

1918 Flu and Responsible Science

The influenza pandemic of 1918 is estimated to have caused 50 million deaths worldwide; 675,000 in the United States. The reconstruction of the 1918 virus by the synthesis of all eight subunits and the generation of infectious virus are described on p. 77 of this issue,* and the sequences of the final three gene segments of the virus are described in a concurrent *Nature* paper.† Predictably, but alarmingly, this virus is more lethal to mice than are other influenza strains, suggesting that this property of the 1918 virus has been recovered in the published sequence. The good news is that we now have the sequence of this virus, perhaps permitting the development of new therapies and vaccines to protect against another such pandemic. The concern is that a terrorist group or a careless investigator could convert this new knowledge into another pandemic.

Should the sequence of the 1918 virus have been published, given its potential use by terrorists? The dual-use nature of biological information has been debated widely since September 11, 2001. In 2003, a committee of the U.S. National Academies chaired by Gerald Fink considered this issue, weighing the benefits against the risks of restricting the publication of such biological information. They outlined the tradeoff between erring on the side of prudence, thus potentially hindering the progress of critical science, and erring on the side of disclosure, thus potentially aiding terrorists. The U.S. National Science Advisory Board for Biosecurity (NSABB) was established to advise governmental agencies and the scientific community on policies relative to public disclosure. This board has begun to deliberate, but the questions are complex, as typified by these papers on the 1918 virus. It is reassuring that the NSABB was asked to consider these papers before publication and concluded that the scientific benefit of the future use of this information far outweighs the potential risk of misuse. People may be reassured that the system is working, because agencies representing the public, the scientific community, and the publishing journals were involved in the decision.

I firmly believe that allowing the publication of this information was the correct decision in terms of both national security and public health. It is impossible to forecast how scientific observations might stimulate others to create new treatments or procedures to control future pandemics. For example, in the *Nature* article, sequence comparisons suggest that the 1918 virus was generated not by incremental changes in the polymerase genes, but by the movement of these genes, in total, from an avian source into a human influenza virus. The availability of these sequences will permit identification of their avian origin and should show why this particular set of genes was selected. Similarly, the results in the *Science* article suggest that the cleavage of a protein on the surface of the 1918 virus, a step critical for virulent infection, may occur by a previously unknown mechanism—a hint that could lead to new drugs for inhibiting this step and thus preventing future pandemic eruptions.

Influenza is highly infectious, and a new strain could spread around the world in a matter of months, if not weeks. The public needs confidence that the 1918 virus will not escape from research labs. All of the described experiments were done in a Biosafety Level 3 laboratory, a high-containment environment recommended by the U.S. Centers for Disease Control and Prevention and the National Institutes of Health on an interim basis, whose use should become a permanent requirement for such experiments. Current evidence suggests that some available drugs and possible future vaccines could suppress infections by the 1918 virus. Given the prospect of another natural influenza pandemic, the recent decision by the U.S. administration to stockpile antivirals for influenza treatment seems wise. Finally, although a sequence of the 1918 virus has been determined and is highly virulent in mice, this may not be the specific form of the virus that caused the pandemic of 1918. An article in the same issue of *Nature*‡ reports the existence of sequence variation in a natural population of influenza virus; yet we have only one sequence for the 1918 pandemic strain, and the reconstructed virus described in the *Science* article was built into the backbone of a laboratory strain. Because a pandemic infection is dependent on many unknown properties, there is no certainty that the reconstructed 1918 virus is capable of causing a pandemic.

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*T. M. Tumpey *et al.*, *Science* **310**, 77 (2005). †J. Taubenberger *et al.*, *Nature* **437**, 889 (2005). ‡S. Salzberg, *Nature* 10.1038/nature04239 (2005).

