

Key to spread of bird flu revealed

Mark Henderson, London
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SCIENTISTS have explained why the bird flu virus does not readily spread from person to person, shedding light on how it would need to mutate to cause a human pandemic.

The H5N1 influenza strain struggles to infect cells high up in human airways, significantly limiting the extent to which victims can pick up the virus and pass it on by coughing and sneezing, research has shown.

The findings, from separate teams in the US and The Netherlands, suggest H5N1 will probably have to evolve substantially if it is to become easily transmissible between people - the key step that would make a pandemic possible.

The research highlights several critical mutations that would ring alarm bells if spotted in virus samples, allowing for improved surveillance of the threat it poses to humans.

While the H5N1 virus is highly virulent when contracted by humans, with 184 cases and 103 deaths confirmed by the World Health Organisation, it does not easily infect people, and all the victims so far picked it up by direct contact with birds.

This resistance to H5N1 stems from the way the virus binds to cells in human airways, the studies show. While ordinary human strains of influenza readily infect cells in the windpipe, only cells much deeper inside the lungs have the right receptors that allow H5N1 to dock with them.

This is important for two reasons: the upper airway is more likely to be exposed to the virus than the inner pockets of the lungs, and infections in the windpipe are also more readily passed on.

When the virus is present only in the lower respiratory tract, it is unlikely to be released by coughing and sneezing. However, people with upper airway infections are likely to expel millions of virus particles with every splutter.

"Deep in the respiratory system, cell receptors for avian viruses, including avian H5N1 viruses, are present," said Yoshihiro Kawaoka, of the University of Wisconsin-Madison, whose study is published in current edition of the journal *Nature*.

"But these receptors are rare in the upper respiratory system. For the viruses to be transmitted efficiently, they have to multiply in the upper system so they can be transmitted by coughing and sneezing," Dr Kawaoka said.

"Our findings provide a rational explanation for why H5N1 viruses rarely infect and spread from human to human, although they can replicate efficiently in the lungs."

The second study, led by Thijs Kuiken, of the Erasmus Medical Centre in Rotterdam, reached similar conclusions and is published in the journal *Science*.

It found the airways of cats and ferrets are affected by H5N1 in similar fashion to humans, making both good animal models for further research.

Dr Kawaoka said the research pinpoints several key mutations in the haemagglutinin protein that the virus uses to bind to cells which would be of grave concern if they were to be identified in H5N1.

"Mutations in the haemagglutinin for avian H5N1 viruses to recognise human receptors are needed for the virus to become a pandemic strain," he said. "No one knows whether the virus will evolve into a pandemic strain, but flu viruses constantly change. Certainly, multiple mutations need to be accumulated for the H5N1 virus to become a pandemic strain."

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