

Responsible Use of Animals in Biomedical Research

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- ▶ 2025 - eliminate word “use” from all slides

Objectives

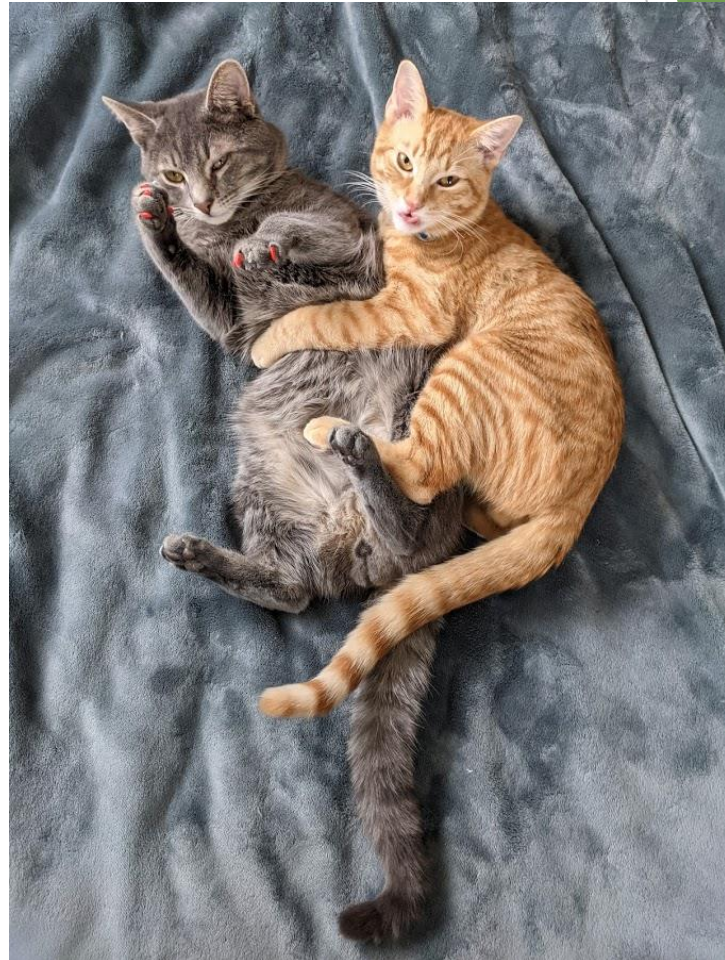
- ▶ Consider & understand the practical approaches to the responsible conduct of animal based biomedical research.
- ▶ Recognize strategies that foster productive, collaborative working relationships & facilitate successful animal research at the University of Pittsburgh.

Discussion Topics

- ▶ Define biomedical research
- ▶ Benefits of animal research
- ▶ Animal species used in research
- ▶ Regulations & guidelines
- ▶ Ethical considerations
- ▶ Compassion fatigue
- ▶ Case discussions

“It’s okay to keep a dog, cat,
or other animal as a pet.”

- A. Agree
- B. Disagree



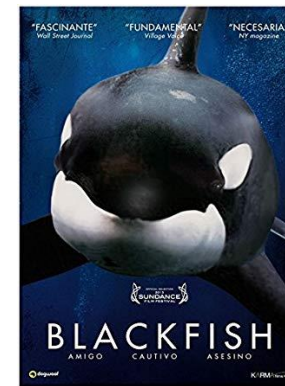
“It’s okay to keep a dog, cat,
or “other” animal as a pet.”

- A. Agree
- B. Disagree



“It’s okay to maintain animals in zoos, exhibits or shows.”

- A. Agree
- B. Disagree



“It’s okay to use animals for sport.”

- A. Agree
- B. Disagree



“It’s okay to use animals for sport.”

- A. Agree
- B. Disagree



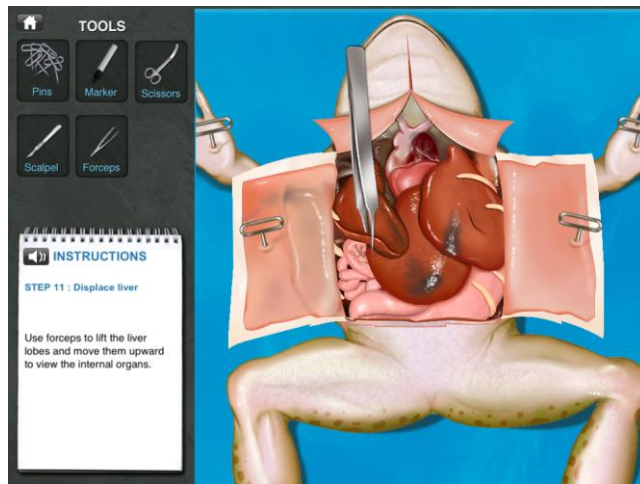
“It’s okay to wear items made of animal products.”

