

## **Animal Research, Animal Welfare, and the Three R's\***

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The last 50 years have witnessed a dazzling array of social and ethical revolutions in Western society. Such movements as feminism, civil rights, environmentalism, affirmative action, consumer advocacy, pro-and anti-abortion activism, homosexual rights, children's rights, the student movement, antiwar activism and public rejection of biotechnology have changed the way in which governments and public institutions comport themselves. This is equally true for private enterprise: to be successful, businesses and institutions must be seen as operating solidly in harmony with changing and emerging social ethics.

Not only is financial success tied to accord with social ethics but, even more fundamentally, freedom and autonomy are as well. Every profession – be it medicine, law or agriculture – is given freedom by the social ethic to pursue its aims. In return, society basically says to professions it does not understand well enough to regulate, “you regulate yourselves the way we *would* regulate you. But we will know if you don't self-regulate properly and then we *will* regulate you.” A classic example of this state of affairs is provided by the fate of the accounting profession after the Enron scandal. Accountants must now dot every “I” and cross every “T”, and their freedom has thereby been eroded.

Animal research is, of course, an institution subject to the same requirements we just described. And, in the 1970s and 1980s, it too was significantly out of step with societal ethics, judging by letters to Congress, media coverage, protests, and demands for new legislation. Beginning in the late 1960s, international concern about the welfare of animals in all aspects of animal use began to emerge, a movement that continues to burgeon. Whereas in Europe the societal focus tended to fall on animal agriculture, in the US it was animal research that first occupied social scrutiny, with agriculture increasingly emerging as a concern over the last several years. There are many reasons for this disparity – agriculture was invisible to the urban population and did not receive a great deal of media attention; Americans until very recently thought farms were Old McDonalds' pastoral units; and most importantly, the U.S. public is both

scientifically illiterate and suspicious of science – as is illustrated by the Creationist movement. In a Pulitzer-Prize winning book published in the 1960s, *Anti Intellectualism in American Life*, historian Richard Hofstadter chronicled the historical roots of anti-intellectualism, and many signs of its current robustness are evident, ranging from public preoccupation with crystals and mystical thought; to the astounding 33.7 billion dollars society spends on evidentially baseless alternative medicine (*Americans Spend Billions on Alternative Medicine* 2009), to the fact that books on crypto-zoology, i.e. the branch of biology dealing with such organisms as the Loch Ness monster, the abominable snowman or Yeti, or the chupacabra, beings not proven to exist, significantly outsell books on zoology.

In any event, the ill-advised responses of the scientific community to public concerns about the ethics of animal research are a matter of historical record. As a person instrumental in the writing of the 1985 laws protecting research animals, I was very involved in researching -- in vain -- for defenses of animal research conducted in ethical terms – after all, the question of our right to hurt animals for human benefit is a legitimate and serious ethical question. I found nothing couched in moral terms, but rather emotional diatribes. For example, in the 1984 film “Will I Be All Right, Dr.”, a frightened child utters the phrase before an operation and the narrator basically affirms that any constraints on animal use would render medicine incapable of curing children. I happened to attend the film’s premier before an American Society of Laboratory Animal Practitioners (ASLAP) group. The only comment came from one laboratory animal veterinarian who affirmed, “I am ashamed and appalled to be associated with a film pitched lower than the worst anti-vivisectionist clap trap”.

Another “argument” could be found in advertisements in national magazines like *Time* saying that over 90% of the animals used in research are rats and mice, and “you kill them in your kitchen anyway”. Judging by the mail I saw coming to Congress, these arguments did not play well in Peoria, i.e. made ordinary people angry, rather than convinced them. Further, the Helms Amendment, declaring rats and mice not to be animals, did not sit well with the public or, for that matter, with many scientists who thought it was absurd that most of the animals used in research are not animals for purposes of the Animal Welfare Act (*USDA has No More to Say over Rats, Mice and Birds* 2001).

One more example of ethical absurdity is provided by a 1982 review of my book, in which I described our proposed legislation that passed in 1985. The review appeared, amazingly enough, in *The New England Journal of Medicine*, and referred to me as “exonerating the Nazis” and supplying a “false cloak of morality for lab trashers” (Visscher 1982). (On a related note, I was put on the Institute for Laboratory Animal Research (ILAR) Council of the National Academies 25 years later.) This was the same week that *The Animals’ Agenda*, a radical animal rights journal, called me a “sellout” for “accepting the reality of science.”

