Human nose too cold for bird flu, says new study

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Avian flu infects the guts of birds.

(PhysOrg.com) -- Avian influenza viruses do not thrive in humans because the temperature inside a person's nose is too low, according to research published today in the journal *PLoS Pathogens.* The authors of the study, from Imperial College London and the University of North Carolina, say this may be one of the reasons why bird flu viruses do not cause pandemics in humans easily.

There are 16 subtypes of avian influenza and some can mutate into forms that can infect humans, by swapping proteins on their surface with proteins from human influenza viruses.

Today's study shows that normal avian influenza viruses do not spread

extensively in cells at 32 degrees Celsius, the temperature inside the human nose. The researchers say this is probably because the viruses usually infect the guts of birds, which are warmer, at 40 degrees Celsius. This means that avian flu viruses that have not mutated are less likely to infect people, because the first site of infection in humans is usually the nose. If a normal avian flu virus infected a human nose, the virus would not be able to grow and spread between cells, so it would be less likely to damage cells and cause respiratory illness.

The researchers also found that when they created a mutated human influenza virus by adding a protein from the surface of an avian influenza virus, this mutated virus struggled to thrive at 32 degrees Celsius. This suggests that if a new human influenza strain evolved by adopting proteins from an avian influenza virus, this would need to undergo further changes in order to adapt to the conditions in the human body.

The researchers reached their conclusions by growing cells from the human airway and infecting them with different human and avian influenza viruses, including H5N1, to see how well the viruses grew and spread. The human influenza viruses grew equally well in the cells whether they were maintained at 37 degrees Celsius, our core body temperature, or at 32 degrees Celsius, the temperature of the nose. In contrast, the four avian influenza viruses tested grew well at 37 degrees Celsius but grew very slowly at 32 degrees Celsius.

When the researchers added proteins from an avian influenza virus to a human influenza virus, the human influenza virus also grew slowly and struggled to replicate at 32 degrees Celsius.

As viruses kill the cells they infect, the researchers also measured the extent of cell death in the model. This showed that at 32 degrees Celsius, far fewer cells died as a result of infection with avian influenza

compared with human influenza, supporting the idea that the avian virus could not thrive at that temperature.

Professor Wendy Barclay, one of the authors of the study from the Division of Investigative Science at Imperial College London, said: "Bird viruses are out there all the time but they can only cause pandemics when they undergo certain changes. Our study gives vital clues about what kinds of changes would be needed in order for them to mutate and infect humans, potentially helping us to identify which viruses could lead to a pandemic.

"It would be impossible to develop vaccines against all 16 subtypes of avian flu, so we need to prioritise. By studying a range of different viruses in systems like this one we can look for warnings that they are already beginning to make the kinds of genetic changes in nature that mean they could be poised to jump into humans; animal viruses that spread well at low temperatures in these cultures could be more likely to cause the next pandemic than those which are restricted," added Professor Barclay.

The research was funded by the Medical Research Council in the UK and by the NIH in the USA.

More information: "Avian Influenza Virus Glycoproteins Restrict Virus Replication and Spread through Human Airway Epithelium at Temperatures of the Proximal Airways" PLoS Pathogens, Thursday 14 May 2009.

Provided by Imperial College London (news : web)