- A. Agree
- B. Disagree

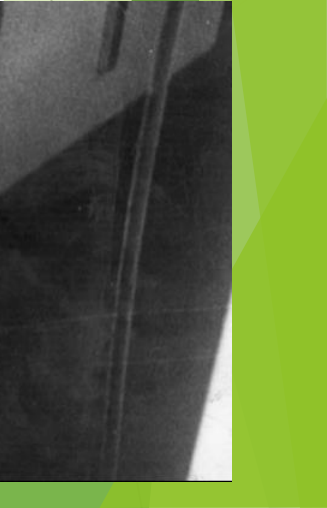


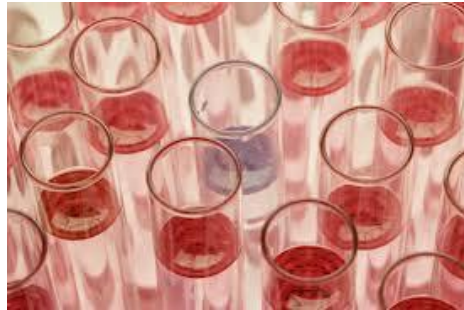
“It’s okay to use animals for educational purposes.”

- A. Agree
- B. Disagree

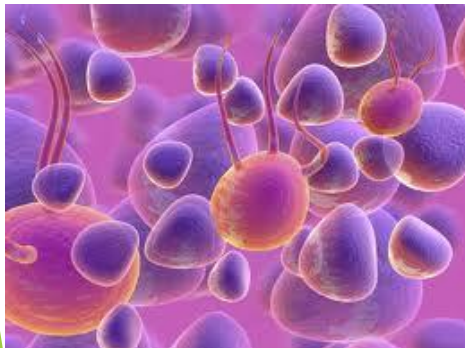


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What is Biomedical Research?



Biomedical research is

- ▶ the study of human *or* animal diseases including the diagnosis, cause, prevention, & treatment of the disease;
- ▶ the development of procedures, drugs & medical devices used to prevent, diagnose, or treat disease;
- ▶ scientific investigations required to understand the underlying disease processes (genetics, immunology, virology, & cellular & molecular basis of diseases);
- ▶ Includes laboratory investigations, clinical trials, environmental studies, etc.

Animals Used in Research



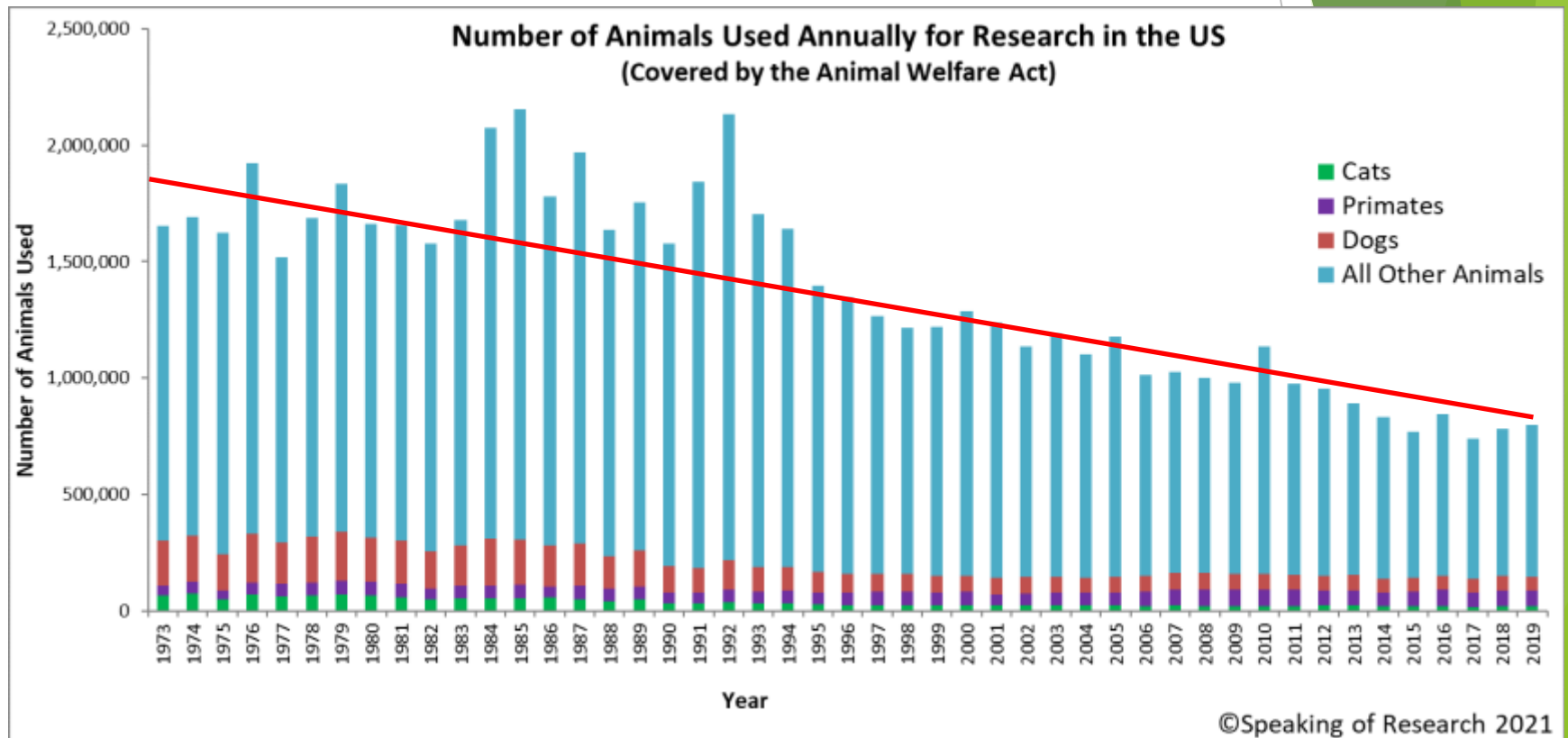
“What are the most commonly used animals in biomedical research?”

