H5N1 Influenza: Evolution and Options for Control

Professor Robert G. Webster, of the Department of Infectious Disease at St. Jude Children's Research Hospital was the special lecturer at this year's ICAAC. Speaking on the topic of the evolution and options available for the control of the deadly H5N1 (avian flu virus) strain, Dr. Webster stressed that the H5N1 virus presents a special threat to the world because of its unique characteristics.

Although it was only identified 10 years ago, H5 shows enormous variability and adaptability. This viral strain has the ability to perform point mutations, reassort itself, and make spontaneous insertions and deletions. To date, H5 has shown no aptitude for recombination. However, Dr. Webster feels it is only a matter of time before this occurs.

The Spanish influenza pandemic (1918) killed 20-50 million people and spread from fowl to man as the H1N1 virus. The 1957, Asian flu killed 1 million and spread through reassortment and replication of the H2N2 virus. The Hong Kong flu (1968) killed 0.5 million and spread through reassortment and replication of H3N2. None of these viruses, however, are as dangerous as the current strains of H9, H7, and in particular, H5.

The H5N1 virus has been evolving into different genotypes and carriers since 1996. The first clade has disappeared, however the second clade has split into three different genotypes and is moving Westward at an accelerated rate. Usually carried by migratory birds and water foul in which the virus is not pathogenic, the virus is deadly in poultry. Surveillance of the poultry markets in South China has documented a 2-3% shedding rate (higher during the winter).

The H5N1 virus first appeared in humans in 2002. A study of a small number of H5N1 influenza victims in Vietnam found evidence of multiple organ dysfunction, diarrhea, and lower respiratory and intestinal tract inflections in the majority of the patients. To date, there have been 251 confirmed infections and 147 human deaths associated with H5.

A new technology, plasmid-based reverse genetics, may prove a quick and effective way to develop a suitable vaccine in the event of a pandemic. Using reverse genetics, scientists can custom make a flu vaccine by assembling genes that code for the desired features [Neumann et al. *Avian Diseases* 2003; Supplement 3] Other research projects aimed at developing a vaccine for this deadly disease include studies in mice using passive immunotherapy with equine hyperimmune globulin $F(ab')_2$ [Lu J, et al *Respiratory Research* 2006] and a clinical trial designed to determine whether having received an H5 vaccine in the past primes the immune system to respond rapidly to another dose of H5 vaccine. Subjects who participate in this study will have participated in a previous vaccine study (involving the A/Hong/Kong/97 virus) during the fall of 1998 at the University of Rochester [http://clinicaltrials.gov/ct/show/NCT00240903].

Dr. Webster concluded his lecture with a call for increased influenza manufacturing capacity. While it is extremely difficult for humans to be infected with the current strains of avian influenza, this is a rapidly evolving virus. A continued focus on vaccine efforts may help mitigate what Dr. Webster sees as an inevitable pandemic.