Molecular epidemiology of infectious diseases: a case for increased surveillance

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Infectious diseases continue to be the leading cause of death worldwide. This is compounded by the rapid emergence both of new infections and of microbial resistance. With new drugs rarely appearing, the threats to public health are becoming increasingly grave. The major challenge for the public health community is to work out a coordinated, global and multidisciplinary approach to preventing and controlling complex infectious disease problems (*1*). Molecular epidemiology is one of the most exciting new fields as it has a direct impact on infectious disease research at all levels — outbreak investigation, surveillance, and intervention strategies involving clinicians, laboratory technicians, microbiologists, immunologists and health workers. Its ultimate purpose is to prevent morbidity and mortality (*2*).

Several methods are available for outbreak analysis or for a global survey of disease patterns. These range from traditional serotyping and serogrouping to genotyping tools such as fluorescent amplified fragment length polymorphism (FAFLP), single strand conformational polymorphism–polymerase chain reaction (SSCP–PCR) or nucleotide sequencing. Many of these methods do not just make it possible to do pathogen profiling for disease correlation but are also powerful enough to assign new species status (*3, 4*).

An epidemiological study of measles cases observed in the United States between 1997 and 2001 was carried out to highlight the utility of virological surveillance (*5*). Molecular typing of the 55 clinical isolates revealed the presence of 11 genotypes. Interestingly, the majority of these represented genotypes D6 (Europe), D5 (Japan) and D4 (Indian subcontinent) and included an unknown genotype (G2). This study concluded that the measles virus genotype reflected multiple imported sources and indicated that no strain of measles was endemic in the United States.

Another study was aimed at characterizing the circumstances in which poliomyelitis occurred in three children in Bulgaria during 2001. The public health response is reported in this issue (pp. 476–481). Serological and faecal surveys of children who were most likely to have been exposed and vulnerable to the virus showed gaps in population immunity and circulation of the wild type-1 poliovirus. Vigorous immunological intervention by vaccination of high-risk children within one month of the onset of paralysis and countrywide supplementary vaccination prevented further spread of the virus. When the poliovirus isolates were sequenced, they were found to be genetically isolated, representing a single evolutionary lineage. These were less than 90% identical to European poliovirus isolates, but 98.3% similar to an Indian strain isolated in 2000. Perhaps the most striking feature of this study was the question of how a poliovirus strain, which was similar to those circulating in the Indian subcontinent reached Eastern Europe.

The most recent disease outbreak of global significance has been the severe acute respiratory syndrome (SARS), with mortality ranging from 3% to 10% of the infected cases, caused by a member of the coronavirus family. Nucleotide sequencing of this virus reveals that it is neither a host-range mutant nor a recombinant between known coronaviruses, but represents a previously unidentified coronavirus group (*6*). Comparative genomic analysis of different isolates suggested that the virus was genetically quite stable, with very minor nucleotide changes. These minor changes, which may not affect the overall functioning of the virus, nonetheless offer a very useful molecular tool for epidemiological studies.

Questions have been raised about the origin of the SARS virus, including the possibility of an animal origin (*7*). In view of the disproportionate association of SARS cases with people working in the food industry, a detailed analysis of the exotic animals sold in Chinese food markets was carried out. A virus was found in civet cats — a species eaten as a delicacy in China — suggesting that it may have been lurking in these animals for some time before moving into humans. Genetic analysis showed that the virus isolated from the civet cat was almost identical to that found in human SARS patients, except for 29 extra nucleotides. It remains to be seen whether this extra sequence actually confers the ability to productively infect humans when linked to some other animal viruses.

The above examples highlight the importance of virological surveillance in understanding the transmission pathways of existing and emerging infections. Unfortunately, in many epidemiological settings, there is much more dependence on serological and other traditional methods, especially in developing countries, and these have much less positive predictive value. The identification of non-endemic genotypes necessarily means that our understanding of the extent of genetic diversity is far from complete. The SARS epidemic has demonstrated the need to improve laboratory capacity to put in place an expanded and strengthened virological surveillance system. ■

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