Medical Hypotheses (2005) x, xxx-xxx



medical hypotheses

http://intl.elsevierhealth.com/journals/mehy

Correspondence

Avian flu virus H5N1: No proof for existence, pathogenicity, or pandemic potential; non-"H5N1" causation omitted

WHO, CDC, Robert Koch Institute (RKI), and Friedrich Loeffler Institute (FLI) claim that H5N1 (avian flu virus) is "highly contagious". Further, Reinhard Kurth, president of RKI, says that H5N1 "threatens potentially all six billion people on earth".

We identified four fundamental questions underlying these claims and requested supporting studies from FLI (which according to the German Government "possesses virus isolates of H5N1"):

- 1. Does H5N1 exist?
- 2. Is it pathogenic to animals?
- 3. Is it transmissible and pathogenic to humans, and does it have pandemic potential?
- 4. Have other causes for observed disease been studied?

FLI responded with four papers: PNAS [1], Science [2], J Virol [3] directed towards questions 1 and 2; EID [4] towards question 3; PNAS [1] towards question 4.

Question 1 (existence). FLI responded with, "H5N1/asia virus can be produced completely in vitro by using reverse genetics. The virus generated this way, also called infectious clone, cannot contain contaminants from sick animals" [translated from German]. However, PCR cannot be used to identify viruses which have not been previously sequenced [5].

The PNAS paper (as the others) does not show or reference the composition of the stock virus — nor does Subbarao et al. (referenced by the EID paper), which claims first characterization of H5N1 disease in a human in 1997 [6]. Though the EID study failed to detect "H5N1" in several of the diseased organs, this anomaly was labelled an "enigma", rather than a "contradiction".

Robert Webster, corresponding author of the PNAS paper and Director of WHO's Collaborating Center for Studies on the Ecology of Influenza in Animals and Birds, informed us that stock viruses "are classified as select agents" and "we are not at liberty to release this information". Without verification, and without purification described in any of these papers, we cannot accept that stock virus is pure and fully characterized. Inquiries for clarification to Webster, CDC Select Agents Program, and FLI received no response.

Question 2 (animal pathogenicity). Papers describe the use of natural routes, but disease was only achieved with extraordinary concentrations, up to 10 million EID per animal. None of the experiments used controls or blinding. The Science paper is highly abstract molecular science, employing elevated concentrations of chimeric variants.

Question 3 (human pathogenicity and pandemic potential). The EID paper is an anecdotal report of a 6-year-old boy from Thailand with severe multi-organ disease. No evidence was given for transmissibility to humans. The scientists found evidence of aspergillosis, and the boy was treated with toxic agents (broad-spectrum antimicrobial and antivirals) before he died.

Subbarao et al. (referenced by the EID paper), describes a previously healthy 3-year-old Hong Kong boy who developed flu-like symptoms in May 9, 1997, and was treated with broad-spectrum antibiotics and salicylic acid, though this is commonly contraindicated. He developed Reye's Syndrome and died eleven days later [7]. A search commenced for causation within a limited range of flu viruses. H5N1 was claimed causative, even though coronaviruses, flaviviruses, enteroviruses,

2 Correspondence

other pathogens and chemicals can also cause flu symptoms. There was no confirmation of prior avian contact. Regardless, warnings of an "explosive pandemic" appeared in this early document, though FLI conceded: "There is no scientific forecasting method that can evaluate the possibility that an influenza virus induces a new pandemic."

Question 4 (non-"H5N1" causation). Neither the Subbarao et al study nor the FLI references consider reasonable, competing theories for disease causation, e.g., environmental and pharmaceutical factors.

Our analysis shows the papers do not satisfy our four basic questions. Claims of H5N1 pathogenicity and pandemic potential need to be challenged further.

References

[1] Hulse-Post DJ, Sturm-Ramirez KM, Humberd J, Seiler P, Govorkova EA, Krauss S, et al. Role of domestic ducks in the propagation and biological evolution of highly pathogenic H5N1 influenza viruses in Asia. Proc Natl Acad Sci USA 2005;102(30):10682—7.

- [2] Hatta M, Gao P, Halfmann P, Kawaoka Y. Molecular basis for high virulence of Hong Kong H5N1 influenza A viruses. Science 2001;293(5536):1840–2.
- [3] Hulse DJ, Webster RG, Russell RJ, Perez DR. Molecular determinants within the surface proteins involved in the pathogenicity of H5N1 influenza viruses in chickens. J Virol 2004;78(18):9954–64.
- [4] Uiprasertkul M, Puthavathana P, Sangsiriwut K, Pooruk P, Srisook K, Peiris M, et al. Influenza A H5N1 replication sites in humans. Emerg Infect Dis 2005;11(7):1036—41.
- [5] Brown TA. The polymerase chain reaction. In: Genomes. 2nd ed. Bios Scientific Publishers; 2002 [chapter 4.3].
- [6] Subbarao K, Klimov A, Katz J, Regnery H, Lim W, Hall H, et al. Characterization of an avian influenza A (H5N1) virus isolated from a child with a fatal respiratory illness. Science 1998;279(5349):393. p. 393—6.
- [7] Hurwitz ES, Barrett MJ, Bregman D, Gunn WJ, Pinsky P, Schonberger LB, et al. Public Health Service study of Reye's syndrome and medications. Report of the main study. JAMA 1987;257(14):1905–11.

David Crowe Torsten Engelbrecht Freelancer, Hein-Hoyer-Strasse 60, 20359 Hamburg, Germany. Tel.: +49 40 42103378 (T. Engelbrecht). E-mail address: tengelbrecht@gmx.net (T. Engelbrecht).