- A. Rodents (mice & rats)
- B. Zebrafish
- C. Cats & dogs
- D. Rabbits & guinea pigs
- E. Monkeys

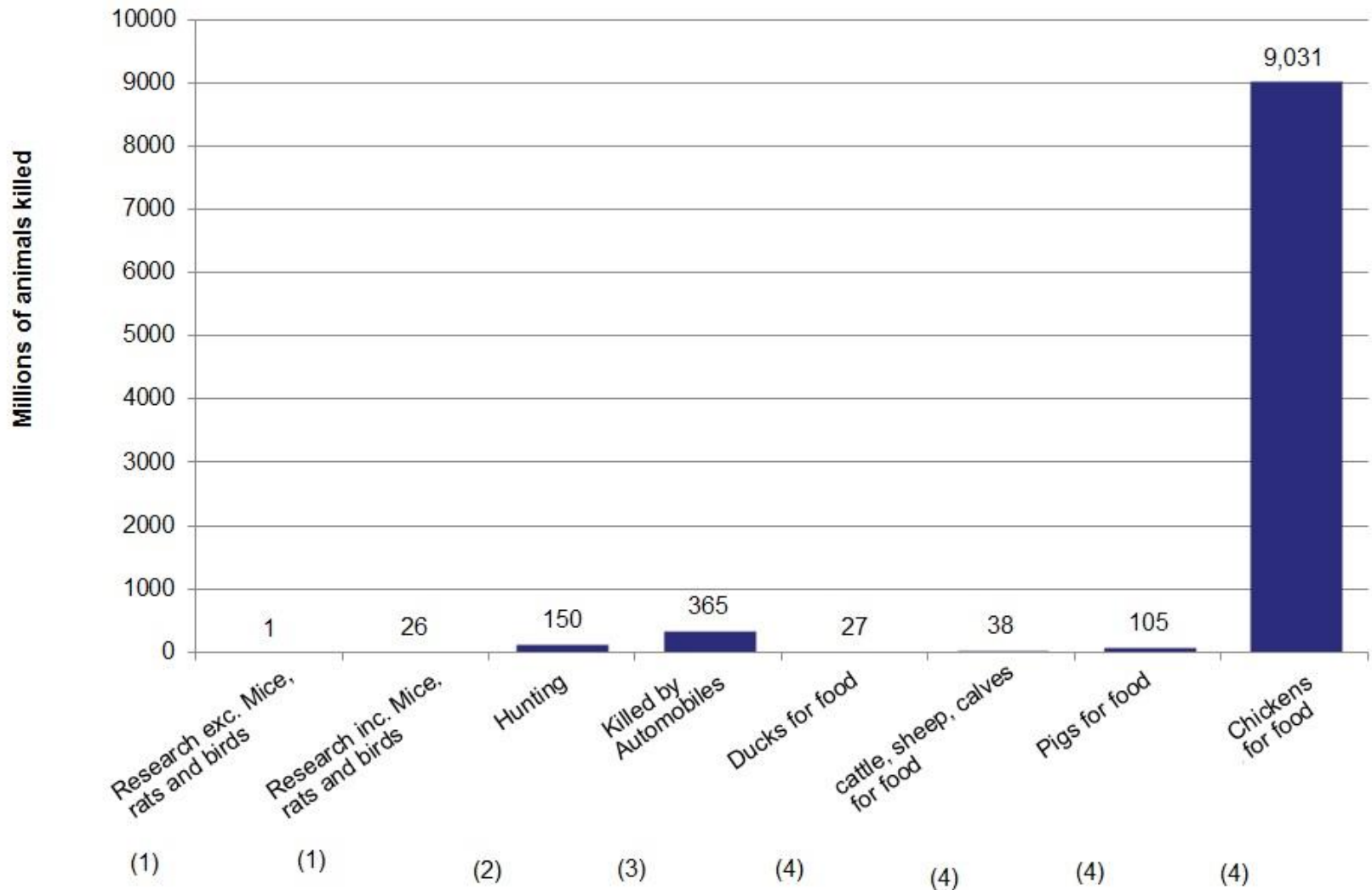
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Annual Animal #'s - US Trends

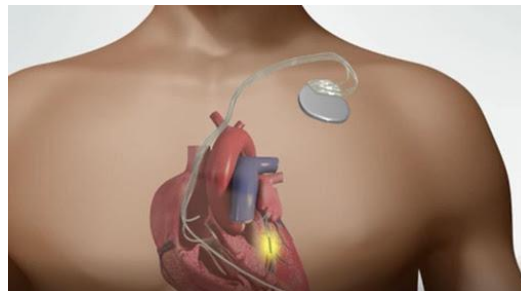


Numbers in Perspective



Benefits of animals in research

- ▶ Vital role in virtually every major medical advance of the last century for both human & animal health. Examples:
 - ▶ Anesthetics, analgesics, antibiotics, vaccines, blood pressure medications, insulin, chemotherapy
 - ▶ Surgical procedures, organ transplants, pacemakers, artificial knees/hips/lenses
 - ▶ Understanding disease processes (HIV/AIDS, Alzheimer's, heart disease, diabetes)



