and a shared sense of responsibility.

According to a newspaper report, Korea's National Board of Bioethics indicated that, in contrast to claims by Hwang's group, information on serious risks of egg donation were not provided to all donors, and that 16 of 100 donors required in-hospital treatment of adverse effects from the procedure (*20*). Even the most stringent regulations also rely on trust.

The responsibilities to mentor students in navigating the pressures of becoming a scientist can pale by comparison to the drumbeat of competition and the expectation to produce. Contemporary research is nested in a plethora of codes, rules, and laws. It is a challenge to inculcate the skills of responsible research let alone the more general set of nontechnical skills and virtues that ennoble science.

Although some research universities now require that doctoral and postdoctoral students complete fairly elaborate courses in ethics, many more treat students to a sandbox morality lesson consisting of the admonition not to lie, cheat, or steal data. The courses may have little effect on future misconduct (*19*). The idea that research training, such as that required in the United States for some federally funded trainees and emphasized by the National Research Council report (*21*), in itself would have prevented fabrication on such a grand scale in South Korea strains credibility.

Teachers must themselves be judged by the authorities in our institutions—not only for their ability to produce science, but also to be scientists of virtue and integrity. The ability to give testimony and to act as a witness can be modeled, and students should be allowed to exercise skills of discernment and skepticism about results that seem unlikely or behaviors that are worrisome without punishment. The lesson to be learned is that we need to do a better job of holding research institutions accountable for setting up systems and mentorship that will produce integrity in its scientists.

References and Notes

1. Seoul National University Investigation Committee, *Interim Report of Professor Hwang Woo-Suk* (Seoul National Univ., Seoul, 2005).
2. S. Shapin, *A Social History of Truth: Civility and Science in 17th Century England* (Univ. of Chicago Press, Chicago, 1994).
3. S. Shapin, *Soc. Stud. Sci.* **14**, 481 (1984).
4. S. Shapin, S. Schaffer, *Leviathan and the Air-Pump: Hobbes, Boyle, and the Experimental Life* (Princeton Univ. Press, Princeton, NJ, 1989).
5. P. Lipton, *Stud. Hist. Philos. Sci.* **29**, 1 (1998).
6. C. White, *BMJ* **331,** 281 (2005).
7. J. Ryu, " Roh aide caught in stem cell scandal," *Korea Times*, 18 December 2005; in English (times.hankooki.com).
8. R. Weiss, *Washington Post,* 24 December 2005, p. A2.
9. International Committee of Medical Journal Editors, "Uniform requirements for manuscripts submitted to biomedical journals" (2005); (www.ICMJE.org).
10. D. Rennie, V. Yank, L. Emanuel, *JAMA* **278**, 579 (1997).
11. Institute of Medicine, National Research Council, *Integrity in Scientific Research* (National Academies Press, Washington, DC, 2002).
12. Bioethics and Biosafety Act, Act no.7150, Korean National Assembly, passed 2003, effective date 1 January 2005.
13. Editorial, "Study shows bioethics awareness lacking," *Dong-a Ilbo* (*East Asia Daily*, Seoul) 25 November 2005; (english.donga.com).
14. T.-G. Kim, "Cloning scientist Hwang to get more funding," *Korea Times*, 3 February 2005.
15. T.-G. Kim, "Hwang honored as 'Supreme Scientist'," *Korea Times*, 24 June 2005.
16. Office for Human Research Protections, U.S. Department of Health and Human Services (HHS), "Guidance on research involving coded private information or biological specimens" (HHS, Washington, DC, 2004); (www.hhs.gov/ohrp/humansubjects/guidance/cdebiol.pdf).
17. HHS, "Public Welfare: Part 46 Protection of Human Subjects," Revised June 23, Code of Federal Regulations (C.F.R.) 45 § 46,102 (2005).
18. D. Magnus, M. Cho, *Science* **308**, 1747 (2005).
19. R. Weiss, *Washington Post*, 22 November 2005, p. A21.
20 J. K. Min, "Stem cell researcher used more eggs than reported," *Ohmy News*, 30 December 2005; (english.ohmynews.com).
21. S. Brown, M. Kalichman, *Sci. Eng. Ethics* **4**, 487 (1998).

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PUBLIC HEALTH

Community Studies for Vaccinating Schoolchildren Against Influenza

A plan to vaccinate schoolchildren against flu presents an opportunity to assess risks and benefits.

M. Elizabeth Halloran* and Ira M. Longini Jr.

The Advisory Committee on Immunization Practices and several states are considering recommending annual influenza vaccination in groups beyond the currently recommended high-risk groups. This offers an opportunity that should not be missed: to conduct a nationwide study of the effectiveness of vaccinating schoolchildren against influenza as a means of reducing community transmission. Some public health officials speak of universal vaccination against influenza, meaning a recommendation for all age groups, but schoolchildren, aged 5 to 18 years, are a prime target as they are generally considered to be the most important source of community-wide transmission. Researchers also believe that the immune systems of children respond better to influenza vaccination than do those in the elderly at-risk population. To realize maximum benefit from a study of such effects, we must prospectively sort out the crucial features to be evaluated: effectiveness, benefits, risks, and costs.

