

H5N1 virus outbreak in migratory waterfowl

A worrying development could help to spread this dangerous virus beyond its stronghold in southeast Asia.

The highly pathogenic H5N1 influenza virus has become endemic in poultry in southeast Asia since 2003 and constitutes a major pandemic threat to humans¹. Here we describe cases of disease caused by H5N1 and transmission of the virus among migratory geese populations in western China. This outbreak may help to spread the virus over and beyond the Himalayas and has important implications for developing control strategies.

H5N1 virus has occasionally been isolated from dead wild birds, usually within the flight range of infected poultry farms^{2,3}. In the absence of evidence that the virus is transmitted within wild bird populations or that migratory birds can carry the virus, it was possible that these birds were dead-end hosts of virus acquired from poultry. On 30 April 2005, however, an outbreak was detected in bar-headed geese (*Anser indicus*) at Qinghai Lake in western China (see supplementary information), which is a protected nature reserve with no poultry farms in the vicinity.

Initially, sick bar-headed geese were recorded on a single islet that contained about

3,000 bar-headed geese as well as some brown-headed gulls (*Larus brunnicephalus*), great black-headed gulls (*Larus ichthyaetus*) and great cormorants (*Phalacrocorax carbo*). Clinical findings included paralysis, unusual head tilt, staggering and neck thrill — all are known features of H5N1 disease in waterfowl. By 4 May, bird mortality was more than 100 a day; by 20 May, the outbreak had spread to other islets, with some 1,500 birds dead.

Overall, 90% of the dead birds were bar-headed geese, with the remainder being brown-headed gulls and great black-headed gulls. We isolated 28 H5N1 viruses from 92 cloacal, tracheal and faecal swabs from all three species, and a further 5 viruses from tissue samples from bar-headed geese. (For details of methods, see supplementary information.)

Sequence comparison revealed that the H5N1 viruses were almost identical across all gene segments. The haemagglutinin gene retains the motif of basic amino acids (QGERRRKKR) in the connecting peptide that characterizes highly pathogenic avian flu. All Qinghai isolates had a Lys 627 mutation in the PB2 gene,

which has been associated with increased virulence in mice⁴. Phylogenetic analysis of these isolates and eight other H5N1 viruses, isolated from poultry markets in Fujian, Guangdong, Hunan and Yunnan provinces during 2005, indicated that the haemagglutinin (Fig. 1a), neuraminidase and nucleoprotein (data not shown) genes of the Qinghai viruses were closely related to the H5N1 virus A/Chicken/Shantou/4231/2003 (genotype V).

However, the other five internal genes, represented by the matrix-protein gene, were closely related to H5N1 viruses isolated from domestic poultry in southern China during 2005, represented by the virus A/Chicken/Shantou/810/2005 (genotype Z) (Fig. 1b). These viruses are therefore characterized as H5N1 genotype Z, but are clearly distinguishable from those that have caused human infection in Thailand and Vietnam (Fig. 1a, b)⁵. This indicates that the virus causing the outbreak at Qinghai Lake was a single introduction, most probably from poultry in southern China.

Qinghai Lake is an important aggregation and breeding site for bar-headed geese that are distributed over central Asia⁶. From September, they migrate southwards to Myanmar and over the Himalayas to India, returning to Qinghai around April⁶. Our findings indicate that H5N1 viruses are now being transmitted between migratory birds at the lake. Although the outbreak could burn itself out, the large migratory bird population at Qinghai Lake makes this unlikely. The viruses might also move to other migratory species that could act as carriers, remaining highly pathogenic for domestic chickens and possibly humans.

Like its precursor, A/Goose/Guangdong/1/96, the current H5N1 virus could become established in bar-headed geese. There is a danger that it might be carried along the birds' winter migration routes to densely populated areas in the south Asian subcontinent, a region that seems free of this virus, and spread along migratory flyways linked to Europe. This would vastly expand the geographical distribution of H5N1. Increased surveillance of poultry is called for because previous experience has shown that control measures become almost impossible once the virus is entrenched in poultry populations.

