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Medical Focus - Avian Flu Essentials

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“The more it spreads in birds internationally, the more opportunities it has to interact with animal and human hosts, increasing the chances it could evolve into a human pandemic virus.”

– Dr. Carissa Etienne, Pan American Health Organization (PAHO) assistant director

Dear Colleague:

In the seventeenth letter of the Avian Flu Essentials series, I would like to discuss some of the evolutionary steps that the H5N1 virus has undergone over the last several years. An estimated 200 million birds have died from H5N1 or been culled as a cautionary response since 2003. The number of reported avian influenza outbreaks and the variety of bird species infected have dramatically increased.

Researchers have striven to elucidate which key mutations are needed to transform H5N1 into a strain which could potentially cause a pandemic. A genetic analysis of the avian virus that was responsible for the 1918 pandemic demonstrated that changes in about 25 out of 4,400 amino acids was sufficient for this change to happen. A study that came out this month suggests that human-to-human transmission has been ineffective to date because the virus currently binds to the lower respiratory tract. A few mutations in the hemagglutinin (H) gene could allow H5N1 to bind to receptors in the upper respiratory tract instead. This would result in enhanced human transmissions because the virus could be shed more easily through coughing.

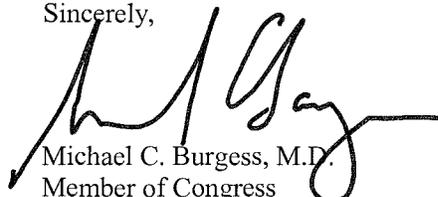
In addition, the virus has evolved into two distinct clades. These genetic variations reflect the spread of the disease and that H5N1 is evolving. An article on the reverse of this letter elaborates on this concept.

Furthermore, a protein has been attributed to disrupt cellular processes and play a role in the high mortality of H5N1. It was reported that the NS1 proteins in this virus originated from an avian source, while the lower mortality avian flu viruses in the 1957 and 1968 outbreaks contained NS1 protein derived from a human source. The individual's own immune response to the virus is also thought to contribute to its mortality. The release of excessive inflammatory chemicals results in more damage to the host's lungs.

The successful infection of mammals by avian influenza is another cause of concern. In October of 2004, zoo tigers in Thailand died of H5N1 after consuming infected chicken. More recently, cats in Germany and Austria have died of avian influenza. The presence of this virus in predatory mammals is due to the fact that they hunt birds, some of which are infected with H5N1. Unlike in humans, the virus is found in the upper respiratory tract of these animals, therefore transmission between cats is more likely to occur and must be monitored more closely.

Steps to minimize cross species adaptability are vital. For example, pets should be quarantined if they become infected with avian influenza. Animals should also be kept indoors if infected birds are found in the area. Adequate surveillance and protective measures are still effective barriers to keep this virus from jumping from poultry to humans.

Sincerely,



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From the Washington Post, *US study defines two clear bird flu strains*, March 20, 2006:

ATLANTA (Reuters) - The H5N1 strain of bird flu in humans has evolved into two separate strains, U.S. researchers reported on Monday, which could complicate developing a vaccine and preventing a pandemic.

One strain, or clade, made people sick in Vietnam, Cambodia and Thailand in 2003 and 2004 and a second, a cousin of the first, caused the disease in people in Indonesia in 2004.

Two clades may share the same ancestor but are distinct -- as are different clades, or strains, of the AIDS virus, the team from the U.S. Centers for Disease Control and Prevention found.

"Back in 2003 we only had one genetically distinct population of H5N1 with the potential to cause a human pandemic. Now we have two," said the CDC's Rebecca Garten, who helped conduct the study.

Speaking to the International Conference on Emerging Infectious Diseases in Atlanta, Garten said the pool of H5N1 candidates with the potential to cause a human influenza pandemic is getting more genetically diverse, which makes studying the virus more complex and heightens the need for increased surveillance.

"As the virus continues its geographic expansion, it is also undergoing genetic diversity expansion," Garten said in a statement.

The H5N1 strain of bird flu has spread across Europe, Africa and parts of Asia and killed about 100 people worldwide and infected about 180 since it re-emerged in 2003.

Although it is difficult to catch bird flu, people can become infected if they come into close contact with infected birds. Scientists fear the virus could mutate into a form that could pass easily between humans, triggering a pandemic in which millions could die.

All influenza viruses mutate easily, and H5N1 appears to be no exception.

"Only time will tell whether the virus evolves or mutates in such a way that it can be transmitted from human to human efficiently," Garten said.

The U.S. Health and Human Services Department has already recognized the two strains and approved the development of a second H5N1 vaccine based on the second clade.

Several companies are working on H5N1 vaccines experimentally, although current formulations are not expected to protect very well, if at all, against any pandemic strain.

A vaccine against a pandemic flu strain would have to be formulated using the actual virus passing from person to person.

For their study, Garten and colleagues analyzed more than 300 H5N1 virus samples taken from both infected birds and people 2003 through the summer of 2005.

The majority of the viruses, including all the human cases, belonged to genotype Z. Now there are two clades of the Z genotype. There were also small numbers of viruses in birds that were genotype V or W or recently identified genotype G.