

Publish and Perish?

In late 2011, the National Science Advisory Board for Biosecurity (NSABB) made an unprecedented recommendation that details of two H5N1 bird flu studies by researchers from the Netherlands and the University of Wisconsin be withheld from publication because they could potentially be used to start a deadly pandemic. In March, following months of controversy and additional review, the board reversed that recommendation. Michael Imperiale, Ph.D., Arthur F. Thurnau Professor and associate chair of the Department of Microbiology and Immunology, has served on the NSABB since its inception in 2005 and explains what's at stake in the debate. ➔

Q: What makes the H5N1 flu so dangerous?

A: There have only been a small number of human cases of H5N1 — just over 600 to date — but the mortality rate is incredibly high, nearly 60 percent. So, while we've been seeing it transmitted from bird to human, rather than human to human — primarily in populations with direct contact with animals, like poultry workers — we've come to know it as a highly lethal virus in humans. In contrast, the mortality rate associated with the 1918 influenza pandemic was around 2 to 3 percent and it killed up to 40 million people; a quarter of the world was infected.

Q: Where does the research at the heart of the controversy fit in?

A: The unanswered question is, "Could this virus start spreading from human to human?" There's been a lot of debate in the influenza community as to whether this is going to happen.

Q: What did the two research teams find?

A: They introduced mutations into the virus based on the fact that avian viruses use different receptors to get into cells than human viruses. They changed the virus so that it would be able to recognize human receptors, and then they took the engineered virus and passaged it through ferrets. When they introduced this virus to ferrets within sneezing distance of non-infected animals — a well-established model for influenza transmission — they found that the passaged virus can be transmitted from ferret to ferret through an airborne route.

Q: What is the scientific value of this type of research?

A: There are three potential benefits. The first is simply confirming that mammal-to-mammal transmission is possible. Another is that it may be useful for vaccine development. And finally, if public health authorities know certain mutations can cause transmissibility, they can watch out for them. Now there are two caveats to that: Presumably these aren't the only mutations that can cause transmissibility, so you don't want to get a false sense of security; and influenza surveillance is not that great. It's been argued that by the time you've seen a particular sequence, it may already be too late.

Q: Why did the board make its initial recommendation?

A: This is the first time we've seen papers and said, "Whoa, this is potentially really dangerous." We had reviewed a couple of papers previously that described the reconstruction of the 1918 influenza virus. In that case, we deemed that publishing wasn't of concern because the sequence of

that virus and how to reproduce the virus from that sequence were already known. Now you could argue with the H5N1 research that someone could also go into the literature and figure out how to do it, but our thinking here was, "Why give them the actual template?"

Q: What kind of response did the board expect?

A: Our hope was that the influenza community was going to stop what it was doing and have a serious discussion about the risks and benefits of this type of research. They did stop what they were doing during a 60-day research moratorium [which was later extended], but it's not clear to me whether they have had any serious discussions during that period. We also were hoping that this would be a wake-up call to the public health community that this issue needs serious attention. Since about 2005, we've been telling the U.S. government — and anybody else who's willing to listen — that we need a better way to deal with this type of research-of-concern. We made some specific recommendations in

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a report in 2007, but in the interim, nothing much happened. One of the good things that came out of this controversy was that on March 29, the government finally did release a policy on dual-use research [research that can be used for good or ill].

Q: What does the policy say?

A: They made a list of 15 agents and toxins and outlined seven categories of experiment that are deemed to be the most dangerous. A federal agency that's funding any research that uses one of the listed agents for one of those categories of experiments must look at it more closely and work with the investigator to think about things like putting restrictions on publication, or maybe

even whether or not the experiment should be done in the first place.

Q: Why did the board change its mind about publication?

A: We had initially recommended that the articles be redacted, but we wanted public health officials and researchers still to have access to the data. We learned, however, that there was no way to accomplish restricted sharing. We were left with two options: publish, or don't publish. So, along with additional information provided by the researchers, the board felt the benefits of publishing outweighed the risks.

Q: Do you think the current dual-use review system is sufficient?

A: I think there needs to be a better system that's truly global in nature, where research like this will be discussed and decisions will be made at an earlier stage in the process, like when someone applies for funding or obtains a result — not when they've already written it up, presented it at a conference and/or submitted it for publication. Local institutional review boards and biosafety committees should be more involved, too.

Q: Where does the debate stand within the scientific community?

A: That's a great question. I'm not sure where the larger scientific community stands on this. I would have loved to have seen senior, well-respected scientists speak out publicly, but there's been this eerie silence, in my view. Certainly, the vocal members of the influenza community said the research should absolutely be published, that no one is going to use influenza as a terrorist weapon. But with respect to the dual-use issue in general, many scientists seem to have the opinion that this doesn't really affect them — either "I'm not doing research that could be misused," or "That's not my responsibility to think about." One of the points the NSABB has emphasized is that there has to be better awareness of the issue and that we as scientists have a responsibility to the public, to show them we're behaving responsibly. They fund our research through their tax dollars and they're the ultimate beneficiaries, through better medicines, better vaccines and better treatments. [M]

Interview by Ian Demsky