While many in this audience are probably not surprised at the absurdity promulgated by radicals, the research community's reaction is shocking. How do we in fact explain the absence of rational ethical discussion of animal research? This question has occupied much of my thinking, writing, and teaching for my entire career.

The answer is to be found in the concept of ideology. An ideology is a set of beliefs that is basic and unquestioned among a population. These beliefs are presuppositional to that population. Those of us who went to religious schools were infused with religious ideology – others are grounded in racist ideology; liberal ideology; Marxist ideology, etc. Essential to ideology is its virtually universal acceptance among certain sub-groups of society, or for certain ideologies such as Nazism, acceptance by the society as a whole.

Twentieth century science has also been captive to an ideology significantly violative of common sense and common morality, that I have called the “common sense of science” and that I learned as a science major in college (Rollin 2006). This ideology was based in the positivistic belief that science deals only with what is testable, observable, and empirical-- facts. Based on this belief, science denied the relevance of ethics to science for, as Wittgenstein remarked, if one takes an inventory of all the facts in the universe, one does not find it a *fact* that “killing is wrong” (Wittgenstein 1965). Hence the belief spread that science is “value-free” in general and “ethics-free” in particular. This positivistic dogma can be found in science texts and in the scientific community's regular failure to engage ethical issues science occasions.

A second component of scientific ideology working synergistically with the first affirmed that science could not talk of consciousness and felt pain in organisms, particularly in animals. Thus 20<sup>th</sup> century biomedical science, despite its Darwinian base, was agnostic and atheistic about animal thought and feeling (Rollin 1989).

This ideology occasioned great harm to science's ability to engage ethical issues. I will illustrate its powerful influence in a series of anecdotes. The first group of stories illustrates the “science is ethics-free” dogma.

1) In about 1990, James Wyngaarden, the then Director of NIH and therefore arguably the chief representative of biomedicine in the U.S., was visiting his alma mater. He was talking to a group of students informally, and was apparently unguarded in his remarks, not realizing that a student reporter for *Michigan State News*, the school paper, was present. The students asked him about the ethical issues associated with genetic engineering. His reply was astonishing: He opined that “though scientific advances like genetic engineering are always controversial, science should never be hampered by ethical considerations”.

2) At an American Association for Laboratory Animal Science (AALAS) meeting in the early 1980's, I ran a full day session on ethics and animal research. At the end, the reporters present converged on the president of AALAS, asking him to respond to my

points. "Oh there are no issues in animal research," he said, "God said we can do whatever we want with animals." (When the reporters asked me to respond, I facetiously said that what he said could not possibly be true. "Why?" they asked. "Because he is at the Blank Vet School," I replied, "and if God chose to reveal himself at a vet school, it would surely be Colorado, which is, after all, God's Country.")

3) In 2001, I was part of the World Health Organization group that was charged with setting guidelines for the use of antibiotics in animal feeds, since their indiscriminate use was driving evolution of resistance to anti-microbial agents and endangering human health. I was asked to give the keynote speech defining the ethical dimensions of the issue. When I finished, I asked for questions. One veterinarian, who was in fact the FDA employee in charge of managing the issue, leapt up and said to me "I am offended!" "By what?" I asked. "By the presence of an ethics talk at a scientific conference. Ethics has nothing to do with this issue. It is strictly a scientific question!" I calmly said, "Let me show you that you are wrong. Suppose I give you an unlimited research budget to determine when to stop or curtail the use of antibiotics in feeds. We do the research and find out that current use levels kill (or sicken) 1 person in 500, or 5000, or 50,000, or 500,000, or 5,000,000. Even when we know this data, it does not tell us where the risk of morbidity or mortality tells us to discontinue such antibiotic use. That is an ethical decision." She then kept quiet for the rest of the conference.

4) A few years before Dolly the cloned sheep was announced, I received a Saturday afternoon call from a research official at the Roslin Institute, asking me to chat about the ethics of "hypothetically" producing a cloned animal. "It's your nickel," I said, finally deploying that wonderful locution stolen from old "hard-boiled" 1940's detective novels and noir films, "Keep talking!" I told them that there were two major concerns: does cloning harm the animal, and does it create social, ecological, or disease dangers. More important than these legitimate concerns, I continued, was what I called "A Gresham's Law for Ethics" (Rollin 1995). Gresham's Law in economics asserts that "Bad money drives good money out of circulation." In the same way, "Bad Ethics drives good ethics out of circulation." So, for example, after World War I, German currency (the Deutschmark) was so inflated that it took a wheel barrow wheel full of them to buy a loaf of bread. In such an economy, rational people pay their outstanding debts with Deutschmarks, not with gold, which they hoard. So too in ethics, I continued. Any new technology, be it the computer or biotechnology, creates a vacuum in social ethical thought, and fear. "What effect will this have on our lives? Is it good or bad? What do we need to control?" If the scientists do not inaugurate rational discussion, that lacuna will be filled by doomsayers with vested interest, such as Jeremy Rifkin. "So", I concluded, "that is your biggest worry. You must create an educated populace on cloning, and help them define the issues, or the public will be told that it 'violates God's will', and how can you respond to that?"

