

RESEARCH AT THE UNIVERSITY OF MARYLAND

DANIEL PEREZ

The Infectious Range of Flu

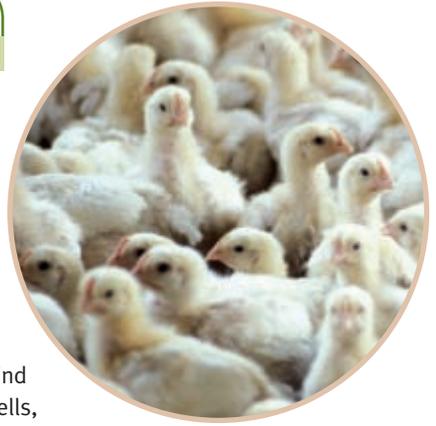
Since the H5N1 strain of avian flu started crossing into people, killing about half the people it has infected, the virus has stoked fears of a human pandemic. Should an infection spread to animals in the United States, poultry farmers and others worry about having to cull large numbers of birds. Contaminated meat could also potentially infect people.

Daniel Perez, an associate professor of veterinary medicine at the University of Maryland, has been studying influenza since 1990. In graduate school, he studied the molecular complex that allows the flu virus to replicate. In 2000, Perez began to focus on avian influenza and the factors that dictate which species a particular strain infects. "Basically, we try to learn what it takes in a virus and what it takes in a host to end up with a productive infection and transmission," he says. "We look at what it takes for viruses to cross species."

The first known cases of human H5N1 infection occurred in 1997. Before then, an H5 strain of avian flu had never been known to cross into humans. The infections immediately raised alarm because H5 strains are particularly deadly. "They are definitely more lethal and we're trying to understand why," Perez says.

PHOTOGRAPHY BY
Edwin Remsberg





Any given year, the approximate number of people infected with the flu is roughly the same, but in some seasons, flu strains are far more virulent. Lethality may or may not be connected to ease of transmission, says Perez. His laboratory studies both the factors that affect transmission of influenza and its virulence. Features on the viral surface and components inside the virus appear to affect both characteristics.

The processes that affect transmission are the main focus of Perez's research. "Transmission seems easy to understand, but it's difficult to study," he says. For instance, consider the number of birds that would have to be exposed to a virus to see whether it infects 10 percent or just 1 percent of the animals. To avoid the statistical problems, Perez and his research team study viral infection rates in cell culture and are working to develop animal models where infection rates are close to all or nothing.

It appears that even very small changes in a flu virus can profoundly affect its characteristics. Perez recently found that changing a single amino acid—or protein building block—in an avian H9 virus allowed it to spread among human cells.

To discover the key properties that allow a virus to spread among different species, Perez and his team usually start with viruses found in nature and test their ability to infect species in the lab, whether chickens, quail, turkey, ducks, mice, or ferrets. The research team looks for changes that appear to help a virus transmit across species and then tests whether those changes actually have the suspected effect by genetically engineering viruses with the same alterations.

Through genetic engineering, the researchers can detect the specific parts of particular proteins that affect the germs' ability to spread or cause illness.

Fortunately, the influenza genome is small, coding for just

10 to 11 proteins depending on the strain, and the functions of the proteins are quite well understood. For example, hemagglutinin proteins on the surface of the virus particle recognize and bind to specific sugars on animal cells, which vary, often in subtle ways, depending on the species.

Flu viruses are prevalent in the intestines of aquatic birds, such as ducks. Viruses that infect ducks are not likely to infect humans directly since humans and ducks do not have the same kind of cell surface sugars. But the structures of human sugars overlap with those found in pigs and also with those found in land-based birds such as chickens, turkeys, and quail.

Perez's group studies in particular detail H9 viruses. These viruses are less lethal than H5 strains but also have the potential to start a pandemic because they are common in birds and able to infect and sicken humans. "We ask how are the viruses changing, and are they changing in ways that make them more similar to human influenza viruses?" says Perez. In the lab, ferrets are used to model transmission to humans, since the two species respond similarly to flu viruses. In fact, the first human flu viruses were isolated from ferrets more than 70 years ago.

Ultimately, Perez and his research group are trying to mimic in a controlled way the changes that the flu virus goes through in nature. In the lab, the researchers not only replicate the changes that happen in nature, but probe and dissect what those changes mean. That level of understanding is the best bet we have for foreseeing and preventing a human pandemic. —Karin Jegalian



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