Episode: *Author Interview: "With What Should We Replace Nonhuman Animals in Biomedical Research Protocols?"*

Guest: Aysha Akhtar, MD, MPH
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Transcript: Cheryl Green

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[bright theme music]

[00:00:03] TIM HOFF: Welcome to another episode of the Author Interview series from the *American Medical Association Journal of Ethics*. I'm your host, Tim Hoff. This series provides an alternative way to access the interesting and important work being done by Journal contributors each month.

Joining me on this episode is Dr Aysha Akhtar, the co-founder and CEO of the Center for Contemporary Sciences and a fellow of the Oxford Centre for Animal Ethics. She's here to discuss her article, coauthored with Mikalah Singer, "*With What Should We Replace Nonhuman Animals in Biomedical Research Protocols?*," in the September 2024 issue of the Journal, *Nonhuman Animal Research*. Dr Akhtar, thank you so much for being on the podcast. [music fades]

DR AYSHA AKHTAR: Thanks for having me, Tim.

[00:00:46] HOFF: So, what's the main ethics point that you and your coauthor are making in your article?

AKHTAR: I think there's been a lot of discussion over the decades about the use of animals in experimentation, and much of the discussion has been focused on what's called the 3 *R*'s, which was a term kind of coined back, I think, in the '70s. But it basically means reduction, refinement, and replacement. And that was supposed to sort of guide the ethical considerations when using animals in biomedical research. So, refinement would mean kind of tweaking an experiment so it may cause a little less harm and suffering to an animal. Reduction means reducing the number of animals used in an experimental protocol. And of course, replacement means replacing animals as much as possible in biomedical research with other methods. So that's been sort of the prevailing mindset when it comes to animals in biomedical research for many years.

But there's been a shift in recent years, and the shift is now moved over to the one *R* principle, which is replacement. We're no longer discussing refinement and reduction. Now we're at the point where we're talking about replacing: How can we replace the use of animals in biomedical research, and how fast can we do it, and with what can we do it? There's a couple of reasons for this shift. One is not only because of the increased awareness of the suffering of animals used in experimentation, but also, there's a shift in the bioethics discussion concerning how relevant is animal experimentation for human health?

So, it's also not only are we talking about, is animal experimentation ethical for animals, but now we're also asking is it ethical for humans? And there's been a lot of systematic reviews and multiple published studies that are showing increasingly that as a whole, whatever role animal experimentation may have played in the past, today, we're finding that it's very ineffective and unreliable in informing human health and in predicting what will be safe and effective in humans.

[00:03:08] HOFF: And so, what do you see as the most important thing for health professions students and trainees specifically to take from your article?

AKHTAR: I think what we need is, the most important thing is, that I'd like for health professionals and students to think beyond the animal testing. We've established a kind of paradigm in medical research where we expect animals to be experimented on before we move on to human clinical trials. And we're now at a point where we really need to change, completely shift that paradigm and start thinking about other ways of testing before we get to human clinical trials. And what I mean by that is using methods, especially methods that have been developed in the past few decades, that are much more effective, proving to be much more reliable, and proving to be much more sophisticated because they're based on human biology.

So, for example, there's human organs on a chip. We can bioprint human organs or miniature human organs in the lab, and this is just a start. But the benefit of these methods is that they are human relevant because they are applicable to our species. And so, not only are these methods, you know, have a great potential to replace animal testing, but they also have a farther, I would say, an even greater potential to be much better at informing human health and much better at telling us whether the vaccines or drugs we take, or might take, will actually work and be safe in us.

[00:04:45] HOFF: And finally, if you could add a point to your article that you didn't have the time or the space to fully explore, what would that be?

AKHTAR: The two points, if I can add, one is that when we talk about the bioethical question of the use of animals in experimentation as it relates to humans, we do know now—and I worked at the Food and Drug Administration for over a decade—we do know now that 90 to 95% of all drugs and vaccines that are found safe and effective in animals end up being unsafe or ineffective in humans, and that's discovered in human clinical trials. Most of the reason, the largest major causes for the failure rate is that the drugs and vaccines are ineffective or unsafe in humans, despite having gone through the animal testing protocol that's required by FDA. So, this is a 90 to 95% failure rate, despite the drugs and vaccines having been tested in at least two different species, per FDA protocol.

So, we have that high failure rate, which is not something that exists in a vacuum. It's a high failure rate. It's a high failure rate that uses our tax dollars. It costs us time. It takes us away from implementing better research models. So, there's an opportunity cost with this high failure rate as well. So, patients are waiting for effective treatments, and as long as we continue to use this failed paradigm of using other species to try to predict

what we'll find in humans, patients are waiting for effective treatments during that time. So there is an opportunity cost, not only in time but also in expense.

[00:06:31] The other thing I would also mention is that not only is there an opportunity cost in time and expense, there's also a great concern that because of the unreliability of animal testing, that we've actually, that pharmaceutical companies and scientists, have actually discarded medications and treatments, maybe even cures, that would have worked and would've been safe in humans, but because of results that were different in other animal species. And there've been a number of near misses that we know of to suggest that this potential abandonment of effective treatments is probably very likely and probably happens all the time because of misleading results in animals.

And then the last thing I would say is that what we really need, what we really need, and I would ask anyone who's listening to this podcast to please help drive a paradigm shift, help start demanding that our governmental agencies, our health agencies start investing and putting much more funding into the development, the refinement, the discovery, and the improvement of more human-relevant testing methods. [theme music returns]

[00:07:45] HOFF: Dr Akhtar, thank you so much for your time on the podcast today, and thanks to you and your coauthor for your contribution to the Journal this month.

AKHTAR: Thank you so much, Tim.

HOFF: To read the full article, as well as the rest of this month's issue for free, visit our site, journalofethics.org. We'll be back soon with more *Ethics Talk* from the *American Medical Association Journal of Ethics*.