New H7N7 bird flu strain discovered that could pose threat to humans

H7N7 virus, found in chickens at markets in China, can kill ferrets, which are used as proxies for people in flu research

Ian Sample, science correspondent
theguardian.com, Wednesday 21 August 2013 18.51 BST

A new strain of bird flu that can infect and kill animals has been found in chickens at live poultry markets in China.

Scientists discovered the strain by accident while testing chickens, ducks, geese and other birds for the H7N9 virus that has infected more than 130 people and killed 40 since it was first detected in March.

The new strain, H7N7, poses a potential threat to people, according to lab tests which found that the virus caused severe pneumonia in ferrets, which are used as proxies for humans in flu research.
An international team led by Yi Guan, a flu specialist at the University of Hong Kong, took samples from chickens, ducks, geese, pigeons, partridges and quail at markets in Shandong and Zhejiang provinces to the north and south of Shanghai, and further samples from markets in Guangdong. They found H7N9 in chickens in Rizhao, Shandong, and the new H7N7 in Wenzhou, Zhejiang.

The discovery that H7N9 still lurks in chickens at markets has raised fears that it could break out again in people and evolve into a more virulent form. Genetic tests suggest that the virus arrived in China with migratory water fowl from east Asia, jumped into domestic ducks, and then into chickens on at least two occasions.

Guan said Chinese authorities may have to close hundreds of live poultry markets for good to prevent lethal strains of bird flu spreading through the human population.

The March outbreak of H7N9 led health officials in China to close scores of live poultry markets in the Shanghai area, but many reopened within a month or two when cases of human infections began to fall. At the time, Keiji Fukuda, an assistant director general at the World Health Organisation, said it was unlikely the virus had "simply disappeared".

Guan's study confirms the virus is still circulating in birds, alongside related viruses that may also be a danger to people. "The virus is still at large. It's still in the birds," Guan said. "We shouldn't think that it will disappear naturally."

Most people who caught H7N9 visited live poultry markets before they fell ill. Markets in Shanghai sell about 175 million chickens a year, 120 million of which are bought live, according to the city's agricultural department.

Since they are the source of so many infections, Guan said, "the authorities should seriously reconsider having live poultry markets in big cities". Instead, the birds should be killed at a central slaughterhouse and sent on to market, to reduce human contact with the live animals.

The Chinese government is considering closing markets in Nanjing and Suzhou as part of a pilot project, and ultimately hopes to shift consumer tastes towards frozen chicken.

Writing in the journal Nature, Guan calls for long-term surveillance of viruses in birds, to give health authorities early warning of dangerous strains that emerge.

"The discovery of a novel H7N7 lineage that can infect ferrets reminds us that even if H7N9 does not return, there are risks lurking amongst the great diversity of avian influenza viruses," said Peter Horby at Oxford University's clinical research unit in Hanoi, Vietnam.
"The data do all point to live poultry markets being a major source of human infections with H7N9 virus," he added. "Moving live poultry markets out of urban areas may reduce the frequency of contact between infected birds or contaminated environments and humans, but there is a range of interventions that could reduce the risks of these markets being hubs for transmission and reservoirs of infection."

In the past, better cleaning procedures, bird-free "rest days", and segregation of animals at markets helped slow the spread of the H5N1 strain of bird flu.
Ducks were bird flu 'melting pot'

By James Gallagher
Health and science reporter, BBC News

Ducks were the melting pot of viruses that led to the new bird flu emerging in China early this year, according to Chinese scientists tracking the evolution of the virus.

Ducks picked up viruses from migrating birds and passed them onto chickens.

The study, published in the journal Nature, showed humans were probably then infected with H7N9 due to contact with chickens at live poultry markets.

There have been 133 human cases of the bird flu and 43 deaths.

The team, including researchers at the Shantou University Medical College, were trying to trace the root of the outbreak.

They took samples from 1,341 chickens, ducks, geese, pigeons, partridges and quail as well as faecal and water samples from live poultry markets.

By comparing the similarities and differences between the genetic codes of influenza viruses in each of the animals, scientists can work out how the virus evolved and spread.

Their report said: "Domestic ducks seem to act as key intermediate hosts by acquiring and maintaining diverse influenza viruses from migratory birds.

"This probably led to outbreaks in chickens resulting in the rapid spread of the [virus] through live poultry markets which became the source of human infections."

Market danger

There have been very few cases since China introduced controls on live poultry markets.

