to train 18 doctors, Hayes said. However, the University of Saskatchewan has now purchased a $30,000 patient simulator that will be ready to use in the next course later this fall, he said.

■ **CONT'D:** Please see Pigs/**A8**

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TraumaMan System | Simulab Corporation - Windows Internet Explorer

http://www.simulab.com/product/surgery/open/traumaman-system

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Overview | Deta

The TraumaMan® been evaluated a Society as an alte for their Surgical R Course. The Trau form designed fo procedures. The S ventilator and fou ankle base for IV sets that allow ea

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- Cricothyroido
- Chest Tube I
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- Needle Deco
- Percutaneous
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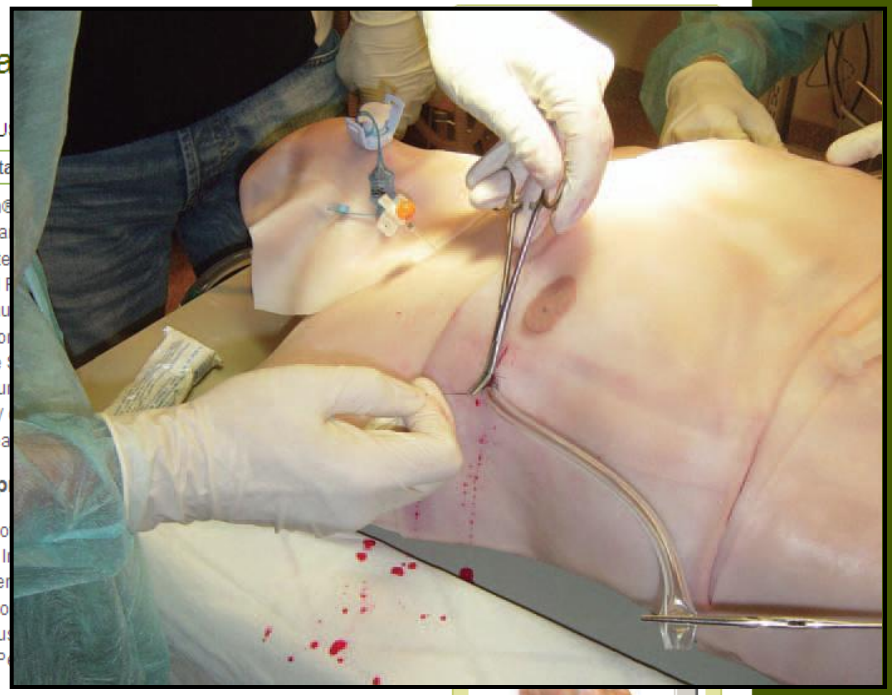

Features and Benefits:

- Anatomically correct human simulator with all the pertinent landmarks for each procedure
- The realistic body form skin and replaceable tissue sets have the highest fidelity touch and dissection of any simulated tissue available today
- TraumaMan is the most flexible training platform available for

Vascular Access Package

Replacement Alternatives to Mammalian Models

- Comparative Substitution using Amphibians (a vertebrate of lower sentience)
  - Acetic Acid Test to determine nociceptive threshold in frogs
  - One drop of increasing concentrations of acetic acid applied to thigh
  - NT is defined as lowest concentration that causes frog to vigorously wipe the leg
  - Acid immediately rinsed off with distilled water, or within 5 seconds if no response

Alternative to Mammalian Models

- Comparative Substitution using Amphibians (a vertebrate of lower sentience)
  - Acetic Acid Test has been shown to give a rank order of the relative analgesic potency of opioids that is highly correlated to rodent models
  - This suggests that analgesic action of opioids in amphibians is predictive of the analgesic effects of opioids seen in humans and other mammals

Alternative to Mammalian Models

- Comparative Substitution using Amphibians (a vertebrate of lower sentience)
  - Comparative substitution is a moderate approach to animal replacement, as a whole animal is still used
  - But evidence indicates that amphibians have less potential for pain (are less sentient) than mammalian models currently in use
  - Whole animals must still be used for pain and analgesia research because cells do not feel pain

CCAC Definitions:

Reduction alternatives refers to any strategy that will result in fewer animals being used to obtain sufficient data to answer the research question, or in maximizing the information obtained per animal and thus potentially limiting or avoiding the subsequent use of additional animals, without compromising animal welfare.

CCAC Definitions:

Refinement alternatives refers to the modification of husbandry or experimental procedures to minimize pain and distress, and to enhance the welfare of an animal used in science from the time it is born until its death.

