

Note

H5N1 influenza in Hong Kong: virus characterizations

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Abstract

In 1997, 18 people were infected in Hong Kong with an avian influenza A(H5N1) virus from chicken. This type of interspecies transmission was never detected before and could have resulted in the development of a pandemic strain. The occurrence suggests that the pig is not needed for the emergence of pandemic influenza virus strains. Characteristics of the strains involved are discussed in relation to the question why, on the one hand, these strains were able to infect humans but on the other hand were not able to start an epidemic. © 2002 Elsevier Science Ltd. All rights reserved.

Keywords: Avian influenza virus; Interspecies transmission; Pandemic influenza

In May 1997, the virus diagnostic laboratory of the Governmental Virus Unit of the Queen Mary Hospital in Hong Kong, head Dr. W.L. Lim, isolated from a tracheal aspirate taken from a severely ill 3-year-old boy from Hong Kong, an influenza A virus that did not react with any of the antisera to current human influenza virus strains. The child died a few days afterwards. Dr. Lim sent the strain for typing to the WHO World Influenza Centres in London and Atlanta and to the National Influenza Centre of The Netherlands. First at the latter centre, the virus was identified by haemagglutination inhibition and neuraminidase inhibition assays and PCR as subtype H5N1 [1]. Subtype H5 is one of the well-known causes of highly virulent fowl plague epidemics in chickens. Soon, the source of the virus could be located in the chicken farms of Hong Kong where, shortly before the child fell ill, a large fowl plague epidemic took place. From this avian epidemic, Dr. K.F. Shortridge from Hong Kong had isolated an H5N1 influenza virus.

Molecular comparison established a very close relationship between the human and the avian H5N1 viruses from Hong Kong [2,3]. In view of the threat of a pandemic developing from this virus, the most important finding was the high similarity between the six genes coding for the internal proteins of the virus. This ruled out the occurrence of reassortment between the avian virus and a current mammalian influenza virus. Such a reassortment is thought to be instrumental for the development of a virus strain with epidemic

potential for humans [4]. In November and December 1997, 17 more cases of human influenza A (H5N1) were detected in Hong Kong, including five additional fatal cases. From 15 patients, the H5N1 virus could be isolated. Fortunately, massive killing of poultry in Hong Kong at the end of 1997 was able to achieve abrupt abolishment of the series of human H5N1 virus infections, well before the usual epidemic influenza period in Hong Kong from February through July. In this period, the chance for reassortment of the chicken virus with a current human influenza A virus would have been greatly increased. Also the 15 new H5N1 isolates closely resembled the H5N1 viruses from chicken.

The haemagglutinins (HAs) of the human and the avian H5N1 viruses from Hong Kong differ by only a few amino acids from each other. They share the amino acids supposed to be involved in the activity of the receptor-binding site. The H5 HAs of the human H5N1 viruses, therefore, had not acquired amino acid substitutions allowing the avian influenza virus to bind to the α -2,6-linked sialic acids which are supposed to prevail in the human respiratory tract. Still, the human H5N1 viruses proved to replicate very well in the lungs of human subjects.

The HAs of the human and the avian H5N1 viruses also have the same multiple basic amino acid sequence motif at the cleavage site [2,3], which is associated with a highly pathogenic phenotype in poultry [5]. In agreement with this finding, all human and avian H5N1 viruses—even after several passages in the mammalian cells of human patients and cell cultures—proved highly fatal for chickens, killing the animals within a few days [2,3,6].

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Detailed nucleotide sequence analyses were performed in several laboratories in an attempt to detect systematic differences between the human and the avian H5N1 viruses which could be involved in the interspecies transmission that occurred in Hong Kong in 1997. These analyses allowed the distinction of two closely related groups of human H5N1 isolates [6,7]. No amino acids could be identified that separated the isolates from human origin from those from avian origin. On the other hand, the consensus amino acid sequences in the internal virus proteins displayed amino acids that were previously found in human influenza virus strains [7]. These “human-specific” amino acids may have facilitated the infection of humans by an avian influenza virus.

From an epidemiological point of view, the most important lesson from the Hong Kong incident is that it clearly demonstrates the possibility of efficient direct crossing of the bird–man barrier by a purely avian influenza virus. Before this event, pigs were generally thought to play an important role as a “genetic mixing vessel” to create reassortant strains with pandemic potential [8]. After the Hong Kong 1997 flu there is no more need for the pig as mixing vessel; humans can probably play this role by themselves.

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