The authors added: "To control H7N9 and related viruses ultimately it is necessary to reconsider the management of live poultry markets in urban areas."

The study also uncovered a similar bird flu called H7N7, which appears able to infect mammals. The scientists said this group of H7 bird flus may "pose threats beyond the current outbreak".

Commenting on the research, Dr Peter Horby, from the Oxford University Clinical Research Unit in Vietnam, said: "This kind of microbial forensics is essential in helping us piece together the origin of novel avian influenza viruses such as H7N9.

"When combined with analyses of poultry production and marketing systems, it can help us identify practices that might reduce the risks of H7N9 and other novel viruses re-emerging.

"Whilst this brings us closer to understanding the pathway to emergence, more detective work is needed to fully reveal the ecology..."
and source of H7N9 viruses, which seem to be concentrated in live poultry markets but elusive elsewhere in the production chain.

"The discovery of a novel H7N7 lineage that can infect ferrets reminds us that even if H7N9 does not return, there are risks lurking amongst the great diversity of avian influenza viruses."
Ducks played key role in China's H7N9 flu outbreak, scientists say

The World Health Organization says that at least 135 people in China have been sickened by the H7N9 flu strain, and 44 have died. Most likely, these victims got the virus from chickens sold in live poultry markets. But where did the chickens get it? From ducks, who got it from wild migratory birds, scientists now say.

In fact, migratory birds that spent time in Hong Kong probably transferred the key N9 influenza genes to domestic ducks at least twice before the H7N9 outbreak began in March of this year, according to a report published Wednesday by the journal Nature.

In addition, wild migratory birds from Eurasia carried an H9N2 flu strain that contributed some genes to the H7N9 strain that went on to infect humans.
But the researchers emphasized the key role of ducks in bringing all the ingredients together to create H7N9.

“Domestic ducks seem to act as key intermediate hosts by acquiring and maintaining diverse influenza viruses from migratory birds, by facilitating the generation of different combinations of [...] viruses, and by transmitting these viruses to chickens,” they wrote.

Influenza viruses are compact infectious agents controlled by only eight genes. They are known by their “H” (hemagglutinin) and “N” (neuraminidase) genes, which contain instructions for the two proteins that stud the exterior of the virus. Hemagglutinin allows flu particles to attach to host cells. After they get inside and replicate, neuraminidase allows the new flu particles to exit and find new cells to infect.

The hemagglutinin in the H7N9 strain has a mutation that has been shown to help the virus replicate in the upper respiratory tract of birds, the researchers reported. But the virus doesn’t seem to have any mutations that make it particularly well-adapted to humans. Nothing in the genetic history of the virus suggests that a mammalian host was key to its evolution, they said.

As the scientists investigated the origin of the H7N9 flu virus, they also discovered a closely related H7N7 virus in chickens sold at live poultry markets in the Chinese province of Wenzhou. The N7 in this strain has been circulating in ducks since at least 2010, they determined.

Although H7N7 has never been detected in people, the researchers wanted to see whether it was capable of sickening mammals. So they infected a dozen ferrets – animals often used as stand-ins for people in flu experiments because their symptoms are similar to ours – and saw signs that the virus became established after two days. Over time, virus particles could be found in the noses, tracheas, lungs and lymph nodes of the animals.

The surprise discovery of H7N7 is a concrete sign that the threat of flu viruses from wild birds extends beyond H7N9, the researchers said.

“The current pandemic threat extends beyond the H7N9 virus,” they wrote. “To control H7N9 and related viruses ultimately, it is necessary to reconsider the management of LPMs (live poultry markets) in urban areas.”
Emergence of H7N9 avian flu hints at broader threat

Evolutionary path shows related virus can infect some mammals, raising concerns about spread.

Beth Mole
21 August 2013

The H7N9 influenza virus did not emerge alone. Researchers have traced the evolution of the deadly avian flu currently spreading in China, and have found evidence that it developed in parallel with a similar bird flu, H7N7, which can infect mammals

Although there is no evidence that this H7N7 strain will infect humans, the authors of a study published today in Nature say that their finding reinforces the idea that H7 avian viruses are constantly mixing and exchanging genetic material — a process known as reassortment — in Asian poultry markets. This raises the threat that H7N7 will reassort and become able to spread to humans.

"H7 is out there in China and not just in the form of this H7N9," says Richard Webby, a co-author of the study and an influenza specialist at St. Jude Children’s Research Hospital in Memphis, Tennessee.

