



Citizens for Alternatives to Animals Research & Experimentation

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October 29, 2019

Dr. Michael T. Osterholm, PhD, MPH  
Director, Center for Infectious Disease Research and Policy (CIDRAP)  
University of Minnesota  
Via email: [mto@umn.edu](mailto:mto@umn.edu)

Dear Dr. Osterholm:

I am writing on behalf of Citizens for Alternatives to Animal Research and Experimentation (CAARE), a national nonprofit organization dedicated to promoting research without using animals. This letter expresses the opinion of our board, staff, advisory board, consultants, and thousands of supporters regarding how to best confront the spread of Chronic Wasting Disease (CWD).

CWD is a prion-related and fatal transmissible spongiform encephalopathy (TSE) affecting wild deer, elk, and other cervids, and is catalogued with other TSEs such as Bovine Spongiform Encephalopathy (BSE, or “mad cow disease”) and Creutzfeldt-Jacob Disease (CJD). So far, CWD has been detected in 26 US states, three Canadian provinces, Norway, Finland, Sweden and even South Korea, and is now recognized not only as an established wildlife disease in North America but as a global epidemic. Thus, CAARE recognizes the pressing need for research into CWD, finding ways to limit transmission among animals, determining the potential risk for interspecies transmission to humans and other species, along with limiting human exposure.

**This is why our organization is urging you to direct resources toward research methods that show genuine promise in generating human-relevant data, and cease to promote or fund inconclusive, expensive and painful animal experiments.**

Such experiments have been conducted for years at the National Institutes of Health Rocky Mountain Laboratories in Hamilton, Montana; the Alberta Institute for Prion Research; and the University of Calgary.

Below are examples of failed, long-term studies using animals for CWD research, all of which involved extremely painful procedures and/or long-term captivity and/or premature death for the animals used. Each applied scientifically questionable methods and yielded inconclusive, human-irrelevant results:

- Titled, “Lack of Transmission of Chronic Wasting Disease to Cynomolgus Macaques.” a 2018 publication<sup>1</sup> reported on a 13-year-long study using 16 macaques. Seven monkeys had a hole

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<sup>1</sup> <https://jvi.asm.org/content/92/14/e00550-18>

drilled into their skull through which infected deer/elk tissue (and one normal elk tissue) was injected into their brains. Another nine macaques had a rubber gastric tube surgically inserted through which infected deer/elk tissue was administered. All 15 inoculated macaques died over the course of the study for reasons including anorexia, aggression toward the human personnel, diabetes, wasting, injuries, depression, and “simply” because the study was declared over. The study concluded that, “... *there was no clinical, pathological, or biochemical evidence suggesting that CWD was transmitted from cervids to CM (cynomolgus macaques).*”

- In another nonhuman primate experiment, 28 squirrel monkeys were used for a multiyear study in which most of the monkeys (11 out of 13) who were infected intracerebrally developed wasting syndrome, tremors, and weakness; of the 15 monkeys infected orally, one was found dead 5 years after infection; another one died of complications from anesthesia; and, finally, other monkeys suffered from extreme weakness, lethargy, and anorexia.<sup>2</sup>
- In yet another study, 108 transgenic mice had infected tissue injected into their brains. Those who were afflicted with prion disease experienced weight loss, difficulty walking, and loss of body control. Since most mice turned up negative for CWD infection, the article notes that the experiment was “unable to show definitive evidence for transmission.”<sup>3</sup>

Significantly, the researchers/authors felt compelled to point out that:

*“... animal models used in the present and previous studies are not infallible at predicting cross-species transmission. Particularly in the case of CWD transmission to humans, there are many differences between humans and the various animals tested; for example, host genetic differences including human PrP allelic variations, possible CWD strain variants, and differences in routes of exposure and dosages” (see footnote 2).*

- Beginning in 2010, a research study in Canada used 21 macaques, some of whom got prions injected directly into their brains via infected steel wire, some had to eat infected cervid flesh, others were exposed via blood transfusion, and other monkeys had to endure intentional cuts, “which were then wrapped in infected deer brain, which was meant to model how a hunter might be exposed to infectious material after getting cut during field dressing.<sup>4</sup> Four of 18 monkeys infected showed clinical symptoms including rapid weight loss and extreme anxiety where they were ‘scared to death’ and crouching into the farthest corner of their cages., shivering, unable to pick up pieces of food ...”<sup>5</sup>

It later became apparent that three out of the four sick monkeys also had uncontrolled diabetes, which the lead researcher acknowledged induces wasting, essentially rendering the findings questionable. Further confounding the experimental outcomes, other monkeys apparently died for reasons unrelated to the study. Finally, the ten macaques still living showed no clinical signs as of July 2017, an average of 7.5 years post-infection. This includes those selected for

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<sup>2</sup> <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2819871/#SD1>

<sup>3</sup> <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6341683/>

<sup>4</sup> [https://www.cste2.org/Webinars/files/CWD\\_Slides\\_FINAL.pdf](https://www.cste2.org/Webinars/files/CWD_Slides_FINAL.pdf)

<sup>5</sup> <https://www.kunc.org/post/bent-out-shape-part-4-next-mad-cow-disease#stream/0>

blood transfusions and skin scarification to “mimic the type of exposure humans have with CWD.”