H. Chen*†, G. J. D. Smith*†, S. Y. Zhang*†, K. Qin*†, J. Wang*†, K. S. Li*, R. G. Webster*†§, J. S. M. Peiris*†, Y. Guan*†

*Joint Influenza Research Center (SUMC & HKU),

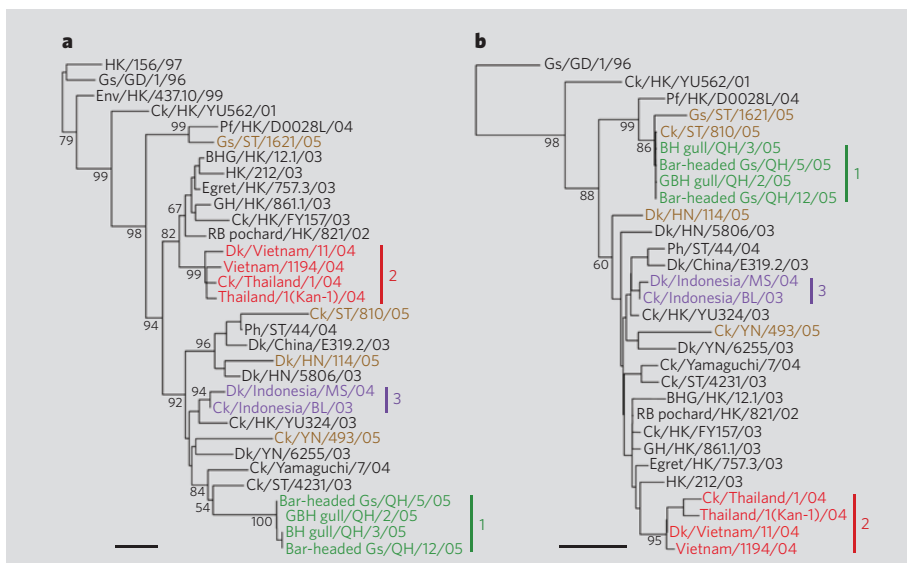


Figure 1 | H5N1 flu strains in wild birds in western China. **a, b**, Phylograms showing the genetic relationship between representative strains for **a**, the haemagglutinin gene (nucleotide positions 25–1,025; scale bar, 0.01 nucleotide changes per site), and **b**, the matrix-protein gene (nucleotide positions 91–956; scale bar, 0.01 nucleotide changes per site). Numbers at branches are bootstrap values from 1,000 replicates. Sources of isolated viruses: clade 1, Qinghai Lake; clade 2, Thailand and Vietnam; clade 3, Indonesia; viruses isolated from southern China in 2005 are shown in brown. BH gull, brown-headed gull; BHG, black-headed gull; Ck, chicken; Dk, duck; Env, environment; GBH gull, great black-headed gull; GD, Guangdong; GH, grey heron; Gs, goose; HK, Hong Kong; HN, Hunan; Pf, peregrine falcon; Ph, pheasant; RB pochard, rosy-billed pochard; ST, Shantou; YN, Yunnan. Sequences have been deposited in GenBank under accession numbers DQ095612–DQ095771.

Shantou University Medical College,
Shantou 515031, China

e-mail: yguan@hkucc.hku.hk

†Department of Microbiology, The University of
Hong Kong, Pokfulam, Hong Kong SAR, China

‡Institute of Zoology, Chinese Academy of
Sciences, Beijing 100080, China

§Virology Division, Department of Infectious
Diseases, St Jude Children's Research Hospital,
Memphis, Tennessee 38105, USA

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Supplementary information accompanies this
communication on *Nature's* website.

Competing financial interests: declared none.

doi:10.1038/nature03974

Published online 6 July 2005.