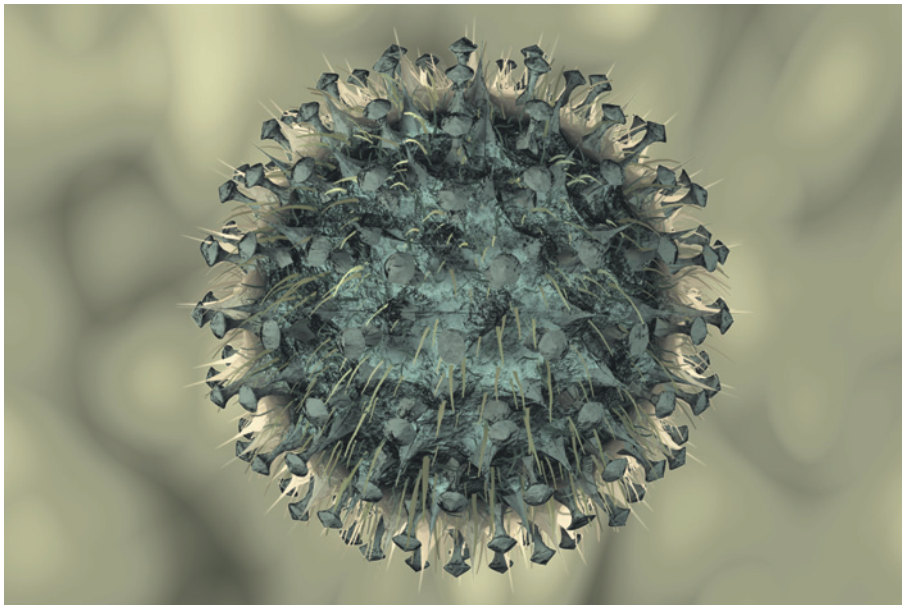
COMMENT



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The fight over flu

A proposal to restrict the planned publication of research on a potentially deadly avian influenza virus is causing a furore. Ten experts suggest ways to proceed.

RON FOUCHIER & AB OSTERHAUS
Globalize the discussion

Erasmus MC, Rotterdam, the Netherlands

So far, most of the human deaths from the deadly H5N1 strain of bird flu have occurred in Asia and the Middle East. Many labs worldwide — including ours — are trying to understand what makes the virus so virulent, and how to stop it. H5N1 research is thus a global issue, yet the entire research community seems to be following the advice of one country.

We are not questioning the unprecedented recommendations last month from the US National Science Advisory Board for Biosecurity (NSABB) to remove key details from the methods and results sections of published papers, including our own, submitted to *Science* (see *Nature* **481,** 9–10; 2012). But we do question whether it is appropriate to have one country dominate a discussion that has an impact on scientists and public-health officials worldwide. This discussion should include the perspective of people in regions where H5N1 has infected humans. Will the NSABB also advise on which international researchers and officials have the right to see the full papers, to help implement urgently needed surveillance and other intervention strategies?

It is not clear whether an international discussion would lead to different recommendations. There is no global equivalent of the NSABB, but many European experts that we have seen quoted in the press believe that the research should be published in full. We don't know the worldwide opinion until a group of experts from all parts of the globe is formed. An issue this big should not be decided by one country, but by all of us.

JOHN STEINBRUNER
A system for redacted papers

Director, Center for International and Security Studies at Maryland, University of Maryland, College Park

If the two papers (submitted to *Nature* and *Science*) describing a transmissible form of the H5N1 virus are the first to be published with key details missing, they probably won't be the last. We need to establish both a short-term and a long-term solution for how the scientific community should handle such a publication. Who decides who should have access to the full details? Who monitors the community so that the details don't get passed around outside the group of experts cleared to receive them?

I believe that the entire process must be regulated by a global health body, ideally the World Health Organization (WHO). Already, a WHO committee oversees all research involving the smallpox virus. A similar, more developed system could work for H5N1 and other deadly pathogens. An international group of experts would approve research involving those agents, decide who will have access to the details of papers that come out of that work, and hold those vetted individuals accountable for what they do with the information. For instance, such a system might allow permitted experts to view papers only electronically, so nothing is on paper. A database could record the privileged few people who have seen the full paper, and what they do with the information. In all likelihood, legal safeguards would be needed to protect the rights of people who receive the sensitive information. Such a process would not offer complete protection against misuse, but it would show the scientific community that the committee is watching what they do.

