

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 haemagglutinin 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 haemagglutinin 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 lycine, 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-haemagglutinin mutation, it signals adaptation to humans, says Alan Hay, director of a WHO influenza laboratory at the NIMR. "There is this glutamic acid-lysine

O. OHSAL/AP

Doctor admits *Lancet* study is fiction

A Norwegian researcher dreamed up the lives and lifestyles of some 900 people — and used them in a study on cancer. Then, last October, Jon Sudbø had his results published in *The Lancet*.

The revelation comes hard on the heels of the Woo Suk Hwang scandal, in which several important advances in human cloning reported by the South Korean researcher turned out to be faked.

The blatant nature of Sudbø's fiction emphasizes questions already being asked about the effectiveness of peer review, even in top journals, and about who should be responsible for catching fraud (see page 243).

The latest deception was discovered by

Camilla Stoltenberg, a director of epidemiology at the Norwegian Institute of Public Health in Oslo, who was catching up on her literature reading over Christmas. Sudbø's paper claims to analyse a public-health database and show that taking anti-inflammatory drugs can reduce the incidence of mouth cancer (J. Sudbø *et al.* *Lancet* 366, 1359–1366; 2005). "I was surprised because it refers to the Cohort of Norway, for which I am responsible," Stoltenberg says. She knew that this could not have been the source of the lifestyle data as the paper claimed.

Last week, Sudbø, who is based at the Norwegian Radium Hospital in Oslo,



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flip," he explains. "Glutamic acid is associated with flu-virus replication in birds, and lysine is in primates."

The Turkey strains are the first in which the polymerase and receptor-binding mutations have been found together. They could make it easier for humans to catch the virus from poultry. But they might also favour human-to-human transmission. This is because the polymerase change helps the virus to survive in the cooler nasal regions of the respiratory tract, and the haemagglutinin mutation encourages the virus to target receptors in the nose and throat, rather than lower down in the lungs. The virus is thought to be more likely to spread through droplets coughed from the nose and throat than from infections lower down.

Hay points out, however, that it is difficult to predict how the mutations will actually influence the virus's behaviour. He adds that just two changes are unlikely to create efficient human-to-human transmission on their own.

Establishing what effects these changes are having on the epidemiology of the current outbreak is a top priority for research teams working in Turkey. "We must learn more about the mild cases and be absolutely sure of whether these viruses are behaving differently from those we have seen elsewhere," says Hay. "It is early days in terms of what we know about the viruses causing these infections."

Researchers are sequencing more strains from the Turkey cases, to see whether they share the mutations and to check for further changes. Samples were expected to arrive in London on 18 January, after being held up for more than a week in Turkey because of the Eid ul-Adha holiday period.

Declan Butler

Will Germany choose a fair elite?

MUNICH

Germany's universities are taking part in a contest that is intended to boost their global standing. But claims that political bias will affect the selection process have sparked debate over whether the top institutions will — or even should — win.

Despite being one of the world's largest economies, Germany's research universities punch below their weight in world rankings. So, in 2004, the then centre-left government created a €1.9-billion (US\$2.3-billion) scheme to name and reward a handful of elite universities.

Each chosen university will receive up to €30 million a year for five years to help them compete with the likes of Harvard, Cambridge and Tokyo. Winners of the first round will be announced on 20 January.

But last week brought allegations that the contest will not be based purely on academic merit. Daniel Guhr, founder of the Illuminate Consulting Group, based in San Diego, California, had

been helping Berlin's Humboldt University to pep up its application. In an interview with Berlin newspaper *Der Tagesspiegel*, he claimed that the competition is bound to be biased by political and regional considerations, and he released details of a study in

"I'm just saying what everyone already knows."

which he predicts the universities most likely to win. For example, Guhr argues that universities with historically strong reputations will have an advantage regardless of their current research status. And that institutes such as the Free University of Berlin and the University of Würzburg in Bavaria — both with strong research programmes — do not have a fair chance because they are geographically close to the favourites, including Humboldt and the Technical University of Munich. "If the decision were solely about scientific excellence, a disproportionate share of the winners would be in southern Germany," he told *Nature*. "Clearly, this would be hard to accept in Germany's federal system."

Guhr adds that he sees such factors as "legitimate and reasonable" — without a political component to the decision, even the strongest universities in the east, for example, the University of Dresden, would have little chance. But he says that biases should be properly acknowledged because of the consequences for the losers. "Funding and attention will focus on the new elite."

The consultant has been almost unanimously criticized for his outburst. Humboldt cut ties with him, and research managers throughout Germany have rejected the idea. "The claims are totally unfounded," insists Eva-Maria Streier, spokeswoman for Germany's main research agency, the DFG, which is running the competition. "Political interests will not play a role in the outcome."

Guhr says he is surprised by the response. "I'm just saying what everyone already knows," he says. Many will be keeping an eye on his predictions when the final results are announced.

Robert Rentzsch



Novel approach:
Jon Sudbø
simply invented
his test subjects.

admitted that the data had not come from that database or any other, but from thin air.

Many details of this case still need to be worked out. There is some indication that Sudbø may have mental health problems. It

is also not clear what his 13 co-authors knew about the fraud — the paper identifies three others as contributing equally to the research, and among the other co-authors are Sudbø's wife and his identical twin. None of the authors could be reached for comment.

The hospital has asked that Sudbø's other work be examined in an independent investigation, to be set up this week by Anders Ekblom, an epidemiologist at the Karolinska Institute in Stockholm, Sweden. But the case is already set to change research policy in Norway. The country's health minister, Sylvia Brustad, announced on 16 January that previously stalled reforms on medical research will probably be law by

the autumn. The new rules would put more responsibility for catching fraud on the shoulders of the institutions where the research was done.

Richard Horton, editor of *The Lancet*, insists his journal is not at fault. "This is all so similar to the Hwang thing that we have just been through," he says wearily. "Peer review is a great system for detecting badly done research, but if you have an investigator determined to fabricate an entire study, it is not possible to pick it up." The mechanism of peer review at his journal is currently being examined as part of the largest study ever conducted into the process (see page 252).

Emma Marris