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INTRODUCTION

Influenza: The State of Our Ignorance

THE STARTLING SPREAD OF H5N1 ACROSS MUCH OF THE GLOBE HIGHLIGHTS OUR vulnerability to the emergence of novel subtypes of influenza virus. Yet despite our fears of pandemic human disease, H5N1 is primarily a disease of birds. Olsen and colleagues (p. 384) outline the unseen network of influenza among migratory birds that spans Earth. H5N1 has engendered alarm not only because it is unusually virulent, laying waste to poultry and causing severe economic losses for farmers, but also because it can, with some difficulty, infect humans and other mammals. So far, the virus has killed more than half of the nearly 200 people known to have been infected. Kuiken and colleagues (p. 394) explore the routes through the obstacles to interspecies transmission (the host species barrier) of viruses. Their analysis focuses on which adaptations are needed to facilitate bird-to-human transfer of H5N1. Examples are provided by Shinya* and in a Brevia by van Riel *et al.* (p. 399). These authors show that the virus preferentially binds to cell types bearing specific surface receptors found deep in the lungs, which may partly explain its poor human-to-human transmissibility.

The combination of ever-unfolding modes of variability (Stevens, p. 404) and symptomless transmission makes identification of the virus slow and hinders the implementation of influenza containment. As Lu outlines in his Editorial (p. 337), we urgently need faster and more robust diagnostic tests for field use (an area we will be covering shortly in our pages). Further articles in this special section describe other tools and approaches for preparedness. Smith (p. 392) summarizes the models that have been developed for tracing the rate and spread of pandemic influenza through human populations, including scenarios for the deployment of drugs and development of vaccines. We might be able to buy some time for vaccine manufacture by stockpiling antiviral drugs for immediate use, but that time may be short. Regoes and Bonhoeffer (p. 389) indicate that the generation and transmission of resistant strains could happen quickly. Unfortunately, our knowledge of influenza transmission is incomplete, and more basic data are needed to make models accurate and to give them predictive weight. Seasonal influenza statistics will provide an important insight into the transmission biology of influenza; Viboud *et al.* (p. 447) have used a large data set from the United States to model annual waves of infection.

In a News story (p. 380), Kaiser explores efforts to develop broader influenza vaccines that protect against new strains and perhaps even all influenza subtypes. Antiviral drugs are also sorely needed to fight a pandemic, but oseltamivir, or Tamiflu, has been in short supply. As Enserink describes (p. 382), Roche and other companies are now ramping up production, while scientists are investigating faster and cheaper synthetic pathways that could make the drug affordable to developing countries. In an accompanying podcast, Wills interviews some of the contributing authors and journalists.

An energetic response to H5N1 does not have to be alarmist. We can marshal existing concern about this particular strain of avian influenza to build a long-lasting international infrastructure to monitor and thwart threats from such emerging infections.

—CAROLINE ASH AND LESLIE ROBERTS

*K. Shinya, *Nature* 440, 435 (2006).

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Research Article p. 404; Report p. 447;
and Podcast at www.sciencemag.org/about/podcast.dtl