This last study cost Canadian taxpayers at least \$8.5 million (as of July 2017), has not been peer-reviewed, and yielded highly objectionable findings. It is unfortunate that these questionable results have been cited as plausible evidence that CWD might jump the species barrier and infect humans, both by CWD-INFO.ORG,<sup>6</sup> and by the American Center of Biology<sup>7</sup> in a report that seemingly contradicts the above-mentioned (and more recent) findings it also published. (See “Lack of Transmission of Chronic Wasting Disease to Cynomolgus Macaques” above.)

Other experiments have shown that ferrets are 100% susceptible to CWD and mink are 25% susceptible to CWD, but only via intracerebral infection, not via oral infection. Squirrel monkeys appear to be “highly susceptible” to CWD; in contrast (aside from the questionable assertions made in the Canadian study cited above), cynomolgus monkeys were found *not* to be susceptible to infection with CWD. The disease has been transmitted to transgenic mice expressing hamster PrP or overexpressing mouse PrP, but not those expressing human PrP via intracerebral infection.<sup>8</sup>

### **More than 15 years of painful animal experiments amount to mere vague science**

The science appears conclusive that these experiments have failed to yield convincing results about the risk of human susceptibility, transmission and exposure, let alone treatment possibilities for CWD.

**After more than 15 years, translational data from animal experiments is vague, and summarized by a systematic NIH review that could only report a “high level of uncertainty” regarding possible transmission of CWD to humans. Specifically, “five epidemiological studies, two studies on macaques, and seven studies on humanized transgenic mice, provided no evidence to support the possibility of transmission of CWD prions to humans.”<sup>9</sup>**

**CAARE strongly concurs with taking proactive measures to confront the spread of CWD, and that a public health intervention is warranted.** We support the authors’ recommended steps (ii-iv) in their Call to Action to advance knowledge of human exposure and transmission risk: *(i) investing additional resources in CWD research, (ii) enacting and enforcing mandatory CWD testing of dead or harvested cervids in all areas of endemicity, (iii) improving management practices to prevent CWD transmission among cervids, and (iv) heightened surveillance of human prion diseases to determine if CWD is transmissible to humans.*”

With respect to additional resources for research, (i), our position is that continued funding of animal models is scientifically unsound and must be replaced by human-relevant testing methods.

**We urge all scientists and public health experts to effectively address the threat of CWD and its unknown transmissibility to humans by ending inconclusive animal studies and replacing them with human-centered methodologies.**

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<sup>6</sup> <http://cwd-info.org/cwd-overview/>

<sup>7</sup> <https://mbio.asm.org/content/10/4/e01091-19>

<sup>8</sup> <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2819871/#R6>

<sup>9</sup> <https://onlinelibrary.wiley.com/doi/full/10.1111/tbed.12612>

Scientists are now equipped to construct and learn from human-mimetic scientific models replicating key components of human biology in the lab. This is in stark contrast to reliance on animal models that have consistently failed to deliver any conclusive insight into how CWD may affect humans.

### **The Way Forward: Human-Derived Models**

Recent work at the National Institutes of Health (NIH) using cerebral organoids engineered from human skin cells demonstrates a promising method to study prion disease, from which actionable, human-relevant data can be collected and utilized in a preventative, risk mitigation strategy.<sup>10</sup> These “mini-brains” are delivering significant results in human prion disease studies, and should be similarly used to clearly understand CWD’s risk to humans.

The human organoid model developed at NIH is but one method for studying human-specific infection and transmission of prion disease. In 2017, research at the University of Edinburgh successfully generated human stem cell-derived astrocytes capable of replicating human prions.<sup>11</sup>

Induced from pluripotent stem cells, astrocytes are non-specialized cells capable of transforming into other cell types, and scientists were able to infect the astrocytes with prions isolated from the brain samples of CJD patients. These diseased astrocytes successfully infected adjacent, healthy cells—the first time such conditions had been created in a lab—significantly enhancing our understanding of prion diseases in people. This achievement has simultaneously paved the way for new treatments combatting CJD while further promoting the efficacy of studying this fatal brain disease without repeating the same cruel, ineffective tests on animals and expecting different results.

The ability to engineer and study lab-grown prion assays continues to expand. As such, the current multiple and unpredictable testing limitations that arise from animal experiments are increasingly removed or reduced for studying CWD using organoids and other advanced 3D cell culture techniques. These methods demonstrate significant promise for better understanding this fatal disease.

**It is clear that CWD animal experiments are not providing human benefit. They are inconclusive, well-funded exercises that cause great pain and suffering in sentient nonhuman animals.**

CAARE believes that the allocation of resources to study CWD should emphasize best practices in developing and deploying innovative, precise, and human-mimetic science.

It is imperative that foundations, researchers, and public health officials concerned with the potential serious risk posed by CWD direct all resources towards effective, human-based technologies in order to truly understand and contain potential human transmission of this fatal neurological disease.

All animal experiments currently conducted at the Rocky Mountain Laboratories, the Alberta Institute for Prion Research, the University of Calgary and elsewhere should be immediately terminated. In the interest of mercy and in recognition for their sacrifice to humans, we believe that all current animal survivors of CWD experiments should be sent to sanctuaries.

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<sup>10</sup> <https://www.nih.gov/news-events/news-releases/niaid-scientists-develop-mini-brain-model-human-prion-disease>

<sup>11</sup> [https://cjd.foundation.org/sites/default/files/grant-downloads/Krejciova%20et%20al%202017%20jem\\_20161547.full\\_.pdf](https://cjd.foundation.org/sites/default/files/grant-downloads/Krejciova%20et%20al%202017%20jem_20161547.full_.pdf)

Sincerely,



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