A pandemic warning?

Introduction of new influenza type-A viruses, carrying different combinations of the viral envelope glycoproteins haemagglutinin (H) and neuraminidase (N), have led to three major pandemics of influenza in humans this century. Phylogenetic evidence suggests that these viruses have originated from avian influenza A viruses, either unchanged or after reassortment with human influenza A viruses. In aquatic birds, all of the known H and N antigenic varieties (15 varieties carry H, nine carry N envelope glycoproteins) apparently circulate in a genetically conserved fashion. Viruses carrying the H1N1, H2N2 and H3N2 combinations were responsible for the Spanish flu of 1918, the Asian flu in 1957 and Hong Kong flu in 1968, respectively[1]. An influenza A virus of the H5N1 subtype has now been identified in a human patient, raising discussions about its potential to spark a new human influenza pandemic.

On 21 May 1997, the fifth day of his hospitalization, a three-year-old boy from Hong Kong died in an intensive-care unit in Hong Kong, with a final diagnosis of Reye syndrome, acute influenza pneumonia and respiratory distress syndrome (ARDS). No indications of other underlying disease, including immunodeficiency or cardiopulmonary disease, were observed. From a tracheal aspirate, we isolated an influenza virus in MDCK and LLC cells. We were unable to grow any pathogenic bacteria from respiratory specimens. In haemagglutination inhibition assays, the virus did not react with ferret antisera to recent isolates of human and swine subtypes. By complement fixation tests we found it to be an influenza A virus, confirmed by an indirect immunofluorescence assay on cells from the original tracheal aspirate.

Haemagglutination inhibition assays using antisera to 14 H subtypes showed that the isolate was an H5 influenza A virus. Biochemical neuraminidase inhibition tests, using antisera to nine N subtypes, indicated that the neuraminidase was of the N1 subtype. Nucleotide sequence analyses of parts of the H and N genes of the virus allowed a phylogenetic comparison with other influenza viruses. Our analyses clearly confirmed that the virus is of the H5N1 subtype (Fig. 1). The H5N1 virus was indeed isolated from the sample of the child, and could not be attributed to a laboratory cross-contamination, as there was no H5N1 virus present in the human diagnostic laboratory. Furthermore, we reisolated the same virus from the original tracheal aspirate specimen.

The contribution of the influenza A H5N1 virus infection to the child's disease, eventually leading to his death, is not yet clear. But the virus identification is important as it is the first documented isolation of an influenza A virus of this subtype from humans. Subtype H5 influenza A viruses can cause lethal avian influenza (fowl plague), a disease that may decimate flocks of domestic poultry. These viruses have so far not been identified in pigs. We feel that the identification of the H5N1 influenza A virus and its presently unknown pandemic potential, should be the basis for an intensive monitoring of the epidemiology and the clinical manifestation of infection with this virus by the international World Health Organization influenza surveillance network.