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Implementation of the 3 R Alternatives

Consideration of the "Three Rs Alternatives" must start during the early stages of animal use planning, together with development of the experimental protocol (rather than as a last minute addition).

Implementation of the 3 R Alternatives

The CCAC requires principal investigators to implement the Three Rs when they are preparing to use animals for a scientific purpose, in the following ways:

- Investigators must consider whether animals are required or whether suitable replacement alternatives exist (Replacement Alternatives)

Implementation of the 3 R Alternatives

- When animals are used, the investigator must consider how best to decrease the number of animals used to a minimum and/or how to maximize the amount of information obtained per animal (Reduction alternatives)

- Investigators must identify potential harms and ways to minimize these (Refinement alternatives).

Implementation of the 3 R Alternatives

The CCAC Three Rs Microsite (http://www.ccac.ca/en/alternatives/index.html) provides information and tools for animal users, including:

- The Three Rs Search Guide, which provides detailed instructions on how to conduct a Three Rs information search in the Step-by-Step Three Rs Search Strategy.

CCAC Three Rs Microsite

Welcome to the Canadian Council on Animal Care (CCAC) Three Rs Microsite.

The use of animals in research, teaching, and testing is acceptable ONLY if it promises to contribute to understanding of fundamental biological principles, or to the development of knowledge that can reasonably be expected to benefit humans or animals. Therefore, in Canada people involved with the use of animals in science (such as investigators, technicians, veterinary personnel and animal care committee members) must prepare and review scientific protocols with a view to replace, reduce, and refine animal use whenever possible. This is the concept of "The Three Rs" (replacement, reduction, refinement) which provides a set of guiding ethical principles that help to minimize harms to animals used in science.

To support implementation of the Three Rs in Canada this microsite aims to provide easily accessible, useful, and relevant information and resources related to Replacement, Reduction and Refinement.

Replacement alternatives refers to methods which avoid or replace the use of animals in an area where animals would otherwise have been used. This includes both absolute replacements (i.e. replacing animals with inanimate systems, such as computer programs) and relative replacements (i.e. replacing more sentient animals, such as vertebrates, with animals that current scientific evidence indicates have a significantly lower potential for pain perception, such as some invertebrates).

Reduction alternatives refers to any strategy that will result in fewer animals being used to obtain sufficient data to answer the research question, or in maximizing the information obtained per animal and thus potentially limiting or avoiding the subsequent use of additional animals, without compromising animal welfare.

Three Rs Search Guide

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Is your Three Rs Search complete?

Animal use protocol worksheet

Three Rs Search Guide

If you plan to use animals for scientific purposes, you must complete an animal use protocol and submit it to an animal care committee for approval prior to commencement of the study. The animal use protocol outlines how the Three Rs will be implemented in the proposed animal-based procedures. To find the most up-to-date information on the Three Rs, investigators typically conduct a structured information search. To assist investigators with this search, the CCAC has produced the Three Rs Search Guide.

The Three Rs Search Guide provides detailed instructions on how to conduct a Three Rs information search in the Step-by-Step Three Rs Search Strategy.

Specific information can be found more quickly by selecting one of the following Quick Info topics:

- CCAC guidelines & policies on animal use protocols
- Where to do a Three Rs literature search
- Questions to assess if your Three Rs search is complete
- Animal use protocol worksheet

We would like to know whether this tool is useful for Canadian investigators and would be grateful if you could send us your feedback at ThreeRs@ccac.ca.

Replacement alternatives refers to methods which avoid or replace the use of animals in an area where animals would otherwise have been used. This includes

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Step-by-Step Three Rs Search Strategy

A Three Rs information search typically requires a multi-database literature search, a review of CCAC guidelines & polices on animal use protocols, a search of Three Rs internet resources, and often, consultations with appropriate experts (such as laboratory animal veterinarians, animal welfare specialists and statisticians). The step-by-step strategy begins with collecting pre-search information and keyword selection, followed by two phases of information searching and review. It may be helpful to fill-out the Animal use protocol worksheet as you work through your Three Rs search.

