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# DATELINE UC DAVIS

News for Faculty and Staff of the University of California, Davis

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## Experts keep wary eye on global flu scene

By Pat Bailey

Somewhere in the world, a farmer tends a small flock of chickens and a few pigs near a rice paddy filled with wild ducks. In this bucolic setting, say UC Davis influenza experts, the perfect storm is building.

Among the chickens, ducks, pigs and farmer moves a family of influenza, or flu, viruses that could one day produce a human flu capable of sweeping the world in a global epidemic.

The influenza viruses have their home base, or "reservoir," in wild duck populations. In ducks, the virus reproduces in the intestinal tract and spreads to other wild ducks and birds, as well as to domestic poultry. These avian influenza, or bird flu, viruses may cause few symptoms in ducks, but can quickly wipe out an entire flock of chickens, killing some on the day they first show symptoms.



Carol Cardona, a Cooperative Extension poultry veterinarian and an authority on avian influenza, surveys some of the feathered residents. Influenza viruses have their home "reservoir," in wild duck populations. Experts like Card specialize in flu viruses that could mutate and cross fire to species. (Debbie Aldridge/UC Davis)

In humans, the flu appears as a severe respiratory infection, complete with a fever, sore throat and It can turn into a fatal form of pneumonia as it shuts down the body's ability to breathe.

"In the American public, people talk about the flu as when you have the sniffles," said Nicole Baum who studies influenza in mice at UC Davis' Center for Comparative Medicine. "What they don't understand is that if you really ever have had the flu, you know you've had it."

The first description of influenza is credited to the Greek physician Hippocrates around 400 B.C., and to Provost Virginia Hinshaw, who spent more than 20 years researching influenza, including studying its characteristics and transmission of influenza viruses.

During an average year, 36,000 people die of influenza in the United States alone, reports the U.S. Center for Disease Control and Prevention. Most vulnerable are the elderly, young children and people whose immune systems are weakened by some other ailment.

"All you have to do to know how bad flu can be is to talk with someone in your family who was alive in 1918," notes Carol Cardona, a Cooperative Extension poultry veterinarian and an authority on avian influenza. "There were many orphans."

During 1918 and 1919, the world experienced a pandemic of influenza. In just four to six months, a strain of flu spread around the world. It reoccurred in several waves over two years, killing an estimated 40-50 million people, according to the World Health Organization.

Scientists who know the deadly potential of the influenza viruses fear that, despite all the advances of modern medicine, just such a pandemic may be looming on the horizon. Recent years have seen an increase in outbreaks of avian influenza, along with the spread of those viruses, in a relatively few humans.

"We started to see birds infecting humans in 1997 in Hong Kong," said Baumgarth. "And in February of that year there was a case of avian influenza in humans in the Netherlands."

While the human flu cases are troubling, scientists are equally concerned that avian influenza seem to have found its way into pigs in some parts of the world.

"The pigs are known as the potential mixing vessel," said Hinshaw, explaining that an avian flu virus and a human flu virus might simultaneously infect a pig who also has swine influenza virus, and then the viruses could swap genetic material. The resulting virus might easily spread to humans, which would mean no immunity to the new strain of influenza.

It's the influenza viruses' uncanny ability to readily change their own genetic makeup that worries scientists. Those who study influenza describe a flu virus as a microscopic ball, surrounded by a membrane. Within the ball, all the genetic material of the virus is contained in just eight gene segments, which have a high affinity for resorting and recombining.

"Mutations in the human flu viruses happen every year, but they are relatively small," said Baumgarth. "The fear out there is that there will be a much bigger change in the virus some year."

"Influenza is kind of sloppy in its reproduction," said Hinshaw. "It can accommodate a lot of 'mistake' changes and still survive."

Every year public health officials and vaccine makers scramble to keep up with the flu viruses' penchant for reinventing themselves. Flu viruses around the world are sampled to determine what virus proteins should be included in the next season's flu vaccine for North America.

For humans, the vaccine is the front line of defense against influenza.

"Influenza is really quite well understood," said Baumgarth. "What really needs to be done, as far as vaccine application, is to find a way to make vaccines in a way that will allow us to rev up vaccine production in the event of an epidemic."

Currently, flu vaccines are grown up in chicken eggs. The speed of vaccine production is limited by the labor-intensive processing method and by the availability of eggs. It takes several months to produce enough stock of vaccine to carry the United States through flu season.

Baumgarth's laboratory is studying influenza in mice, focusing on a group of B-1 cells in mice that produce antibodies against infection, even when the animal is not experiencing an infection.

"If one understands how those cells are active, one could exploit them," she said. "I could imagine that understanding B-1 cells could result in making vaccines that are more broadly protective."

For avian influenza expert Cardona, flu poses a threat both to public health and the economic stability of the California poultry industry.

"When a bird dies, the producer loses everything invested in that bird," she said. "But more than the economic fear that could arise could keep people from eating poultry. For that reason, our poultry producers are strongly allied to prevent influenza from coming into the United States."

Because avian influenza can be spread through birds, the United States forbids importation of live birds from countries infected with avian influenza, Cardona said.

Perhaps some of the greatest points of vulnerability for California are the flea markets, swap meets and auctions where live birds are sold on a small scale.

Because these sales venues are the "perfect setup for the transmission of the virus," Cardona visits these venues to educate both buyers and sellers, telling them how to protect their birds against infection and to recognize the symptoms of a sick bird.

In addition to her laboratory work, examining how long the influenza vaccine is active in chickens, Cardona works extensively with commercial poultry producers to provide them with the information they need to safeguard their flocks against infection and to recognize health problems in their flocks.

"People talk about the threat of bioterrorism, but this virus doesn't need that kind of help," Cardon

She advises producers to keep their birds -- even free-range flocks -- in secure chicken houses, to restrict visitor access to their farms and to educate their employees against purchasing birds at markets that include birds smuggled in from infected countries.

"We've also really tried to instill the concept of the good-neighbor policy," she said, noting that producers are encouraged to establish agreements with other nearby poultry farms to not move any birds if a problem is suspected and to notify neighboring producers of such problems.

Both human and avian health officials are hopeful that such preventive vigilance and research aimed at developing new vaccines will help keep the dreaded flu pandemic at bay.

"Through research, we've made a lot of progress," said Hinshaw.

"We now have a much better understanding of the virus, we know now that it has a huge reservoir nature, and we have better drugs for treating influenza. And basic influenza research has been amazingly helpful in understanding diseases like AIDS and SARS (Severe Acute Respiratory Syndrome)."

Despite these advances, however, she stresses that the many strains of human and avian flu, will not go away.

"Influenza," said Hinshaw, "is very much a survivor."

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