National Collaborating Centre for Infectious Diseases
Centre de collaboration nationale des maladies infectieuses

Purple Paper

Composition and Role of the 2010-2011 Northern Hemisphere Seasonal Influenza Vaccine in the Post-Pandemic Period

WHO Recommendations for Influenza Vaccines for Use in the 2010-2011 Northern Hemisphere Influenza Season

WHO recommends that the 2010-2011 northern hemisphere seasonal influenza vaccine include [1]:

- an A/California/7/2009 (H1N1)-like virus (pandemic H1N1 2009 virus; pH1N1)
- an A/Perth/16/2009 (H3N2)-like virus
- a B/Brisbane/60/2008-like virus.

Basis and Process of Seasonal Influenza Vaccine Virus Selection

The WHO recommendations for the composition of seasonal influenza vaccines are based on information on global influenza activity collected through the WHO Global Influenza Surveillance Network (GISN). The Network was established in 1952 and has expanded since, comprising 134 National Influenza Centres (NICs) in 104 countries with 5 WHO Collaborating Centres (CCs) and 4 Essential Regulatory Laboratories (ERLs) in the USA, the UK, Australia and Japan [2].

Global influenza surveillance is a year-round activity beginning with the collection of clinical specimens from patients with influenza-like symptoms. Together, the NICs collect more than 175,000 clinical specimens annually [2]. Upon receiving patient samples from laboratories in their own countries, NICs isolate the influenza virus and conduct preliminary testing to determine the virus type (influenza A or B) and subtype (for influenza A). A selection of virus isolates representative of the influenza epidemic in the country, both temporally and geographically, is sent by each NIC to the WHO CCs for further characterizations [3].

Key Points

- Who recommends that the following viruses be used for influenza vaccines in the 2010-2011 influenza season in the northern hemisphere:
  - an A/California/7/2009 (H1N1)-like virus (pandemic H1N1 2009 virus; pH1N1)
  - an A/Perth/16/2009 (H3N2)-like virus
  - a B/Brisbane/60/2008-like virus.
- Recommendations are based on epidemiological, genetic and serological tests on influenza virus isolates collected through the WHO Global Influenza Surveillance Network between September 2009 and January 2010.
- On August 10, 2010, WHO announced that the world has moved into the post-pandemic period.
- During the post-pandemic period, pH1N1 appears to be taking on the behaviour of a seasonal virus and co-circulating with other seasonal influenza strains. However, pH1N1 will likely continue to affect younger age groups disproportionately as seen during the 2009 pandemic.
- Current influenza activity in temperate countries in the southern hemisphere (Argentina, Chile, New Zealand, Australia, and South Africa) provides us with information on possible influenza scenarios during the winter months in the northern hemisphere. Whereas seasonal influenza A/H1N1 viruses are undetectable in all five countries, influenza pH1N1, A/H3N2 and B viruses have been reported and their proportions in circulation in each country have been variable.
- The recommended trivalent seasonal vaccine for the northern hemisphere 2010-2011 season will provide protection against influenza pH1N1, A/H3N2 and B viruses.

Each year the WHO CCs receive approximately 2,000 influenza isolates for examination of the viral antigenic and genetic properties to determine the direction of evolution (i.e. away from currently circulating strains and from vaccine strains) [2, 3]. In addition to antigenic and genetic analyses, the WHO CCs, in collaboration with key national laboratories involved in registration and quality control of influenza vaccine – Food and Drug Administration (FDA, USA), National Institute of Biological Standards and Control (NIBSC, UK), and Therapeutic

Goods Administration (TGA, Australia) – conduct immunological tests of sera collected from immunized adults and sometimes children. These serological studies determine whether or not vaccines based on older viruses can still provide protection against contemporary viruses, and are another way to determine if the antigenicity of recent viruses has changed significantly from previously circulating strains [2, 3].

The WHO GISN enables WHO to recommend twice annually the composition of the influenza vaccine for the subsequent influenza season in the northern and southern hemispheres [4]. In February and September, respectively, representatives from the CC and ERLs meet as an advisory committee to finalize analyses of the influenza epidemiological data and to select influenza virus strains for the upcoming vaccine. In addition to antigenic and genetic characteristics of the circulating influenza viruses, the committee also considers the viruses' prevalence, geographic distribution and rate of spread to base its vaccine recommendations. While representatives from the NICs, academia and other partners may participate as observers and provide input to the discussion, recommendations are made by advisers only. Representatives from the vaccine industry do not participate in or observe the vaccine composition meetings [4]. More than 250 million doses of the seasonal influenza vaccine are produced each year based on the WHO recommendations [2].

