

Commentary: Trust but Verify

LISA JONES-ENGEL

“Trust is the foundation for ethical treatment of animals in research.” This is what a longstanding member of my Institutional Animal Care and Use Committee (IACUC) wrote to me in response to an article I requested he read following another bruising and ethically bereft monthly IACUC meeting. Written by Jonathan Kimmelman and published in *PLoS Biologist*, the piece touched on some of the insufficiencies that plague the ethical oversight of animal research. I had highlighted the following passage for my IACUC colleague:

...animal care committees—far from mere bureaucratic after-thoughts—play a critical role in shaping what questions are asked in research and how such questions are resolved. Among other things, such committees grant scientists the moral license for pursuing research that might otherwise be deemed inhumane or unethical. In so doing, they signal to scientists and others what sorts of research practices are proper and which ones are not, and scientists who want to get their protocols approved quickly learn to internalize these norms.¹

My hope was that Kimmelman’s words would find more purchase than my own had with this senior scientist. However, what I have learned during my tenure on my institution’s IACUC is that persuasive, eloquent prose is inadequate. My IACUC colleague(s) argue that ‘trust’ in the objectivity of the study sponsors; ‘trust’ in the integrity and morality of the principal investigators, veterinarians, and institutions; and ‘trust’ in the neutrality of the oversight bodies is all that is needed to ensure that there are adequate ethical limits in place on the use of animals in research. Fortunately, Hope Ferdowsian and colleagues have proposed a set of ethical principles that would encourage the animal research community to ‘trust’ but verify.²

Unfortunately, I despair when I consider how unlikely it would be that the current animal research community would embrace ethical principles similar to those outlined in the Belmont Report. As Thomas Kuhn noted in *The Structure of Scientific Revolutions*, paradigm shifts rarely happen when people are confronted with compelling evidence. Rather, revolutionary change can only occur when the current generation of scientific leaders and policymakers is replaced by another.³

As a biological anthropologist I study the human-primate interface. My research examines the consequences of interactions between humans and rhesus (*Macaca mulatta*), long-tailed (*M. fascicularis*), and pig-tailed (*M. nemestrina*) macaques. These three species of macaques have for decades formed the simian backbone of the primate biomedical research community. I focus on these species because they are synanthropic; they thrive in the niches that humans create as we change the environment. However, the macaques’ ecological and behavioral flexibility make them vulnerable in an unexpected way. Their pervasiveness in urban and peri-urban environments makes them an easy target for traffickers. It is difficult to appreciate how many Asian macaques have been removed from habitat countries

to laboratories in North America and Europe. In the 1940s and 1950s, approximately 100,000 rhesus macaques were trapped and exported annually from India as scientists desperately sought a cure for polio.⁴ Jonas Salk's polio vaccine required approximately 3,000 rhesus macaque kidneys to produce every one million doses, though the use of macaques in research was not limited to the development of life-sparing vaccines.⁵ The emergence of the National Primate Research Centers, which were established to ensure that scientists would have the specialized resources needed to conduct primate research, owe their origins to the millions of macaques removed from the wild during the 1940s and 1950s.⁶ However, by the late 1960s rhesus macaque populations in India had declined by 90%.⁷ This staggering population decrease, coupled with the revelation that the United States had violated a 1955 agreement which required that (1) use of Indian rhesus macaques be restricted to medical research and vaccine production, (2) the US Public Health Service certify every project using the Indian-origin macaques, (3) the US establish an Advisory Committee on Rhesus Monkey Requirements, and (4) the monkeys were to be used humanely, and explicitly not used in atomic blast experiments or space research, led to an eventual ban on the exportation of Indian-origin rhesus macaques to the US.⁸ The Indian ban, decried by US researchers as evidence of the scientific ignorance and disregard for human health among international governments and animal activist organizations, resulted in renewed interest in other macaque species across Asia as well as other primate taxa across the globe.⁹ Macaque species continue to dominate in research with more than a million long-tailed macaques being extracted from Southeast Asia and Mauritius between 1975 and 2011.¹⁰

Animal research has for centuries operated under the principle that human benefits outweigh the needs or rights of animals. So, when I read the call by Ferdowsian and colleagues for parity for animals used in research, and their request that issues related to consent, harm, and lack of benefit to experimental subjects be addressed, I wondered what this would look like for macaques. Because, from my vantage point, the treatment of these *nonhuman* primates by the international research community has, to date, violated virtually every conceivable ethical principle and certainly all of the ethical principles that are applied to *human* primate research subjects.

The Belmont Report was published one year after Indian society took the unprecedented moral stance to no longer allow their country's rhesus macaques to be used in research. To understand their decision, one needs to appreciate that, in the predominantly Hindu society, rhesus macaques are acknowledged as the 'children' of the anthropomorphic monkey deity Hanuman, who is revered for his devotion, selflessness, protectiveness, trustworthiness, and accountability.