For basic information on conducting information searches (i.e. use of operators etc.), refer to Search Basics

Step1: Collect pre-search information

Before beginning a Three Rs search, investigators should gather as much information as possible about the proposed animal use (i.e. experiment, test, training procedure). This includes:

a. the working title of the project and the scientific objective(s);

b. a description of the proposed animal model;

c. descriptions of the proposed procedures on animals;

d. descriptions of what could potentially cause pain and distress in the animals;

e. descriptions of any known species-specific considerations;

f. the expected Category of Invasiveness (refer to CCAC policy statement;

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CCAC guidelines and policies on animal use protocols

- Terms of reference for animal care committees
- CCAC guidelines on: animal use protocol review
- CCAC policy statement: categories of invasiveness in animal experiments
- CCAC policy statement: ethics of animal investigation

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Where to do a Three Rs literature search

Lists of Three Rs-related search terms

- FRAME (Fund for the Replacement of Animal in Medical Experiments) Planning a Search: Search Terms and Strategies.
  - guidance on selecting search terms and a list of Three Rs-related terms
- Animal Welfare Information Center. Animal Use Alternatives Thesaurus Terminology - Alphabetical Listing
- European Centre for the Validation of Alternative Methods (ECVAM) ECVAM Database Service on Alternative Methods to Animal Experiments
  - choose *Thesaurus* from upper right hand corner of screen.

Database resources

- Altweb. Databases
  - a table of Three Rs-related research, teaching and testing databases that describes the type of information in each database
- UCDavis Center for Animal Alternatives Information. Guide to Bibliographic Databases for Alternatives Searching
  - organizes databases by Three Rs-related keywords
- CCAC Three Rs Microsite. Databases of humane teaching alternatives
- CCAC Three Rs Microsite. Testing and Three Rs

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Questions to assess if your Three Rs search is complete

To assist in deciding if your Three Rs search is complete, it may be useful to review the following questions:

- Is the proposed experiment or test duplicative?
- Are there any in vitro techniques that could replace use of animals?
- Have any computer simulations been developed that relate to the study?
- Are there any alternative animal models of lower sentience?
- Is there useful and current information about the proposed animal model?
- Has a particular strain of animal been shown to be more sensitive to the effects that will be studied?
- Is there information on the proposed model that might allow the use of fewer animals or might reduce any pain experienced by the animals?
- Could in vitro methods be incorporated into the protocol in any way to reduce the number of animals used (e.g. for early screening)?
- Have any statistical models been developed for use in this type of study, and would these affect the design of the experiment?
- Is there a way to decrease the level of invasiveness of the protocol without compromising the scientific objective?
- Could the proposed anesthetics, analgesics or other drugs pose a confounding influence on the experimental outcome?
- Is there information about assessing welfare and the level of pain of the animals?

Implementation of the 3 R Alternatives

The CCAC Three Rs Microsite (http://www.ccac.ca/en/alternatives/index.html) provides information and tools for animal users, including:

- Information on special topics such as **Wildlife Research and the Three Rs** and **Teaching and the Three Rs**

Wildlife Research and Three Rs

For CCAC purposes, the term "wildlife" refers to free ranging and captive wild vertebrates, including amphibians, reptiles, birds, fish and mammals. This includes all introduced and indigenous species, as well as domestic animals that have become feral. Many types of research involve the use of wildlife, including studies of populations, behaviour, and ecosystems. In these types of studies, it may be difficult to apply the Three Rs, especially when the goals of the research value the needs of whole ecosystems over the welfare of individual animals. These situations place the ethics of animal use outside of conventional "experimental use" and traditional application of the Three Rs.

Therefore, to balance the needs of wildlife research and wild animals, the CCAC recommends that investigators use the following definitions to guide their implementation of Three Rs in wildlife research:

Replacement - Animals may be used only if the investigator's best efforts to find a replacement by which to obtain the required information have failed.

Reduction - The fewest animals appropriate to provide valid information and statistical significance should be used.

Refinement - The most humane, least invasive techniques must be used with the goal of minimizing pain and/or distress.

The animal's physical and psychological well-being should always take precedence over considerations of cost and convenience.

(This section has been adapted from Section B.3. Ethics on the Use of Wildlife of the CCAC guidelines on: the care and use of wildlife)

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Animal welfare and wildlife research

Experimental procedures involving wild animals are of special animal welfare concern for the following reasons:

- There is a general lack of peer-reviewed research on the welfare implications of field studies, for example quantifying the stress of capture and handling, the effects of telemetry devices, and recovery from surgical procedures.

- There is limited knowledge of welfare indicators for many wildlife species.

Wildlife Research and Three Rs

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- **Reduction** - The fewest animals appropriate to provide valid information and statistical significance should be used.

