

## NEWS

# Alarms ring over bird flu mutations

Scientists studying virus samples from the human outbreak of avian flu in Turkey have identified three mutations in the virus's sequence. They say that at least two of these look likely to make the virus better adapted to humans.

The Turkey outbreak is unusual, because of the large family clusters of cases; the fact that many of those infected have only mild symptoms; and the speed with which infections have arisen — twenty cases, including four deaths, in less than two weeks. So scientists are urgently trying to establish whether the virus is behaving differently in this outbreak from previous ones in Asia. In particular, international teams are investigating the possibility that the virus is moving between people.

"With such a large number of cases within such a short period of time, human-to-human transmission is something that we've had to consider," says Maria Cheng, a spokeswoman at World Health Organization (WHO) headquarters in Geneva.

As *Nature* went to press, samples from the first two teenagers in the country to die had been sequenced by a WHO collaborating centre at the National Institute of Medical Research (NIMR) in London.

The results so far are not comforting. The first mutation found, announced last week, involves a substitution in one sample of an amino acid at position 223 of the haemoagglutinin receptor protein. This protein allows the flu virus to bind to the receptors on the surface of its host's cells.

This mutation has been observed twice before — in a father and son in Hong Kong in 2003, and in one fatal case in Vietnam last year. It increases the virus's ability to bind to human receptors, and decreases its affinity for poultry receptors, making strains with this mutation better adapted to infecting humans.

The same sample also contained a mutation at position 153 of the haemoagglutinin protein, *Nature* has learned. Cheng says this information was not included in WHO statements, because "it is not clear what role this particular change plays".

Finally, both samples from the Turkish teenagers show a substitution of glutamic acid



The recent outbreak of bird flu in Turkey has thrown up viruses with mutations that threaten humans.

with lysine, at position 627 of the polymerase protein, which the virus uses to replicate its genetic material. This mutation has been seen in other flu sequences from Eurasian poultry over the past year. It was also present in the one person who died during an outbreak of H7N7 in the Netherlands in 2003, and in a few

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people in Vietnam and Thailand.

The polymerase mutation is one of the ten genetic changes that gave rise to the 1918 pandemic flu virus. Like the 223-haemoagglutinin mutation, it signals adaptation to humans, says Alan Hay, director of a WHO influenza laboratory at the NIMR. "There is this glutamic acid-lysine

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