Because dangerous pathogens are a global issue, any procedure would need buy-in ▶

from all countries, who would have to give the committee binding jurisdiction over research involving extremely dangerous agents. This will take some time. In the short term, the WHO or some other global health organization should immediately establish an ad hoc committee to review who should receive access to the full H5N1 papers, and ensure that the details do not circulate widely.

Most importantly, these discussions should not be controlled by officials focused on national security. H5N1 is primarily a matter of public health. If there is a threat of bioterrorism, let it be judged by a global health organization, which can set rules that do not deprive scientists of information that could save millions of people in the case of a natural pandemic. If national-security organizations become involved, they will vet scientists on the basis of citizenship, and will be inclined to discriminate against those countries in which terrorists have found refuge. But some of those countries are among the few that have experienced human deaths from H5N1, and are most likely to witness the origins of a natural pandemic. It is crucial that scientists and other experts are judged on their qualifications, not on their nationality. If the world is to accept the process, national-security officials cannot be allowed to dominate the discussion.

N. SHRESTHA/EPA/CORBIS

South Asian countries such as Nepal are among the most likely to be hit by avian flu epidemics.

KWOK-YUNG YUEN

The Hong Kong perspective

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As a scientist working in Hong Kong — the site of the first human epidemic of infection by the highly fatal H5N1 virus — I appreciate the public-health significance of knowing which mutations confer airborne transmissibility in an animal model. The new, much-debated research provides this information. Finding similar genomic signatures in animal or human viruses collected from the WHO Global Influenza Surveillance Network may alert public-health workers to an impending epidemic of unthinkable magnitude or severity. But I also appreciate the possibility that such mutants could cause a global disaster if accidentally or deliberately produced and released into animal and human populations. Consequently, I support the recommendation from the NSABB to remove key details from the papers describing this work.

Biological warfare is familiar to people living in this part of the world. During the Sino-Japanese War in the 1930s and 1940s, scientists and physicians of the Japanese army's Unit 731 infected civilians and prisoners of war in Manchuria, China, with *Yersinia pestis*, the bacterium behind the Black Death, which was first identified in plague patients in Hong Kong in 1894. When the unit found that the bacteria caused severe organ damage when serially inoculated into prisoners of war, the unit began spreading plague-contaminated fleas in China, causing outbreaks.

Censoring scientific data for publication will not stop rogue individuals or nations from developing a deadly and highly transmissible form of H5N1, but it would at least buy some time to find and stockpile the appropriate antivirals, immunomodulators and vaccines to protect against most variants of H5N1. Even if the publications omit the methods for making such a deadly virus, the genomic signatures associated with airborne transmissibility should be known to the directors of all public-health laboratories in the WHO surveillance network, after they sign an agreement of confidentiality.

D. A. HENDERSON

The ultimate biological threat

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The H5N1 influenza strain poses a potential biological hazard far more serious than any we have ever known. It is a virus that is capable of killing half its victims, a proportion greater than that for any other epidemic disease. Were that coupled with the transmissibility of a pandemic flu virus, it would have characteristics of an ultimate biological weapon unknown even in science fiction (see *Nature* **480,** 421–422; 2011). We should not publish a blueprint for constructing such an organism.

LYNN KLOTZ &
ED SYLVESTER

Worry about lab infections

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Asian bird flu is just one of the extremely dangerous pathogens researched in laboratories throughout the world. Along with the two labs that created a potentially contagious form of H5N1, at least 40 others worldwide investigate deadly, highly contagious pathogens not currently present in human populations, such as the SARS virus and the recently resurrected 1918 pandemic flu virus. Public-health experts worry about natural pandemics, and governments worry about the risk that these pathogens pose to national security — but the probability of accidental release is likely to be much higher.

We have analysed the likelihood of escape from 42 labs, using 1% as the estimated probability of an escape from a single lab in a single year. This approximates the historical probability, obtained by dividing the documented number of escapes of these pathogens (3, each involving the SARS virus) by our estimate of the total number of lab-years of research on these pathogens since 2003 (more than 300 lab years). Lab infections can easily spread: in 2004, after the only natural SARS outbreak in humans was contained, two graduate students lab-infected with SARS in Beijing infected seven others, causing one death.

Our analysis shows that the probability of an escape from at least one of 42 labs in a single year is 34%; within less than 4 years,