tional Institute of Allergy and Infectious Diseases at the National Institutes of Health in Bethesda, Md., and his collaborators. In their analytic review of the recent pandemic that was posted on mBio in September, they consider the histories of this and other pandemic influenza viruses dating to the late 19th century in their quest to understand the survival pressures that H1N1 now faces.

After the H1N1 virus emerged, it quickly circulated worldwide. Now, however, its levels are much reduced relative to its first season. Its further public health impact will depend directly on population immunity, according to Fauci and his collaborators. Several factors determine population-wide immunity, including “prior exposures to cross-reacting viruses and vaccines, the extent of infection with H1N1, and the relative proportion of the population vaccinated against the virus in 2009–2010.”

Population immunity in the United States is extensive, and “likely to rise substantially with administration of vaccines in the 2010–2011 influenza season,” the researchers note. An estimated 60 million people—most of them older than 55—were immune before the disease struck; another 62 million were vaccinated, and an additional 61 million became infected with H1N1, suggesting a population immunity of about 59%, according to the report. This estimate is conservative in the face of the low rate of infections among individuals older than 50. Moreover, the report authors add, “Standard measurements may underestimate immunity.”

Based on earlier pandemics, population immunity might be even greater. For instance, during the 1957–58 pandemic, individuals who presumably had been exposed to influenza viruses but who lacked cross-reactive antibodies “seemed nevertheless to have been protected, as were some people with low-level, cross-reactive antibodies against distantly related viruses,” Fauci and his collaborators point out. “If the 1976 vaccine is protective without contributing high-level neutralizing antibodies, as many as an additional 8.3% of the population might be partially or fully protected by it, even more than 30 years later.”

During previous pandemics, influenza viruses remained in circulation through “explosive recurrences” in previously unexposed (1889) or partially immune (1918) populations, via antigenic shift among descendants of the 1918 H1N1 virus that swept the world during 1957 and 1968, via reassortments of viral genes, and through antigenic drift. But compared to human populations that endured earlier explosive recurrences of influenza, the current U.S. population has a high (and still increasing) level of immunity to the H1N1 virus.

As for antigenic shift, evidence from the last four pandemics suggests that influenza viruses with only 3 of the 16 possible HA antigens can infect humans. The U.S. population already has high immunity against two of the HA antigens that were not found on pandemic H1N1. Thus, the researchers suspect that antigenic shift might offer the virus a real, but limited advantage. Further, since 1918, antigenic shifts were accompanied by a drop in severity of subsequent flu virus infections.

Antigenic drift is another possible means to keep the virus from going extinct. It can be aggressive, as in H3N2, or lackadaisical, as in seasonal H1N1. Its public health consequences remain difficult to predict.

In any case, the H1N1 flu virus is destined to change or go extinct. Unless major antigenic change occurs, those older than 50 should be “substantially protected” with annual flu vaccines. The authors recommend that those under 50 should be aggressively targeted for vaccination, for the sake of individual protection as well as for contribution to . . . herd immunity.”

“This is a very nice paper that synthesizes much of our knowledge about how influenza viruses behave after emerging in the human population, in order to better understand the future of the 2009 pandemic strain of H1N1,” says Justin Lessler of the Johns Hopkins School of Public Health in Baltimore, Md. “I tend to agree with their speculation that, if this virus survives, it will likely continue to cause only low to moderate mortality. However, as they point out, influenza often surprises.”

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Manganese Complexes Protect D. radiodurans against Radiation Damage

Microorganisms such as Deinococcus radiodurans depend on the antioxidant effects of divalent manganese [Mn(II)] complexes to survive ionizing and ultraviolet radiation, thus avoiding “death by protein damage,” according to Michael J. Daly of the Uniformed Services University of the Health Sciences in Bethesda, Md., and his collaborators. Their emphasis on Mn(II) complexes departs from the views of other researchers, some of whom point to unusual DNA repair proteins and others to the capacity of such cells to produce nitric oxide and components of a general checkpoint system (Microbe, January 2010, p. 8). Details of these recent findings appear in the September PloS ONE.

The radiosensitivities of different bacterial species relate directly to the susceptibility of their proteins to radiation-induced oxidation. While impaired DNA double-strand break (DSB) repair provides the best available correlation with radiation-induced cell-killing, protection of proteins in radiation-resistant bacteria by
Signs of HIV Vulnerability, Possible Susceptibility to Vaccine

“HIV is vulnerable” to specific alleles within the HLA major histocompatibility system, suggesting this virus could be held in check by a properly constructed vaccine, according to Bruce Walker of the Ragon Institute of MGH, MIT, and Harvard in Charlestown, Mass., who spoke during the symposium “Viruses and the Host Response,” convened at the 50th Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC), in Boston, Mass., last September. By studying gene profiles of more than 1,500 individuals whose HIV infections are under control without antiviral drugs, he determined that the genetic control points apparently all lie within HLA loci along chromosome 6. Further, specific amino acids within HLA seem to be crucial for holding HIV in check, keeping it from taking over host-cell “machinery,” perhaps by forcing HIV mutations that undermine its fitness, he says. In terms of developing a vaccine, he adds, “There’s a lot more to do, but there are places for us to look.”

Mn(II) complexes generally provides an explanation for extreme resistance without invoking the need for novel repair pathways or unusual forms of DNA packaging, Daly says. For example, radiosensitive bacteria such as Pseudomonas putida are killed by ionizing radiation because consequent reactive oxygen species (ROS) readily inactivate their DNA repair and replication proteins, thus leading to unrepaired DSBs and cell death.

Daly and his collaborators studied four unrelated bacterial species, D. radiodurans, P. putida, Escherichia coli, and Thermus thermophilus. When protein-free extracts from the latter three microorganisms were mixed with proteins from E. coli and exposed to gamma radiation, the E. coli proteins were extensively oxidized. However, when they used a comparable extract from D. radiodurans enriched in peptides, Mn(II), and orthophosphate, the E. coli proteins were highly protected against radiation-induced damage.

“The big advantage Mn(II) complexes have over antioxidant enzymes is that the complexes, when at high intracellular concentration, bathe and protect all of the proteins all of the time,” Daly says. “In contrast, antioxidant enzymes provide only localized protection within cells, which is not very helpful if a radical suddenly forms right next to you as a protein. The DNA repair proteins of D. radiodurans work so efficiently because they are highly protected from ROS.”

“A key agreement with the authors that protein damages play an important role in cell death, but the ability of Deinococcus radiodurans to survive high doses of ionizing radiation is achieved by a combination of various proteins and mechanisms,” says microbiologist Suzanne Sommer of the Université of Paris-Sud in Paris, France. “A single key to radioresistance, be it a protec-

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