As I suspected, it was as if our conversation had never taken place! Some years later, Dolly was announced to a completely uninformed public. Time/Warner did a survey one

week after the announcement. And, fully 75% of the U.S public affirmed that cloning “violated God’s will!” (*CNN/Time* 1997).

Scientific ideology’s denial of consciousness and pain is also easy to illustrate, as the following vignettes show:

1) In the early 1980s, when my colleagues and I had pretty well drafted the key concepts of our proposed federal laboratory animal legislation and Colorado Representative Pat Schroeder had committed to carrying it forward, we were told by congressional aides that we needed to provide clear evidence of the need for such law, both because the medical research community was a major financial contributor to congressional campaign war-chests, and because that same community claimed to be already controlling pain in research animals. In essence, I was charged with proving they were not. I did so by doing a literature search on analgesia for laboratory animals or, indeed, any animals. What did I find? Two references: one of which said there ought to be papers on this issue, and one saying we don’t know much, and proceeded to list the little bit that was known, namely the efficacy of aspirin and morphine for some pain. If analgesia were indeed widely used, I told Congress, I would have been able to find a significant literature on its theory and practice. Textbooks of veterinary anesthesia before the late 1980s did not even mention felt pain, i.e. that pain that *hurt* (Lumb 1963; Lumb and Jones 1972).

2) Around 1980, when I was developing and pressing the federal legislation for laboratory animals adopted in 1985, I was invited by AALAS to discuss my reasons for supporting legislative constraints on science on a panel with half a dozen eminent laboratory animal veterinarians. By way of making my point, I asked them all to tell me what would be the analgesic of choice for a rat used in a limb-crush experiment, assuming analgesia did not disrupt results that were being studied. The consensus response was, in essence, “How should we know? We don’t even know for sure if animals feel pain!” Interestingly, five years later after the laws passed, I phoned one of those veterinarians, pointing out that as of now, he was *required* to know the answer to my question. He then rattled off five different analgesic regimens. I asked him, “You were agnostic five years ago, where did you get your information?” “From the drug companies!” he said. Puzzled, I asked if they now worked on rat analgesia. “No”, he said, “but all human analgesics are tested on rats.” The point is that he knew this five years earlier, but did not then see it as relevant to rat pain.

3) In 1982, I debated a famous pain physiologist who argued that since the electrochemical activity in the cerebral cortex of the dog, the information processing area, was different from that of humans, the dog did not “really” feel pain. In my rebuttal, I pointed out that he did pain research on dogs and extrapolated the results to people. Thus either his speech was false, or his life’s work was.

Researchers thus did painful things to animals, shielded by an ideology that distanced them from ethics and denied pain. Indeed, the research community also did atrocious things to human subjects in virtue of the same ideological denial. Until the late 1980s, human infants experienced open heart surgery without anesthesia using paralytic drugs because “babies can’t feel pain, or “don’t remember it so it does not matter.” Ironically, the public credibility of science was another victim of this ideology.

If science is value-free, it is conceptually impossible to condemn data falsification, cheating, and other behaviors dubbed “misconduct in science,” a major issue for the research community. Implausibly, such behavior has sometimes been dismissed as evidence of “temporary insanity” (Rollin 2006). In fact, proliferation of such behavior has ironically created a demand that science and ethics be taught! But teaching it is not easy in the face of entrenched ideology. And it is very labor-intensive.

When we drafted the federal laws for laboratory animals, a major purpose of these laws was to undercut ideology, since few things less powerful than law can displace widespread ideology. I had been arguing for years against scientific ideology claims. First of all, science is fraught with value judgment and even ethical judgments. To affirm that double blind randomized clinical trials are better sources of knowledge than the Magic 8 Ball is a value judgment. To demand higher statistical certitude when testing the safety of a human drug versus an animal drug is an ethical value judgment. To say that the value of the knowledge gained from an invasive animal experiment is of greater significance than the animal pain or death is again an ethical judgment. To fund the study of cancer but not baldness is again an ethical judgment. And so on. And to do pain research on animals is to affirm that they feel pain, or else they are poor models.