Ducks, in particular, act as living mixing bowls for avian viruses. Domestic species encounter a large catalogue of wild-bird viruses, which swap genes to form versions that can spread to chickens and to humans.

Better surveillance of Chinese bird populations is needed to monitor the emergence of dangerous viruses such as H7N9, says lead author Yi Guan, an influenza specialist at the University of Hong Kong. In China, the virus has infected 135 people and resulted in 44 deaths since February. "This is a very different influenza ecosystem from other countries," says Guan.

Tracking changes

Guan's team sampled wild birds and poultry markets around Shanghai in April, weeks after the H7N9 outbreak began there. The researchers collected throat and intestinal swabs from 1,341 birds, including chickens, ducks, geese, pigeons, partridges and quails, plus 1,006 water and faecal

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samples from bird markets. About 10% of samples tested positive for an influenza virus; of those, 15% were an H7 virus.

When the team sequenced the two viruses’ genomes and compared them to other bird-flu strains, they found H7N9 and H7N7 to be hybrids of wild Eurasian waterfowl strains, such as H7N3 and H11N9. The scientists think that those viruses swapped genes in domestic ducks before spreading to chickens, where they traded genes with a common chicken virus, H9N2. That improved the viruses’ ability to spread in chickens, which live in close contact with humans.

So far, the latest H7N7 strain has not infected a human. But Guan and his team found that ferrets could become infected with the virus, suggesting that a spread to humans is possible.

"It really shows that the emergence of these types of viruses can happen at any time," says Camille Lebarbenchon, a viral ecologist at the University of Reunion Island in St Denis, France, who has also studied the evolution of H7N9 using archived viral sequences\(^2\).

David Morens, an influenza researcher and senior adviser at the US National Institutes of Health in Bethesda, Maryland, says that the evolutionary pathway that the viruses followed suggests that more surveillance and better sanitation practices at poultry markets are crucial to monitoring risks to human health.

But Ian Lipkin, an epidemiologist at Columbia University in New York City, says that surveillance is not a foolproof solution. "It’s inevitable that something is going to slip through the cracks."

*Nature*  doi:10.1038/nature.2013.13584

**References**

New deadly flu launched by live bird markets

The new strain of bird flu that killed at least 40 people in China this year likely evolved through close contact between ducks and chickens in markets selling live birds, according to a genetic analysis published in the journal Nature. At least 130 people became infected during the outbreak, which began in March.

“We clearly identified that the source of human infection came from the infected chickens, not any other types of birds,” said Yi Guan, a professor of virology at the University of Hong Kong and one of the study authors. The analysis also shows the virus was shed from the birds' oral or upper respiratory tract, not from fecal material. According to Yi, this suggests that H7N9 reasonably well adapted to infect humans, a finding that's supported by other research.

The research group also discovered a previously unrecognized variety of bird flu – an H7N7 strain, with a genetic makeup similar to the novel H7N9 strain. The H7N7 strain was also able to infect mammals in laboratory conditions.

Any variety of influenza is broadly characterized by two of its proteins: the type of hemaglutinin (“H”) and the type of neuraminidase (“N”).

The highly technical analysis concluded that domestic ducks likely served as a melting pot, acquiring a variety of influenza viruses that typically circulate in wild birds. That stew resulted in a strain that shared genetic material with influenza viruses that were already established in the chicken population. The combination was made possible by ducks and chickens being in close contact in live poultry markets, or LPMs.

“This probably led to outbreaks in chickens, resulting in the rapid spread of the novel reassortant H7N9 lineage through LPMs, which then became the source of human infections,” the authors wrote. New infections came to a halt after LPMs in China were ordered shut on a temporary basis.

“At the moment we all have our fingers crossed and have intensive surveillance in place,” said Dr. William Schaffner, who chairs the department of preventive medicine at Vanderbilt University. “Fortunately H7N9 has stopped (for now),” which Schaffner also attributes to the serious interventions at poultry markets in China.

While the markets played a crucial role in the emergence of the novel flu strain, Yi said it is possible to operate them more safely. He told CNN that chickens should be kept separate from ducks and other poultry, and that markets should be closed one or two days per month for thorough cleaning. Beyond that, Yi warns that regular testing is needed to spot potentially dangerous viruses before they start to spread.

“Most important is to conduct influenza surveillance. You need to know what kind of viruses are circulating in these birds at the markets.”

Post by: Caleb Hellerman - CNN Medical Supervising Producer
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