DOI:10.1111/irv.12081
www.influenzajournal.com

Improving influenza vaccine virus selection: report of a WHO informal consultation held at WHO headquarters, Geneva, Switzerland, 14–16 June 2010

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Keywords influenza vaccine viruses, vaccine virus selection, WHO recommendations.

Please cite this paper as: Ampofo *et al.* (2013)Improving influenza vaccine virus selection: report of a WHO informal consultation held at WHO headquarters, Geneva, Switzerland, 14–16 June 2010. Influenza and Other Respiratory Viruses 7(Suppl. 2), 52–53

This article provides a summary of the findings presented at a WHO informal consultation on improving influenza vaccine virus selection held at WHO headquarters, Geneva, Switzerland, 14–16 June 2010.[1]

Global Influenza Surveillance network

Since 1952, the WHO Global Influenza Surveillance and Response System (GISRS) has played a key role in monitoring the evolution and distribution of influenza viruses as well as making recommendations on virus strains to be used in human influenza vaccines. The GISRS also monitors, provides risk assessments of potential pandemic viruses and offers guidance on appropriate public health responses. A number of recent events including the expanded role of GISRS following the adoption of the International Health Regulations in 2005, growing awareness of the continued threat posed by H5N1 and reflection on the 2009 H1N1 pandemic marked a good opportunity to revisit vaccine virus selection, and in June 2010, a WHO informal consultation was held in Geneva, Switzerland, to critically review the process by which vaccine virus strains are selected.

Vaccine virus selection process

The vaccine virus selection process involves a high level of coordination and relies on continual integration of virological data and epidemiological information from National Influenza Centres (NICs), antigenic and genetic characterization of viruses by WHO Collaborating Centres (WHO-CCs) and the preparation of suitable reassortants and reagents for vaccine standardization by Essential Regulatory Laboratories. Collaboration and coordination between human and animal influenza networks are also critical to the vaccine virus selection process in terms of the improved integration of data on animal and human viruses, the identification of unusual human influenza A viruses, the evaluation of pandemic risk and the selection of candidate viruses for pandemic vaccines.

Global surveillance of influenza activity is a crucial component to the virus selection process, and through training workshops, assessments and donation, significant increases in trained laboratory personnel and equipment have been realized, with resulting expansion in both geographical surveillance coverage and in the capacities of NICs and other laboratories. These gains have led to a

significant increase in the volume of information reported to WHO on the spread, intensity and impact of influenza. Other initiatives such as the WHO Shipment Fund Project have facilitated the timely sharing of clinical specimens and virus isolates and contributed to a more comprehensive understanding of the global distribution and temporal circulation of different viruses.

Improving the vaccine virus selection process

Advances in molecular diagnosis and the accumulation of genetic sequence data have aided in ensuring the optimal effectiveness of vaccines. However, there remain a number of challenging constraints including variations in the various assays, the possibility of complications resulting from non-antigenic changes, the limited availability of suitable vaccine viruses and the requirement for recommendations to be made up to a year in advance of vaccine use due to production constraints.

Despite the availability of newer assay technologies that may be amenable to automation (e.g. advanced recombinant DNA and protein technologies) and difficulties in standardizing results across laboratories, the haemagglutination inhibition (HAI) assay is likely to remain the test of choice for the antigenic characterization of viruses in the foreseeable future as it is a simple, rapid and reproducible surrogate assay for virus neutralization. Other technologies such as microtitre neuraminidase inhibition assays may also have an impact on both vaccine virus selection and vaccine development.

Microneutralization assays based on measuring virus replication, cell viability or neuraminidase activity are an important complement to the HAI assay in virus antigenic characterization. Improvements in the use and potential automation of such assays should facilitate large-scale serological studies, while other advanced techniques such as epitope mapping should allow for a more accurate assessment of the quality of a protective immune response, and aid the development of additional criteria for measuring immunity.

Standardized seroepidemiological surveys to assess the impact of influenza in a population could help to establish well-characterized banks of age-stratified representative sera as a national, regional and global resource while providing direct evidence of the specific benefits of vaccination. Such surveys would not only strengthen the comparability of serological data generated at different laboratories but facilitate the comparison of antibody response to different viruses.

Technological advances in areas such as high-throughput genetic sequencing and bioinformatics data collection and analysis, together with the ongoing accumulation of X-ray crystallographic data of relevant viral haemagglutin epitopes, should accelerate understanding of the genetic and phenotypic changes that underlie virus evolution and aid in predicting the influence of amino acid changes on virus antigenicity.

Complex mathematical modelling techniques are increasingly being used to shed light on the evolution and epidemiology of influenza viruses. However, without a fuller understanding of the underlying evolutionary and biological process involved, their value in predicting the timing and nature of future antigenic and genetic changes is likely to be limited. The use of less complex, non-mechanistic statistical algorithms, such as those already used as in antigenic cartography, and phylogenetic modelling is more likely to be useful in aiding vaccine virus selection and assessment of the pandemic potential of avian and other animal influenza viruses.

Conclusion

The WHO GISRS and its partners are continually working to identify improvements, harness new technologies and strengthen and sustain collaboration. Continued progress relies on strong surveillance systems and the establishment and maintenance of cross-cutting collaborations. WHO will continue in its central role of coordinating worldwide expertise to meet the increasing need for influenza vaccines and will identify and support efforts to improve the vaccine virus selection process, including periodic review of the vaccine virus selection process via international consultations.

Conflict of interest

The authors have no potential conflicts to declare.

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