Despite the force of these arguments, I never dislodged anyone’s ideological beliefs, anymore than showing a racist who affirms, “All black people are stupid,” a smart black person disconfirms their ideology. Thus, just as Civil Rights law helped undo racist ideology, we believed that laws aimed at scientific ideology might help undo it.

Mandated protocol review has certainly introduced ethical discussion into animal research science. Questions discussed range from whether we should allow a researcher to do a surgery they are not expert in, to whether we should allow food deprivation for motivation in a psychology experiment. How much pain should we allow if science is studying pain? Or pain control? Should we apply the same degree of scrutiny to mice as to dogs? If a protocol using horses is asking the same logical sort of question as one using mice, and the horse protocol gets by with 10 horses, should we allow the other protocol to use 1000 mice? Should universities do invasive contract research and training for private entities? Should universities allow research into “pest” extermination? Should researchers be allowed to feed live prey in research? And, although the law says we cannot address this question, I never found an institution that did not conduct a cost benefit analysis about whether the result of a given piece of research justifies the animal suffering it takes to achieve it.

Such discussions are of course not restricted to committee members – they soon become common coin in an institution and thus at least some of the “value free” component of scientific ideology has been successfully eroded by the law. The law has also been spectacularly successful regarding pain control. Since 1985, we have gone from the pathetic two papers I found on animal analgesia to what one of my anesthesiologist colleagues estimates is between eight and ten thousand papers, with a correlative increase of analgesic use. And, equally heartening, the research community has begun to realize that the ways in which animals can be miserable go far beyond physical pain – fear, loneliness, boredom, anxiety, social isolation are obvious examples.

Is it the case, then, that everything is fine – that we have transcended or are at least in the process of transcending ideology, and are now on the right road? Not so fast. There are still a number of issues that researchers are morally and prudentially obligated to address.

I’ve indicated earlier that failure to accord with societal ethical demands by a profession can rapidly erode autonomy. This year was the 50<sup>th</sup> anniversary of Russell and Burch’s classic book, *The Principles of Humane Experiment of Technique* (Russell and Burch 1959), wherein they articulated the notion of the 3 R’s – Reduction, Refinement and Replacement. The 3 R’s are taken quite seriously in Europe – last February I gave the keynote speech to some 300 people celebrating the anniversary in Utrecht. It is clear that part of what society had in mind when it began to morally question animal research was alternatives. This is clearly recognized in the European Union; less so in the U.S. A recent study entitled “Journal editorial policies, animal welfare, and the 3 R’s” published in the *American Journal of Bioethics* (Osborne, Payne and Newman 2009), clearly demonstrates that adherence to alternatives is nowhere near as prevalent as it should be anywhere in the Western World, given societal ethical concern for research animals.

In the words of the abstract, this study “evaluates the editorial policies of a randomized sample of English language peer-reviewed journals that publish original research involving the use of animals. The aim is to identify whether journals have editorial policies relating to the use of animals in research that they are prepared to publish and whether any policies are likely to promote animal welfare and dissemination of information of the 3Rs (reduction, refinement, replacement) within the scientific community. The results demonstrate that a significant proportion of journals publishing original research involving animals do not have any editorial policy relating to the use of animals. Of those journals that do have policies, the majority simply request that the research be carried out in accordance with standard regulatory requirements” (Osborne, Payne and Newman 2009).

The maximum possible score for journals emphasizing animal welfare and the 3Rs in the study is 12. The average score across 288 journals was a dismal 1.51 – the maximum score of any journal was a 9 (Osborne, Payne and Newman 2009, p. 56).

This is an ominous portent for animal research. It shows clearly that the research community has not taken seriously socio-ethical demands. As Dr. Albert Koltveit of the *Journal of the American Veterinary Medical Association* told me when I addressed the Society of Biology Journal Editors, “journal editors are the guardians of the gates for animal welfare” – what journals demand, authors do. As the authors of the study say, journals must revise their policies in the area.