Foundation for Biomedical Research



[ABOUT](#) [ANIMAL RESEARCH](#) [NEWS](#) [BLOGS](#) [PROGRAMS](#)



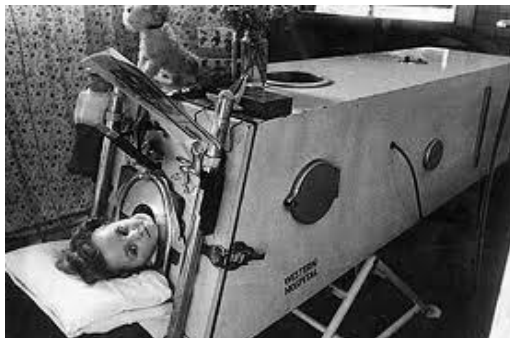
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Year	Nobel Laureate	Animal Model	Contribution to Modern Medicine
2023	Katalin Karikó and Drew Weissman	Mice	For their discoveries concerning nucleoside base modifications that enabled the development of effective mRNA vaccines against COVID-19
2021	David Julius and Ardem Patapoutian	Mice	For their discoveries of receptors for temperature and touch
2020	Harvey J. Alter, Michael Houghton and Charles M. Rice	Chimpanzees	For the discovery of the hepatitis C virus
2019	William G. Kaelin, Jr., MD, Gregg L. Semenza, MD, PhD, and Peter J. Ratcliffe, MD, FRS, FMedSci	Mice	Their groundbreaking research that has led to an understanding of how cells in the body adapt to changing oxygen availability.
2018	Dr. Tasuku Honjo and James P. Allison, PhD	Mice	For their discoveries in cancer therapy via inhibition of negative immune regulation