- **Refinement** - The most humane, least invasive techniques must be used with the goal of minimizing pain and/or distress.

Teaching and Three Rs

The CCAC takes as its premise that the use of animals in science is acceptable ONLY if it promises to contribute to understanding of fundamental biological principles, or to the development of knowledge that can reasonably be expected to benefit humans, animals or the environment. Animals used for educational purposes are not being used to discover, prove or develop new ideas or techniques, but rather to demonstrate principles which are already well-known or to learn manual skills and techniques. Thus, before engaging in any discussions on the use of animals for the purposes of teaching, efforts should initially focus on finding a replacement alternative.

In the case where no replacement alternative is used, justification should be provided for the use of animals over the use of replacements such as models, videos, and computer simulations. The level and type of training of the students (graduate/postgraduate, specialized/non-specialized) are important considerations in ascertaining the need to use animals. Painful experiments or multiple invasive procedures on an individual animal, conducted solely for the instruction of students in the classroom, or for the demonstration of established scientific knowledge, cannot be justified.

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What is a humane teaching alternative

Humane teaching alternatives are educational aids and/or teaching approaches that can replace unnecessary animal use or complement existing humane education. Typically, humane teaching alternatives are used in combination to meet existing teaching objectives and to provide other educational outcomes that cannot be met through animal use. General examples of alternatives in teaching include:

- film and video;
- models, mannequins and simulators;
- multimedia computer simulation;
- ethically-sourced animal cadavers and tissue;
- clinical work with animal patients and volunteers;
- student self-experimentation;

alternative
- Databases of humane teaching alternatives
- **Testing and Three Rs**
- **Wildlife Research and Three Rs**

ADDITIONAL RESOURCES

- **Animal Care Committees**
- **Ethical Review**
- **Humane Science Courses**
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- **Three Rs Centres Worldwide**

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What is a humane teaching alternative

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- film and video;
- models, mannequins and simulators;
- multimedia computer simulation;
- ethically-sourced animal cadavers and tissue;
- clinical work with animal patients and volunteers;
- student self-experimentation;
- in vitro labs; and
- non-invasive field studies.

(This section has been adapted from Jukes & Chiuia [2006])

For more information on the use of humane teaching alternatives, the following resources may be useful:

- Altweb (2007) *Alternatives in Education: An Introduction*.
- Balcombe J. (2000) *The Use of Animals in Higher Education: Problems, Alternatives, and Recommendations*. 104pp. Washington DC: Humane Society Press.
  - This book examines animal use in education from a humane and ethical perspective.

"Emily" K-9 Positioning Mannikin

Item# 300

Prepare students to properly position dogs for abdominal surgery, spay and neutering, x-rays, advanced spinal stabilization, spinal recumbrance, and more. Because this model replicates the movement of a live canine in resistance and natural movement, you can safely practice technique before working with live animals. Articulated on both sides, Emily features shoulder and hip joints with realistic rotation and 90° flexation. Knees, elbows, carpal and hock joints also have 90° range of motion. Model comes complete with carrying case, kneeling pad, and brush.

"Advanced Airway Jerry" K-9 CPR Mannikin

Item# 505

A full size K-9 mannikin, realistic airway, representations of trachea, esophagus, and epiglottis present. Working lungs, Designed to perform endotracheal placement, compressions, Mouth-to-Snout resuscitation, Artificial pulse, Designed to splint and bandage, disposable & cleanable parts, and realistic features.

Accessories included: Carrying case w/kneeling pad, endotracheal tube, syringe, brush, 5 disposable lungs.