When the public thinks of ethics and animal research it thinks of “alternatives to animals.” When we wrote our legislation in the 70s and 80s, there was in fact a competing bill being written, called the Research Modernization Act. I attended a meeting of those drafting the law, whose focus was on alternatives. At the meeting, I asked the woman behind the law, “What do you mean by an alternative?” Waving her hands, she replied, “Oh you knew, a plastic dog that howls when you cut it and bleeds ketchup that they can do their experiments on.” I intentionally wrote her off as scientifically illiterate and not to be taken seriously, yet I soon found that such a view was all too common. Some congressional staffers, for example, asked me why, if we can send a man to the moon, we can’t model a mouse on a computer. My response has always been, “if we could model a mouse on a computer, we would not need to.” In other words, if we knew enough about mouse physiology and cell biology and metabolism to create a computer replicate of the mouse, we probably would not need to bother, as we would know the full biology of the animal.

But we cannot underestimate the degree of scientific illiteracy rampant in the U.S. public. First described with regard to intellectuals in universities by C.P. Snow in the 1950s as “the two cultures in conflict” i.e. science and everything else, there is little reason to believe things have improved. As Keith Black MD wrote in the Cedars-Sinai Neurosciences Report (Black 2004),

America’s best and brightest used to go into science and medicine, but no longer. The United States consistently ranks in low comparison to other developed countries on assessments of scientific literacy. “One half of the American public does not know the earth goes around the sun once a year, and believes that the earliest humans lived at the same time as the dinosaurs.” [NSF]..... A 1996 National Assessment of Educational Progress survey found that 43 percent of high school seniors did not meet the basic standard for scientific knowledge.

Dr. Jon Miller of Northwestern, who studies scientific literacy in the U.S., affirms that only 20-25% of Americans are “scientifically savvy and alert... [the rest] don’t have a clue” (Dean 2004). According to Miller, U.S. adults didn’t know what molecules are, fewer than a third know that DNA is the key to heredity, and only 10% know what



radiation is. 16% of high school science teachers are Creationists. Two thirds of the U.S. public wants creation taught along with evolution, according to a 2004 CBS news poll (Dean 2004).

This should not surprise us, given Richards Hofstadter's Pulitzer Prize winning 1964 book mentioned earlier, pointing out the deep current of anti-intellectualism in American history going back to the founding of this country. And not only is the U.S. anti-intellectual; we are openly hostile to science. As Jeffrey Sacks wrote in *Economist*, Sept. 22, 2008: "By anti-intellectualism I mean an aggressively anti-scientific perspective, backed by disdain for those who adhere to science and evidence". And consider that stem cells and biotechnology have been widely rejected.

All this noted, it is easy to see why the Research Modernization Act had a good deal of support, and might have passed had it been the only proposal. It would have cut the biomedical research budget by up to 60% and put that money into "alternatives" as described earlier. And given the results of the AJOB article, it is not hard to imagine a disillusioned public again supporting a similar bill.

It is sometimes forgotten that Russell and Burch described three varieties of alternatives, Reduction, Refinement, and Replacement. The laws of 1985 have, through the IACUCs, driven more careful attention to statistics, probably resulting in a net reduction of animals used, though sometimes leading to a demand for more animals when the power of an experiment is deemed insufficient. The basic thrust of these laws is refinement and thus much has been done with regard to pain control, though distress has lagged behind. So it is essential to stress to the public the refinement and reduction that has been achieved.

Replacement has not done well, and that is a problem when it is what society generally understands by "alternatives." This is due in part to the innate conservatism of science, possessed of an "if it works don't fix it attitude." Great progress in replacement has been made in toxicology, particularly regarding cosmetic testing. But more money and educational effort must be expended to accelerate replacement.

One more area must receive more attention to augment animal welfare and decrease animal suffering. While at most 15% of research animals are deployed in projects involving pain and suffering, almost 100% are kept under conditions that violate their biological and psychological needs and natures. During the 1980s, Dr. Tom Wolfle and I stressed the ethical need for developing housing for animals that fits their natures. There is certainly some effort in that direction, but not enough. I helped accelerate some of it as external reviewer for the 1996 Guide. When the Colorado Federation of Animal Welfare Administrators toured our research facility, their only complaint was the impoverished and sterile environments in which the animals were kept, and they were correct. I have no problem with talking of "animal happiness", which I define as fulfilling

their nature and the needs flowing therefrom. We should aim not only at the alleviation of suffering but also the promotion of animal happiness.

Let us recall the need for constantly monitoring societal ethical concerns, and for staying abreast of them in our actions. Failure to do so can mean loss of freedom and the advent of onerous and restrictive regulation.

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