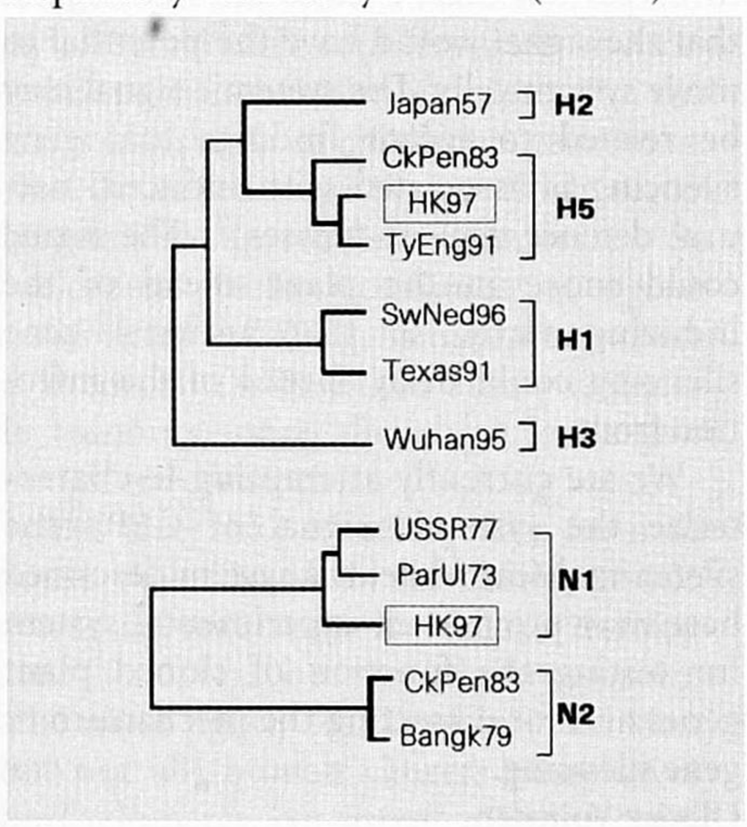

Figure 1 Phylogenetic relationship of the H and N genes from the human virus isolate A/Hongkong/156/97 (HK97) and the corresponding genes from selected influenza A viruses. Japan57, A/Japan/305/57 (H2N2); CkPen83, A/chick/Pennsylvania (H5N2); TyEng91, A/turkey/England/5092/91 (H5N1); SwNed-96, A/swine/Netherlands/609/96 (H1N1); Texas91, A/Texas/36/91 (H1N1); Wuhan95, A/Wuhan/359/95 (H3N2); USSR77, A/USSR/90/77 (H1N1); ParUl73, A/parrot/Ulster/73 (H7N1); Bangk79, A/Bangkok/1/79 (H3N2). Sequences were from GenBank or nucleotide sequence analysis using the Dye Deoxy Terminator kit (Applied Biosystems, Foster City, CA). Alignment was done with 827 nucleotides (38–865) of the H genes and 200 nucleotides (1–200) of the N genes by PILEUP (GCG, Madison, WI). Phylogenetic trees were constructed in Phylip (Felsenstein, Seattle, WA) using DNAPARS and DRAWGRAM.

J. C. de Jong, E. C. J. Claas
A. D. M. E. Osterhaus
National Influenza Centre of The Netherlands, Erasmus University Rotterdam and National Institute of Public Health and the Environment, Dr. Molewaterplein 50, 3015 GE Rotterdam, The Netherlands
R. G. Webster
Department of Virology and Molecular Biology, Saint Jude Children's Research Hospital, 332 North Lauderdale Street, Memphis, Tennessee 38105-2794, USA
W. L. Lim
Government Virus Unit, Queen Mary Hospital, Department of Health, The Hong Kong Special Administrative Region

1. Webster, R. G. *et al. Microb. Rev.* **56,** 152–179 (1992).

Conical beams from open nanotubes

Electron guns are indispensable devices that are widely used in household and industrial appliances. Field electron-emitting sources (which emit electrons by tunnelling effects in electric fields), with their small size, small energy spread, high current density and no requirement for heat, have distinct advantages over thermionic emitters. We have made a field electron emitter from hollow, open-ended carbon nanotubes.

The most commonly used material for field emitters is tungsten, which operates only under ultra-high vacuum conditions. It is for this reason that field electron emitters have not been widely adopted commercially. Carbon nanotubes have intrinsically suitable properties for acting as field emitters: sharp tips with a nanometre-scale radius of curvature, high mechanical stiffness, chemical inertness and electrical conductivity. Indeed, field emission from an individual multi-walled nanotube (MWNT)[1] as well as from assemblies of MWNTs[2,3] has been shown under conventional high-vacuum conditions. But there have so far been no microscopic studies of the geometrical or atomic structure of the emitting regions of nanotube tips.

Using field-emission microscopy (FEM)[4], we have now observed emission patterns from two kinds of MWNT — ordinary MWNTs with closed caps and open-ended MWNTs (Fig. 1). We retrieved the first type from the core of a cathode deposit produced by a carbon arc. We produced the open-ended type from the first using a purification process, by which graphite grains and nanoparticles were removed by oxidation with the aid of $CuCl_2$ intercalation[5]. We

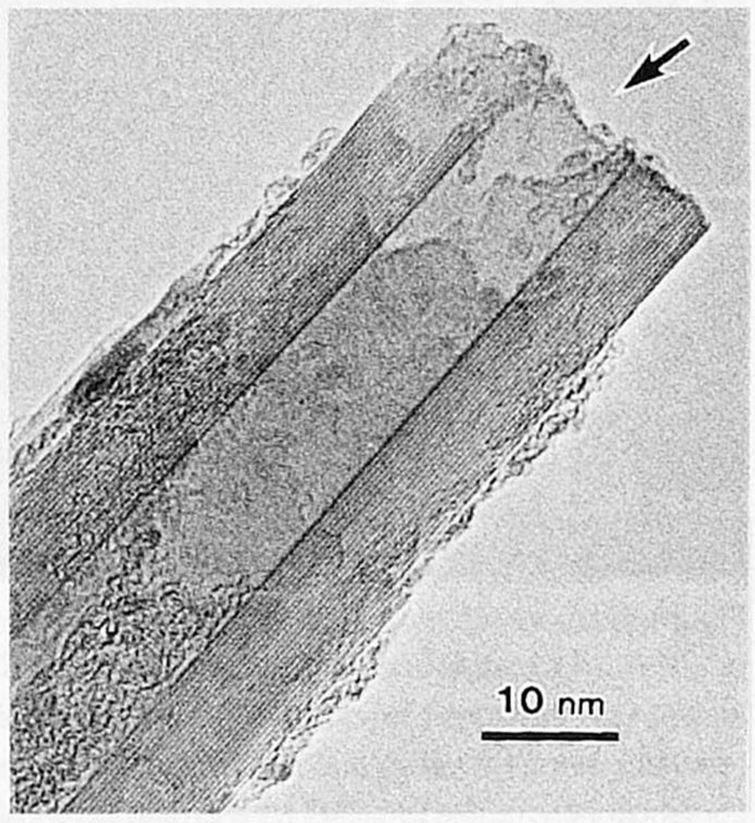

Figure 1 Transmission electron microscope image of the open end of a multi-walled carbon nanotube. The exposed cavity is indicated by an arrow. The cap of the nanotube was removed using a purification process that included oxidation.