The children of Hanuman have paid an enormous price to improve human health and welfare. Yet, despite the millions of monkeys that have been consumed by the research and pharmaceutical industries, there has been virtually no effort to contribute to the *in situ* conservation or study of these animals in the wild.¹¹ Is it any wonder that the laboratory animal technicians, veterinarians, researchers, IACUC members, US Department of Agriculture and National Institutes of Health officials, the public, and, to a lesser extent animal activists have so little understanding of the rich emotional needs, complex social lives and the drive for self-determination that these monkeys possess? The decimation of wild-macaque populations for the international research trade is registered, if at all, merely as a breakdown of the supply chain. There is no champion, no Jane Goodall for

macaques, no one with the scientific, political, and social reach to step forward and demand that the end-users meet that lowest of ethical bars and provide some measure of benefit for these nonhuman primates that have given so much to humans. If free-living macaques are not benefitting in some measure from the research that is being conducted on their captive brethren, then are we not obligated to exclude macaques from research altogether?

If I turn my eye to the other animals that are commonly used in research—for example, rodents, pigs, and fish—I am more hopeful that the institutional structures that have impeded the adoption of rigorous, clearly defined ethical principles can be surmounted. However, before we can contemplate extending or adapting the Belmont Report principles for research animals, we need to change the structure and required training for members of Institutional Animal Care and Use Committees (IACUCs). The 1985 Amendment to the Animal Welfare Act stipulated that the composition of a five-member IACUC reflect the necessary veterinary and scientific expertise and the nonscientific (public and institutional unaffiliated) concerns that surround the use of animals in research. Such a balance of priorities and expertise was expected to ensure that the ‘needs’ of the science did not overshadow animal welfare. Unfortunately, most large institutions now possess 20 or more member IACUC monocultures, where 90 percent of members are personally and/or institutionally invested in animal research. This ‘stacked-deck’ approach is highly problematic, as studies continue to show that increasing the breadth and depth of IACUC membership is critical to improving research reproducibility, overall research quality, and animal welfare.¹² If “[t]rust is the foundation for ethical treatment of animals in research,” then it is well past time for IACUCs to live up to the public trust placed in them. They must reemerge as ethically-grounded, principle-driven, diverse, and independent bodies worthy of such trust.

Animals have no voice. Therefore, their surrogates on the IACUC must be galvanized and empowered to speak for them, calling out ethical inconsistencies and ensuring that animals are protected from harm. Hanuman’s children are vulnerable. We must protect them as we would protect our own.

Notes

1. Kimmelman J. *The XV Collection: Ethical Oversight in Ethical Oversight of Animal Research* [Blog Post]; available at <https://blogs.plos.org/biologue/2019/01/11/the-xv-collection-ethical-oversights-in-ethical-oversight-of-animal-research/> (last accessed 9 May 2019).
2. Ferdowsian H, Johnson LSM, Johnson J, Fenton A, Shriver A, Gluck J. A Belmont Report for a Animals? *Cambridge Quarterly of Healthcare Ethics* 2020;29(1):19–37.
3. Kuhn T. *In the Structure of Scientific Revolutions*. Chicago, IL: University of Chicago Press; 1962.
4. Nijman V, Healy A. Present day international primate trade in historical context. In: Wich SA, Marshall AJ. *An Introduction to Primate Conservation*. Oxford, UK: Oxford University Press; 2016, 129–41.
5. Baicus A. History of polio vaccination. *World Journal of Virology* 2012;1:108–14.
6. Newbern L. National Primate Research Centers–North America. In: Fuentes A. *The International Encyclopedia of Primatology*, Hoboken, NJ: John Wiley and Sons; 2017.
7. Southwick CH, Siddiqi MF. Partial recovery and a new population estimate of rhesus monkey populations in India. *American Journal of Primatology* 1988;16:187–97. See also Southwick CH, Siddiqi MF. Population trends of rhesus monkeys in villages and towns of Northern India, 1959–65. *Journal of Animal Ecology* 1968;37:199–204.
8. India bans export of rhesus monkeys. *International Primate Protection League Newsletter* 1978;5(1).

Commentary: Trust but Verify

9. Rensberger B. Export ban on monkeys poses threat to research. *New York Times* 23 January 1978, A1. See also Mack D, Mittermeier RA. *The International Primate Trade, Volume 1: Legislation, Trade and Captive Breeding*. Washington DC: TRAFFIC; 1984.
10. See note 4, Nijman, Healy 2016:136–37.
11. Nijman V, Nekaris KAI, Donati G, Bruford MW, Fa J. Primate conservation: Measuring and mitigating trade in primates. *Endangered Species Research* 2011;13:159–61.
12. Pritt SL, Hammer RD. The interplay of ethics, animal welfare, and IACUC oversight on the reproducibility of animal studies. *Comparative Medicine* 2017;67:101–05.