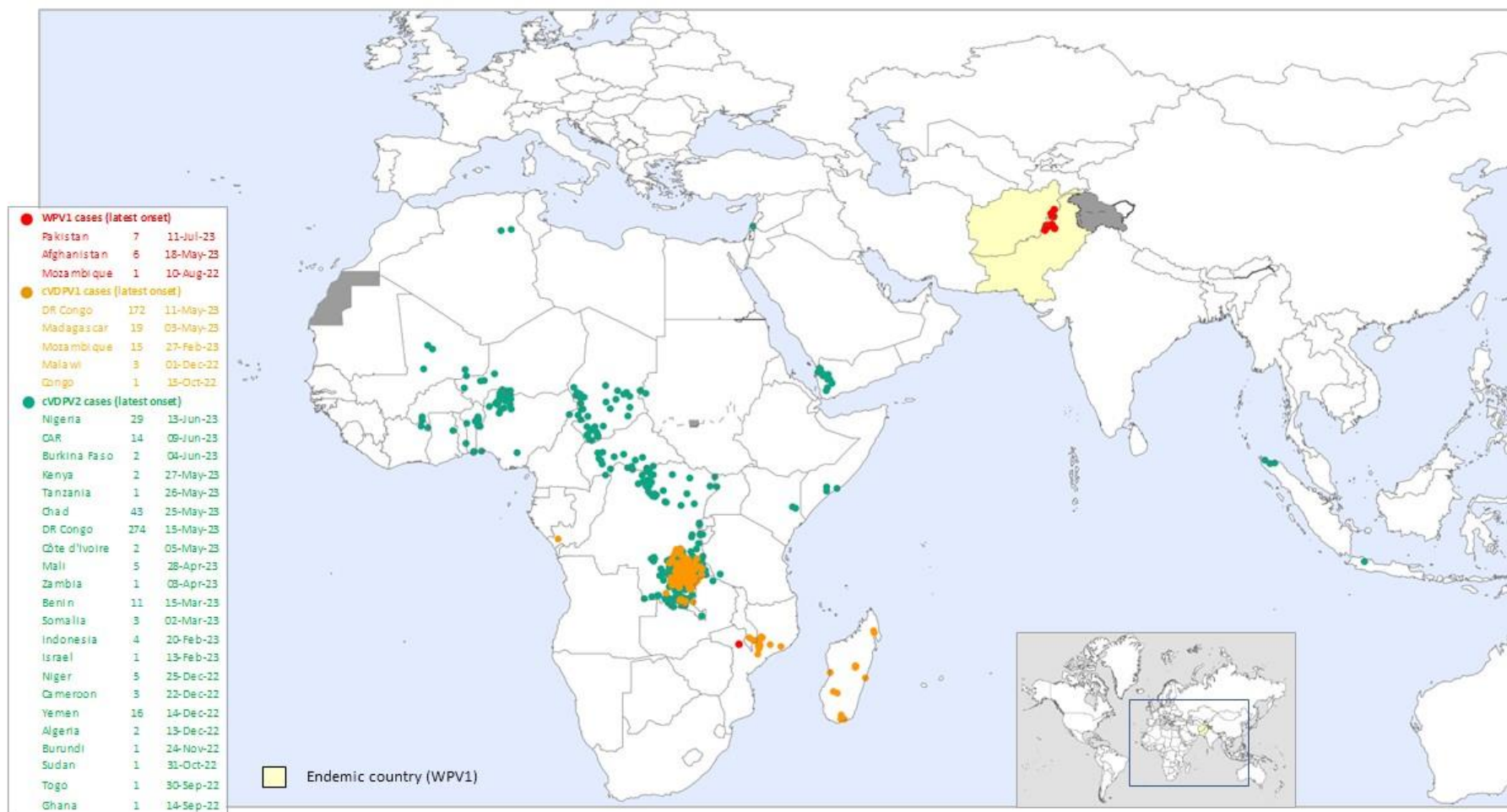
Poliomyelitis

- ▶ AKA polio
- ▶ Signs: mild flu-like symptoms to paralysis (arms, legs, airways)
- ▶ Was one of the most feared diseases in the world
 - ▶ 1940 - 1950s: >500,000 affected, mostly children
- ▶ Salk inactivated vaccine & Sabin live attenuated vaccine → near worldwide eradication



Polio Global Eradication Initiative

Global WPV1 & cVDPV Cases¹, Previous 12 Months²



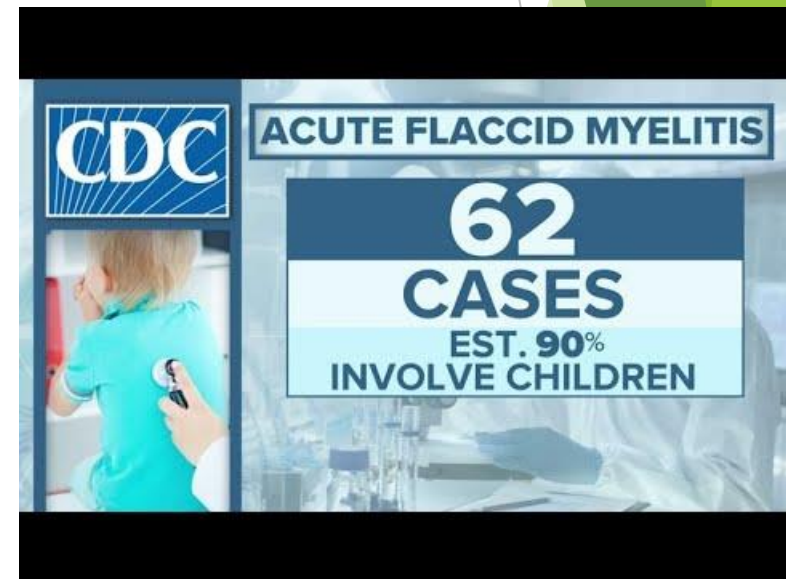
¹Excludes viruses detected from environmental surveillance; ²Onset of paralysis: 09 Aug. 2022 to 08 Aug. 2023

Acute flaccid myelitis (AFM)

- ▶ Rare but serious condition
- ▶ Affects the nervous system causing muscles & reflexes to become weak
 - ▶ May be irreversible
 - ▶ May lead to death
- ▶ Increases in AFM cases since 2014, 90% cases involve kids
- ▶ Referred to as a “polio-like” condition, but patients tested negative for polio
- ▶ 739 confirmed cases reported since 2014
 - ▶ 13 confirmed (as of 12/1/23) in 2023 (1 in PA)