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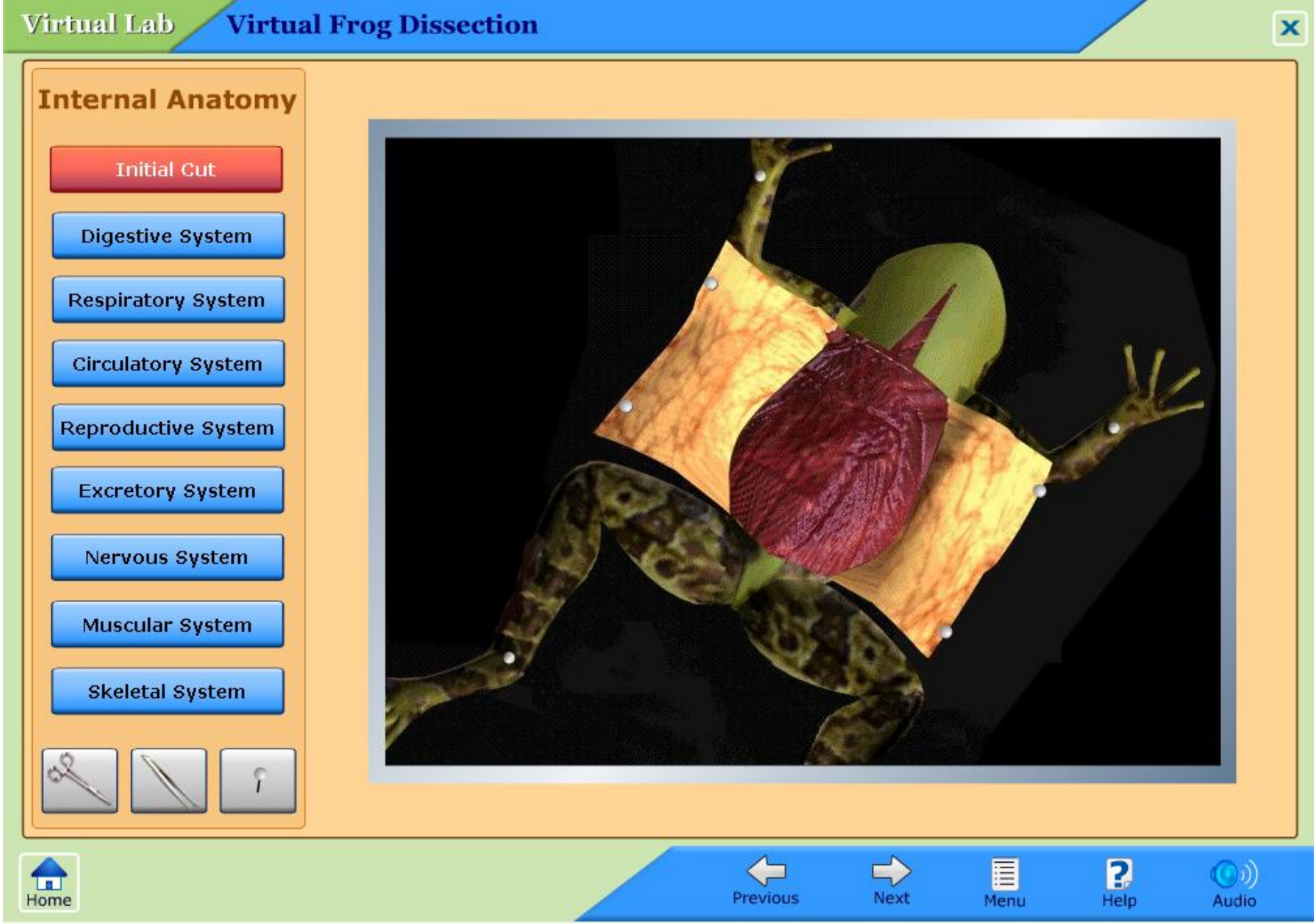

http://www.mhhe.com/biosci/genbio/virtual_labs/BL_16/BL_16.html

Implementation of the 3 R Alternatives

The CCAC Three Rs Microsite (http://www.ccac.ca/en/alternatives/index.html) also provides information and tools for animal care committees to enable them to assess whether the animal user has implemented the Three Rs

Animal Care Committees

The Three Rs microsite was created, in part, to assist animal care committee members in finding easily accessible, useful and relevant information and resources on the Three Rs - Replacement, Reduction and Refinement alternatives. Therefore, the CCAC encourages animal care committee (ACC) members to use the entire microsite as a resource. (However, the information on the site is not meant to supplant CCAC guidelines, and will not be used as a basis for recommendations made in CCAC Assessment reports.)

Potential questions to consider during protocol review to encourage implementation of the Three Rs

- Is the proposed experiment duplicative?
- Are there any *in vitro* techniques that could replace use of animals?
- Are there any alternative animal models of lower sentience (i.e. invertebrates)?
- Is there useful and current information about the proposed animal model?
- Is there information on the proposed model that might allow the use of fewer animals or might reduce the pain experienced by the animals?
- Could in vitro methods be incorporated in any way into the protocol to reduce the number of animals used (e.g., for early screening)?
- Have statistical methods been used to determine sample sizes?
- Is there a way to decrease the level of invasiveness of the protocol without compromising the scientific objective?
- Is there information about assessing welfare and the level of pain of the animals?

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Questions?

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