Influenza Activity, September 2009 – January 2010

Influenza illness was observed worldwide between September 2009 and January 2010. During this period, which coincided with the second wave of the 2009 pandemic and the "normal" influenza season in the northern hemisphere, pH1N1 had largely displaced the seasonal influenza A/H1N1, A/H3N2 and B strains and predominated as the major circulating strain. In the southern hemisphere, pH1N1 activity had declined to sporadic levels by September in most countries. In tropical regions, pH1N1 activity was widespread but had declined in all but a few countries. All in all, many regions experienced much higher influenza activity than in the same period of the previous year due to the circulation of pH1N1 outside their usual influenza season [1].

In spite of the much lower seasonal influenza activity than in previous years worldwide, low numbers and sporadic activity of seasonal influenza A/H1N1 and A/H3N2 viruses were reported in some countries in Africa, the Americas, Asia, Europe and Oceania. In the case of seasonal influenza B virus, while its activity had been intermittent in Asia, Australia and New Zealand, some African and European countries, and many countries in the Americas, its activity, albeit sporadic, was more significant in Canada, the USA and the Russian Federation. In Bangladesh and China, activity from seasonal influenza B viruses achieved regional levels. By January, influenza B viruses became predominant in China [1].

Antigenic and Genetic Characteristics of Recent Influenza Virus Isolates

Influenza A/H1N1 viruses

The vast majority of A/H1N1 viruses detected worldwide between September 2009 and January 2010 were pH1N1. Antigenic and genetic tests revealed that pH1N1 has remained homogenous and closely related to the A/California/7/2009 virus strain used in the monovalent pandemic vaccine [1].

Of the few seasonal influenza A/H1N1 viruses isolated, most were antigenically and genetically closely related to A/Brisbane/59/2007 – the virus strain included in the seasonal influenza vaccine for the past two seasons in the northern hemisphere [1].

Influenza A/H3N2 viruses

Recent seasonal influenza A/H3N2 viruses generally fell into two genetically distinct groups, but all were antigenically closely related to the current southern hemisphere vaccine virus A/Perth/16/2009 [1].

Influenza B viruses

Since 1988-1989, two antigenically distinct lineages of seasonal influenza B viruses have been circulating in varying proportions in different countries at different times. These are referred to as B/Victoria/2/87 and B/Yamagata/16/88 lineages. Thus selection of one influenza B virus lineage over the other primarily depends on which virus lineage might predominate in the forthcoming season in that hemisphere [5].

Between September 2009 and January 2010, both influenza B virus lineages circulated; however,

B/Victoria/2/87 lineage viruses continued to predominate. Recent influenza B/Victoria/2/87 lineage virus isolates were antigenically closely related to the vaccine virus B/Brisbane/60/2008 [1].

Serological Studies

As part of the comprehensive analysis for each seasonal influenza vaccine composition recommendation, serological studies are conducted using sera collected from individuals vaccinated with last year's vaccine to determine if immunity to older influenza viruses could still protect against contemporary strains. However, due to the worldwide predominance of pH1N1, sera from children, adolescents, younger adults and the elderly who had received the 2009-2010 seasonal influenza vaccine was tested against seasonal influenza A/H3N2 and B viruses only. To assess the protective effect of the monovalent pH1N1 vaccine, separate panels of sera from children, adolescents, younger adults and the elderly who took part in the pH1N1 vaccine trials were analyzed [1].

Monovalent pandemic vaccines containing influenza A/California/7/2009(H1N1)-like antigens stimulated similar levels of antibody against the vaccine virus strain and a representative pH1N1 isolate.

Seasonal vaccines containing influenza A/Brisbane/10/2007(H3N2)-like antigens induced a lower level of cross-reacting antibody against recent A/H3N2 isolates than against the vaccine virus (average reduction: children, 67%; adolescents, 53%; younger adults, 57%; the elderly, 66%).

Seasonal vaccines containing influenza B/Brisbane/60/2008-like antigens induced similar levels of antibody against the vaccine virus and recent B/Victoria/2/89 lineage isolates, but induced somewhat lower cross-reacting antibody levels against recent B/Yamagata/16/88 lineage viruses (average reduction: children, 20%; adolescents, 0%; younger adults, 33%; the elderly, 37%).

Thus, based on the combined epidemiological, genetic and serological analyses, the WHO recommends that the influenza vaccine for the 2010-2011 northern hemisphere season include:

- an A/California/7/2009 (H1N1)-like virus (pandemic H1N1 2009 virus; pH1N1)
- an A/Perth/16/2009 (H3N2)-like virus
- a B/Brisbane/60/2008-like virus.