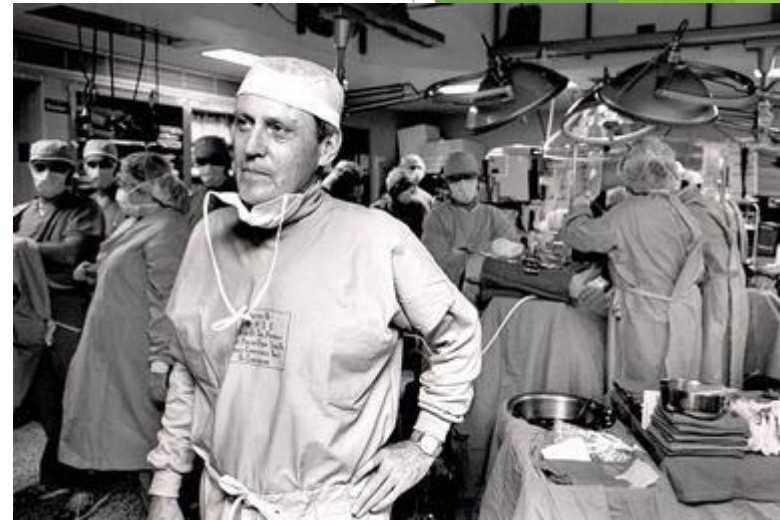
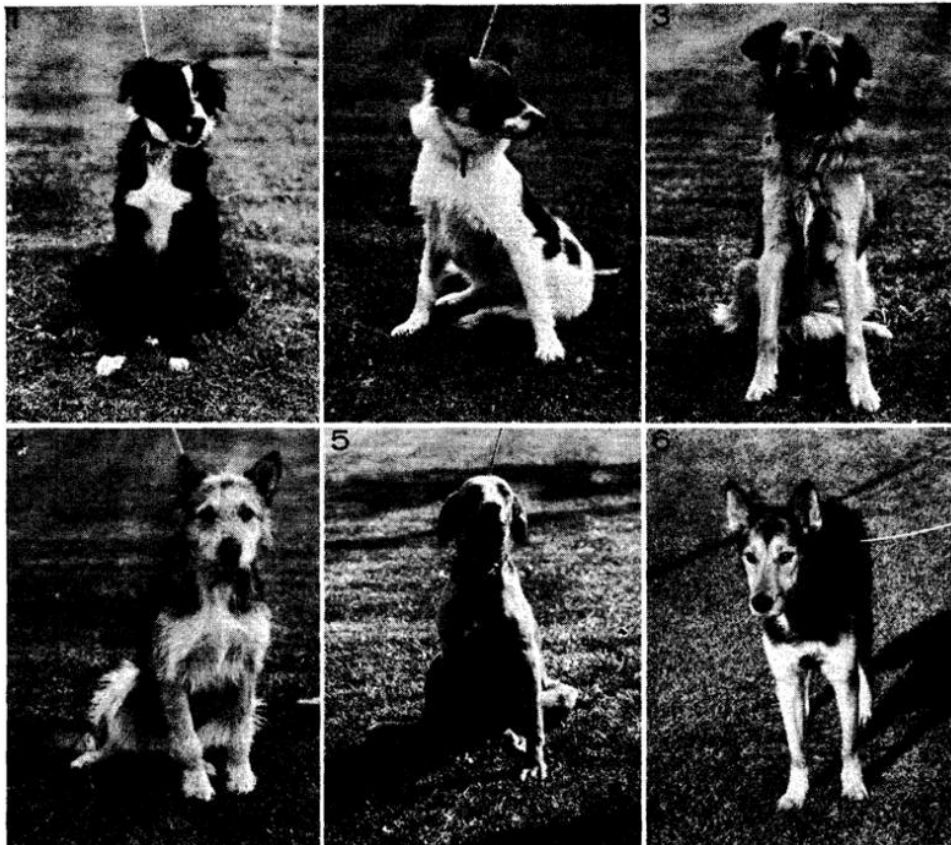
U.S. health officials alarmed by paralyzing illness in kids

Last year there were 228 confirmed U.S. cases of acute flaccid myelitis, a rare, mysterious and sometimes deadly paralyzing illness that seems to ebb and flow on an every-other-year cycle.





EXPERIMENTAL AND CLINICAL OBSERVATIONS AFTER HOMOTRANSPLANTATION OF THE WHOLE LIVER (Starzl, 1965)

