COMMENTARY

ENCOURAGING DEVELOPMENTS CONCERNING AVIAN INFLUENZA

By the late summer of 2006, global concerns about an avian influenza pandemic had lessened. In large measure, this was due to the waning of cases in countries such as Thailand and Vietnam, and the absence of evidence of significant further spread among sylvatic bird populations elsewhere in the world. Improved surveillance and containment of outbreaks among domestic poultry flocks as well as public health education efforts aimed at instructing people how to handle sick and dead birds have all contributed to reducing spread of the disease.

Despite these successes, the disease has still episodically appeared in Thailand, where two deaths occurred by mid summer. The last was in a 21-year-old man who had handled poultry that had died from an H5N1 infection. Of greater epidemiologic concern were several deaths in Indonesia in mid-year that appeared to be a cluster among family members. Nonetheless, the overall epidemiologic situation as of late summer 2006 was one of reduced transmission to humans.

Efforts to isolate the H5N1 virus from some 29 bird species in Alaska, where the East Asia/Australia and the Pacific/Americas flyways overlap, have, as of August 2006, produced negative results. The U.S. Departments of Agriculture and the Interior have allocated $29 million for the testing of wild birds in Alaska and the western United States. As of the summer of 2006, 3,772 samples had been tested from Alaska, all of which were negative. This positive situation was not altered by the discovery of low pathogenicity H5N1 infections in swans in Michigan in mid-August.

These encouraging epidemiologic and environmental developments have been complemented by recent biological studies that examined the transmissibility of the H5N1 avian influenza virus when it was reassorted with the H3N2 human influenza virus. The result of an international collaborative effort involving scientists from the U.S. Centers for Disease Control and Prevention (CDC), the Centro Nacional de Biotecnologia in Spain, the National Institute of Hygiene and Epidemiology in Vietnam, and the Center for Biomedical and Pharmaceutical Research and Development in Indonesia, these investigations, headed by T.R. Maines of CDC, were
conducted in a ferret model which provides valid comparisons for transmission among humans.

The significance of these findings is further bolstered by the fact that both the 1957 and the 1968 pandemics were due to avian-human reassortant influenza viruses that in the process of reassorting “had acquired human virus-like receptor binding properties.” The ferret model used in these experiments essentially confirmed the efficient transmission of H3N2 and the poor transmission of H5N1 in humans.

Maines et al. found that when they created an H3N2 reassortant virus into which avian virus internal protein genes had been incorporated, the resulting virus efficiently replicated but was inefficiently transmitted. When they inserted four to six human influenza virus internal protein genes into the H5N1 virus, the resulting reassortant virus exhibited poor replication and no transmission. As a result, the authors conclude that “the human virus H3N2 surface protein genes alone did not confer efficient transmissibility, and that the acquisition of human virus internal protein genes alone was insufficient for this 1997 H5N1 virus to develop pandemic capabilities, even after serial passages in a mammalian host.” The authors further note that their experimental results highlighted “the complexity of the genetic basis of influenza virus transmissibility and suggest that H5N1 viruses may require further adaptation to acquire this essential pandemic trait.” In essence then, the current 1997 H5N1 avian influenza virus is not yet poised to begin a pandemic through reassortment of its genetic material with that of current H5N2 influenza viruses.

However, this very encouraging finding does not exclude the possibility that H5N1 might eventually acquire human-to-human transmissibility capabilities through further adaptation or its potential to mutate into a human pandemic virus of the type responsible for the 1918 influenza pandemic. It has now been shown that the 1918 influenza virus was an entirely avian-like virus that mutated and adapted to humans, and that it was not a reassorted virus such as those that caused the 1957 (H2N2) and the 1968 (H3N2) human pandemics.

The encouraging news, however, is that H5N1 does not appear at present to have the ability to become a human pandemic virus through the biological mechanism of reassortment with the prevailing H3N2 human influenza virus. This very important finding by Maines and his colleagues coupled with all of the worldwide public health initiatives focused on H5N1 provide hope that a human pandemic of avian influenza may yet be averted.
REFERENCES