Role of the Seasonal Influenza Vaccine in the Post-Pandemic Period

On August 10, 2010, Dr. Margaret Chan, the Director-General of WHO, declared that the 2009 pandemic had ended and the world has entered the post-pandemic period [6]. At this time, the activity and severity of pH1N1 remains unpredictable. While pH1N1 will likely take on the behaviour of a seasonal virus and co-circulate with other seasonal influenza strains, it would likely retain some characteristics of the original pandemic virus in the immediate future.

In the post-pandemic period, cases and localized outbreaks due to pH1N1 are expected to continue to occur. In particular, areas of some countries that were less severely affected during the pandemic could still experience significant outbreaks. As of August 20, 2010, India and New Zealand continue to report significant pH1N1 transmission, with geographical pockets experiencing intense localized epidemics [7, 8]. Furthermore, at least in the immediate post-pandemic period, groups at high risk of severe or fatal illness during the pandemic will probably remain at heightened risk. Although the number of such cases could diminish gradually, it is likely that the pH1N1 virus will continue to disproportionately affect younger age groups, including pregnant women. In addition, a small proportion of otherwise healthy people may also develop acute respiratory distress syndrome – a unique phenomenon observed during the pandemic that is not typically seen during seasonal epidemics [9]. It is impossible to predict if this pattern of pH1N1 transmission will be sustained over the long term or whether and when this will change; therefore, public health authorities must remain vigilant and respond accordingly as their regional influenza situation becomes more clear.

In the meantime, current influenza activity in temperate countries in the southern hemisphere can provide us with a forecast on the possible influenza scenarios during the winter months in the northern hemisphere. Argentina, Chile, New Zealand, Australia, and South Africa – the five southern hemisphere countries with ongoing influenza surveillance – have experienced levels of influenza-like illness (ILI) that are similar to levels seen during inter-pandemic periods and are markedly lower than those of the 2009 pandemic.

Whereas seasonal influenza A/H1N1 viruses are undetectable in all five countries, influenza pH1N1, A/H3N2 and B viruses have been reported and their proportions in circulation in each country have been variable [7, 10].

South Africa was the first country to report considerable active influenza transmission in the southern hemisphere. Influenza activity there has been geographically uneven [11]. The current influenza epidemic began and rose sharply in early June 2010, peaked during early July 2010, and has since stabilized and gradually declined. To date, seasonal influenza A/H3N2 and B viruses form the majority of viruses detected, the latter of which has been associated with a greater proportion of severe acute respiratory infection (SARI) cases in the country. Pandemic influenza A/H1N1 viruses have only been detected sporadically [12, 13].

In New Zealand, the national consultation rate for ILI continues to increase, as of 20 August 2010. Influenza activity, as indicated by rates of ILI, hospitalization, and absenteeism, has been focally intense in areas of the country that had experienced milder epidemics during the previous winter 2009 pandemic wave. The overall rates of ILI and number of severe and fatal cases remain well below the levels during the 2009 winter; however, the current epidemic has yet to peak. The majority of influenza viruses detected during this time have been pH1N1 [7, 8, 14, 15].

In Argentina, Chile, and Australia, overall influenza activity and respiratory diseases remain low and below levels observed during recent, mild, pre-pandemic influenza seasons. All three countries have reported a mix of influenza pH1N1, A/H3N2 and B viruses. While pH1N1 has predominated in all three countries since the beginning of the winter season, influenza B viruses have become the majority in Argentina and Chile in the week ending in 8 August 2010 [7, 16-24]

Based on the influenza trends in the southern hemisphere so far, it is therefore reasonable for the WHO to recommend a trivalent seasonal vaccine, composed of the influenza pH1N1 virus, A/H3N2 and B viruses, for the southern hemisphere 2010 and northern hemisphere 2010-2011 seasons. Recent published studies indicate that seroprevalence against pH1N1 in populations in various regions following the 2009 pandemic waves ranges from 20%-50%, hence many people are still susceptible to infection [25-31]. The situation is compounded by the fact that pH1N1 may continue to disproportionately affect younger age groups. Therefore, vaccination against pH1N1 will continue to play an important and integral role in the public health effort to prevent and control the spread of pH1N1, and to reduce excess morbidity and mortality due to pH1N1 in the post-pandemic period. Moreover, the trivalent vaccine will also provide protection against seasonal influenza A/H3N2 and B viruses that will likely co-circulate with pH1N1 during the winter months in the northern hemisphere.

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