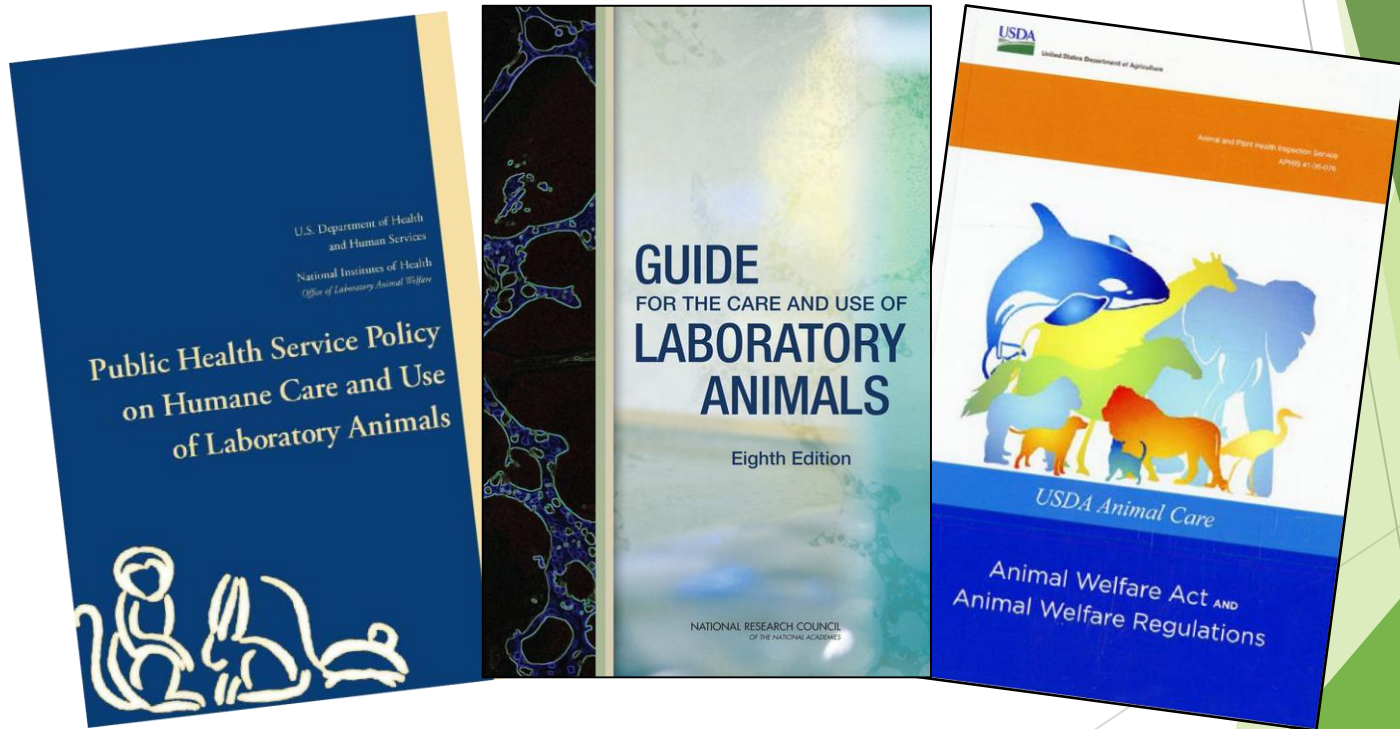


Regulations and Guidelines

- ▶ Federal, state and local laws, regulations, & guidelines
- ▶ institutional policies
- ▶ voluntary accreditation (AAALAC)



Primary Guidance Documents



Primary Guidance Documents

- ▶ Public Health Service Policy on Humane Care and Use of Animals (PHS Policy)
- ▶ USDA Animal Welfare Act & Regulations (AWA&Rs)
- ▶ Guide for the Care and Use of Laboratory Animals (“the Guide”)
- ▶ The American Veterinary Medical Association (AVMA) Guidelines for the Euthanasia of Animals

Institutional Oversight - Pitt

- ▶ Mandated by federal animal welfare regulations
 - ▶ Institutional Official (IO)
 - ▶ Institutional Animal Care and Use Committee (IACUC)
 - ▶ Attending Veterinarian
- ▶ Other regulators
 - ▶ Pitt policies
 - ▶ EH&S
 - ▶ Radiation safety
 - ▶ DLAR
 - ▶ Office of Research Protections
 - ▶ Institutional Review Board (IRB)



AAALAC international

- ▶ Voluntary accreditation
- ▶ Peer-review process
- ▶ Site visitation every 3 years
- ▶ Pitt accredited since 1983



The background features abstract, overlapping green geometric shapes, primarily triangles and polygons, in various shades of green, creating a modern, layered effect on the right side of the slide.

Beyond legislation

Ethical Considerations

- ▶ In addition to laws and regulations, researchers and animal care technicians are guided by ethical considerations for the proper care and use of animals.

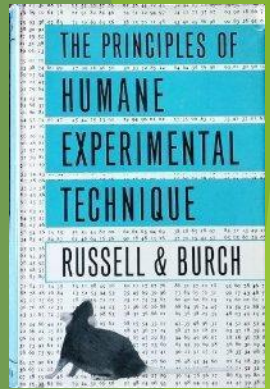


US Government Principles for the Utilization and Care of Vertebrate Animals Used in Teaching, Research and Training (cliff notes version)

1. Transit, care, & use adhere to federal regulations.
2. Consider relevance of study to human or animal health.
3. Appropriate species & # used
4. Minimize distress, comfort, pain
5. If more than momentary pain, relieve pain
6. Humanely euthanize at appropriate time
7. Living condition appropriate for the species
8. Qualified personnel
9. Exceptions can't be decided by research, must be IACUC

“The Three Rs”

- ▶ **Reduction**: ↓ the # of animals used with no loss of useful information. May be achieved:
 - ▶ ↓ variables through good experimental design
 - ▶ rigorously control conditions of experiment
- ▶ **Refinement**: a change in the experiment that results in a reduction or replacement of animals, or in a reduction of pain, stress or distress animals experience.
- ▶ **Replacement**: use of an
 - ▶ inanimate system as an alternative (e.g., a computer model or program)
 - ▶ cell or tissue culture
 - ▶ replacement of sentient animals (usually vertebrates) with less sentient animals (usually invertebrates)





Tom L. Beauchamp & David DeGrazia

Beyond the 3R's

- ▶ Social benefit
 - ▶ No Alternative Method
 - ▶ Expected net benefit = amount of benefit x likelihood of achieving it
 - ▶ Sufficient value to justify harm
- ▶ Animal Welfare
 - ▶ No unnecessary harm
 - ▶ Basic needs
 - ▶ Upper limits to harm

Right vs. Privilege


- ▶ The use of animals in research, teaching and testing is not a right but a privilege. It is incumbent upon every researcher to use that privilege responsibly.

Compassion fatigue



Caring
For
Caregivers

- ▶ What: *“The reduced capacity in being empathetic and the consequent behaviors and emotions resulting from knowing about a traumatizing event experienced or suffered by a person.”*
 - ▶ Sadness, apathy, isolation, difficulty concentrating, bottled-up emotions, excessive complaints, lack of self-care, poor professional relationships, employee turnover
- ▶ Why: *The expectation that we can be immersed in suffering and loss daily and not be touched by it is as unrealistic as expecting to be able to walk through water without getting wet” ~ Remen, 1996*
- ▶ Who: research personnel, vet staff, animal care staff, administrators, supervisors, IACUC



*"I could never
do your job.
I love animals
too much."*

I think you meant to say:
"Thank you for your service."