Highly pathogenic avian influenza A (H5N1) and its potential to unleash a pandemic are recently in the news. Aside from reducing community-wide transmission of seasonal influenza, vaccinating schoolchildren against influenza and putting its evaluation into place would prepare us for an organized response to an influenza pandemic, whenever it occurs. Our predictions suggest that if limited doses of vaccine were available, as might be expected during a pandemic, vaccinating schoolchildren would be the most efficient approach to reducing overall numbers of influenza cases.

A combination of vaccinating schoolchildren and older adults would be most effective for reducing influenza deaths (*1, 2*) Results from influenza simulations that we have conducted indicate that vaccinating just 20% of the schoolchildren would do more in reducing overall mortality in adults over 65 years old than vaccinating 90% of the adults over 65 years of age (see chart, page 616, top). Even though schoolchildren and young adults have not been considered at high risk of dying of influenza, annual morbidity is still high, with illness attack rates in schoolchildren exceeding 10% most years. Thus, the benefits would not be limited to the older population.

Expanding annual influenza vaccination would give vaccine manufacturers the incentive of a guaranteed market so that they would be willing to increase production capacity and stabilize the influenza vaccine pipeline. This improves our preparedness for a pandemic strain.

Arguments against and hindrances to vaccinating schoolchildren against influenza need to be taken seriously. Despite the benefits, children already receive many vaccinations, and parents and children balk at the idea of yet another, especially if needed annually. However, even if coverage were incomplete, community-wide benefits could be obtained provided that vaccination rates were 50% or higher, not to mention the direct protection of the vaccinated children. Use of a nasally administered live-attenuated influenza vaccine (LAIV) (*3*) might be an alternative to the traditional shots with killed vaccine. Influenza

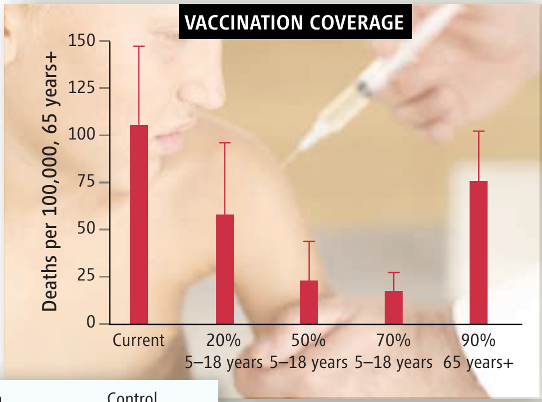
The authors are with the Program of Biostatistics and Biomathematics, Fred Hutchinson Cancer Research Center, Seattle, WA 98109, and the Department of Biostastistics, University of Washington, Seattle, WA 98195, USA

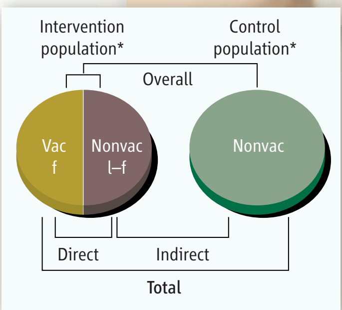
*Author for correspondence. E-mail: betz@u.washington.edu

vaccination is generally safe, with mild local reactions, such as soreness at the injection site with the killed vaccine, or runny nose with the LAIV, and, especially in persons with no previous exposure to influenza virus antigen, mild systemic reactions such as myalgia, fever, and malaise (*4*). Guillain-Barré syndrome was associated with the 1976 swine influenza vaccine, but not proven in later vaccines (*4*, *5*). Numerous logistical uncertainties remain to be worked out. Who would pay for the additional immunizations? Would distribution be through schools or physicians' offices? Who would carry the liability protection for potential or alleged injury due to vaccination?

We are not starting on a blank page. Attempts have been made before to demonstrate the community-wide effectiveness of vaccinating schoolchildren against influenza. Just before the epidemic in 1968, Monto and colleagues vaccinated 85% of the school-age children in Tecumseh, Michigan, against influenza, which resulted in a 67% decrease in the influenza-like illness attack rate in Tecumseh compared with neighboring Adrian (*6*). In an ongoing community vaccination study in Central Texas with LAIV, Glezen and colleagues are attempting to demonstrate that vaccinating schoolchildren reduces the incidence of influenza-like illness in adults (*7*). Although these studies are rigorous, they each have only one or two comparison communities.

A larger-scale study with numerous comparison communities is needed. A study in several schools in the former Soviet Union used a nonspecific outcome as well, so the results are difficult to interpret (*8*). A compelling example of the need to plan evaluation prospectively is provided by the Japanese national vaccination strategy, which, for over two decades until 1987, was targeted at schoolchildren precisely to reduce epidemic influenza. A retrospective reassessment suggesting that the Japanese strategy reduced excess deaths among elderly adults (*9*) is open to criticism because it is based on nonspecific mortality data over time. The time trends could result from factors not related to influenza vaccination. More recently, the province of Ontario, Canada, has been promoting widespread vaccination for all age groups. The analysis of the Ontario experience suffers from weaknesses similar to that of the Japanese. A recent review of 14 studies concluded that further evidence is needed of the indirect effects of influenza vaccination in children (*10*). Although mathematical models of the population-level effects of vaccination offer useful guidance, they cannot replace data from an actual study.





Simulated effects of vaccine interventions and study designs. (**Top**) Simulated mean number of deaths per 100,000 in the elderly population and 90% upper confidence limits under the current vaccination coverage in the United States and under different additional levels of coverage in school-aged children or the elderly. The current coverage in the United States is about 5% in children aged 5 to 18 years, 23% in adults aged 19 to 64 years, and 68% in the elderly aged 65+ years. Simulations based on model described in (*5*). (**Bottom**) Types of effects of interventions against infectious disease and different study designs based on comparison populations for their evaluation [adapted from (*10*)].

So, what are essential aspects of a successful study? The primary goal has to be evaluating whether increased coverage in schoolchildren would reduce the overall influenza illness attack and death rates in the community as a whole. Comparisons should be made between places where expanded coverage was implemented and those where current recommendations remained in place (see chart, this page, bottom) (*11*). Although we could propose simply vaccinating children in half the states in the first year, followed by the rest of the states the next, it is neither feasible nor desirable. More tractable units of coverage are school districts, communities, cities, counties, or individual states. Enough pairs of units must be included to ensure that the study has statistical power to detect and estimate an effect. The more units are included in the study, the smaller is the chance that any observed differences in influenza incidence would be due to chance. Also, to allow for the possibility that, one year, the vaccine might be mismatched to the circulating strains or that the influenza season is particularly mild, the study should be continued for two or more years. This would also allow progressive inclusion of more communities. Such a geographically staggered introduction would permit vaccine production to ramp up for the increased demand and would give time to monitor potential safety concerns.

A vital factor in the success of such a study is the accurate and consistent diagnosis of influenza. Currently, influenza incidence is measured using nonspecific case definitions, such as pneumonia and influenza-like illness. If virologic confirmation of a random sample of influenza-like cases is done, the proportion of confirmed influenza-positive cases can be used to estimate the proportion of the nonspecific influenza-like cases that were in fact truly influenza (*12*, *13*). The importance of virologic confirmation in obtaining accurate estimates is highlighted by the Texas study above in which the direct protective efficacy of LAIV was estimated to be 18% (95% CI: 11, 24) by using a nonspecific case definition, and 79% (95% CI: 51, 91) when surveillance cultures were included (*13*).

Many people alive today remember the large mobilization in the 1950s for the polio vaccine trials. Two important differences are that a study of the effect of vaccinating schoolchildren against influenza would involve a licensed rather than an experimental vaccine and would measure the overall effects on reducing transmission, morbidity, and mortality, rather than just the direct protective effects.

We propose nationwide mobilization for a study of influenza vaccination. Similar to the polio vaccine study (*14*), a large study of influenza vaccination will need to be conducted by a partnership of academia, government, and industry. Government could provide the public health access, guidance in operations, and policy, as well as some funding for the research. Industry could provide vaccine and guidance in safety evaluation. Academia could provide expertise in innovative design and central coordination of the study.

Vaccination of schoolchildren will be a massive effort if introduced nationwide. Why not plan for its proper evaluation now?

References and Notes

1. R. Patel, I. M. Longini, M. E. Halloran, *J. Theor. Biol*. **234**, 201 (2005).
2. I. M. Longini, M. E. Halloran, *Am. J. Epidemiol.* **161**, 303 (2005).
3. R. B. Belshe *et al*., *N. Engl. J. Med*. **20**, 1405 (1998).
4. Side Effects and Adverse Reactions: Inactivated Influenza Vaccine (www.cdc.gov/flu/professionals/vaccination/sideeffectsinact.htm), accessed 18 December 2005.
5. R. E. Neustadt, H. V. Fineberg, *The Swine Flu Affair: Decision-Making on a Slippery Disease* (University Press of the Pacific, Honolulu, 2005).
6. A. S. Monto, J. A. Davenport, J. A. Napier, T. F. Francis, *Bull. World Health Organ*. **41**, 537 (1969).
7. P. A. Piedra *et al*., *Vaccine* **23**, 1540 (2005).
8. L. G. Rudenko *et al*., *J. Infect. Dis.* **168**, 881 (1993).
9. T. A. Reichert *et al*., *N. Engl. J. Med*. **344**, 889 (2001).
10. R. Jordan *et al*., *Vaccine*, published online 26 September 2005 at www.science.direct (10.1016/j.vaccine.2005.09.017), in press.
11. M. E. Halloran, C. J. Struchiner, *Epidemiology* **2**, 331 (1991).
12. M. E. Halloran I. M. Longini, *Am. J. Epidemiol*. **154**, 391 (2001).
13. M. E. Halloran *et al*., *Am. J. Epidemiol*. **158**, 305 (2003).
14. T. Francis *et al*., *Am. J. Public Health*, **45**, 1 (1955).
15. D. Weycker *et al*., *Vaccine* **23**, 1284 (2005).

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