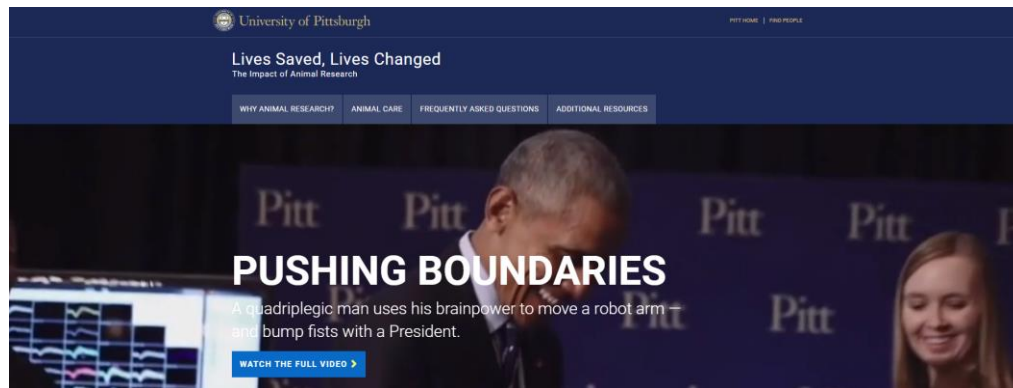
Focus Question Case

- ▶ 2019-USDA closed its lab studying toxoplasmosis in cats
 - ▶ Cats are definitive hosts
 - ▶ Some stages of lifecycle can be cultured, but not the stage in cats
- ▶ 3000 kittens enrolled in studies from 1982-2019
 - ▶ Infected orally, housed for ~2 wks, euthanized
 - ▶ Estimated that # people infected ↓ ~50% as a result of this work
- ▶ ~40-60 million people infected in the US (~11% of population over 6 years of age)
- ▶ ~40-60% of US cats are naturally infected
 - ▶ Treatable vs. curable

Toxoplasmosis questions

- ▶ Is there value to these studies involving cats for toxoplasmosis research?
- ▶ Is it ethical to adopt out experimentally infected cats?
- ▶ An alternative model uses manipulated mice, but manipulation cause severe illness to mice. Is this a better solution than using cats?

<https://www.animalresearch.pitt.edu/>



RESEARCH IMPACT: AT A GLANCE

AGING

ALZHEIMER'S DISEASE

BRAIN-MACHINE INTERFACE

CANCER

MENTAL HEALTH

ORGAN TRANSPLANTS

PARKINSON'S DISEASE

POLIO

HIGHLIGHTS

- Nonhuman primates are essential to our knowledge of the human brain.
- Researchers have used mouse models to help determine the disease's genetic factors and to pioneer immunotherapy treatments as well as a possible drug-free treatment.



PITT'S CONTRIBUTIONS

In 2004, Pitt's [William Klunk](#) and [Chester Mathis](#) completed the first human study of Pittsburgh Compound B. This PET-scan dye, which was first tested in animals, proved an effective way to make the hallmarks of Alzheimer's visible in living people for the first time.

6

Million Americans living with
Alzheimer's

500000

New diagnoses expected in 2018

Questions?



POOKIE
LIVING WITH DIABETES

MAGGIE
HEART FAILURE SURVIVOR

Animal research saves animals.
Get the facts about animal research at www.researchfacts.org.
An international campaign from the Foundation for Biomedical Research ©2009

BUDDY
AFTER HIS HEART SURGERY

LUCY
AFTER HER KIDNEY TRANSPLANT

Photos of animals that have survived serious diseases are the heart of the Foundation for Biomedical Research's campaign promoting animal research for the sake of animals.

Focus Question Case #2

- ▶ A technician performs husbandry duties for an animal research facility. This technician expresses very strong vegan beliefs and is adamantly against the use of animals for food, fur and fiber.
- ▶ Is this an ethical incongruity?

Focus Question Case #3

- ▶ You have a research grant funded by the NIH & are preparing to write additional grant proposals based on the very promising data collected from your animal studies. You are also writing the 3-year renewal of your animal protocol to submit to the IACUC when you realize that you have been performing experimental animal procedures for the past 18 months that are not described on the current version of the protocol. Technically you have been working “off protocol”. Although no animals experienced any adverse events from the unapproved experimental procedures, the data generated over the past 18 months cannot be paid for using NIH funds and the work should not be published. The university expects you to self report this to the IACUC and OPR that will likely result in the IACUC notifying OLAW.
- ▶ What do you do?

Focus Question Case #4

- ▶ You are a research technician in a lab that studies cancer models in mice. You are studying a new tumor type that grows rapidly causing ulceration of the tumor due to lack of a fully developed blood supply. The IACUC protocol states that animals with ulcerated tumors must be euthanized. Your PI is submitting an IACUC modification, which has not been approved yet, to keep the animals and treat them with topical antibiotic ointments. Your PI asks you to treat the current cohort of mice with ointment because he doesn't want to lose the data from these animals and the modification should be approved soon.
- ▶ What do you do?

Focus Question Case #5

- ▶ You are eating lunch with your best friend and she's telling you about the rough morning she had. She works in a laboratory that uses dogs in their animal research studying new potential treatments for myocardial infarction. While checking on an animal that underwent a surgical procedure yesterday, the animal growled and snapped at the individual when she examined the surgical incision site. She confessed that she hit the dog in response to his growling/snapping. Then she confides that it's not uncommon for her to "smack" the dogs every once in a while to remind them who's the master. You are aware of the IACUC policy for anonymously reporting animal welfare concerns.
- ▶ What do you do?