

## INFLUENZA VACCINATION: A CALL FOR ACTION

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Influenza is a disease of global importance as a cause of morbidity and mortality, particularly among older adults and people of all age groups who have underlying high-risk conditions.<sup>1,2</sup> Influenza and its complications are responsible for 150,000 excess hospitalizations and 10,000 to 40,000 deaths annually in the United States, with 80% to 90% of these deaths occurring among individuals 65 years and older.<sup>2,3</sup> It is estimated that the annual cost of influenza in the United States is at least \$12 billion.<sup>3,4</sup> In Austria, 104 million schillings were spent on influenza-related hospitalizations in 1990.<sup>5</sup> In view of the recurrent and enormously widespread disease caused by influenza viruses, effective prevention is an important public health goal in order to decrease the burden of illness, deaths and costs resulting from influenza.

Typically, influenza illness is characterized by sudden onset of fever, chills, myalgia, prostration, headache, sore throat, pharyngitis, nonproductive cough, abdominal pain and vomiting. Unlike infection with other common respiratory viruses, influenza can cause lingering malaise and depression for several weeks. Two important features of influenza infection give it a special significance: the high rate of influenza-related pulmonary complications and deaths, and the epidemic nature of the disease.

Influenza viruses are orthomyxoviruses of three antigenic types—A, B, and C. However, only types A and B cause epidemic disease. Influenza A is classified into three separate subtypes based on the hemagglutinin (H) and neuraminidase (N) antigens. Antigenic variations in these antigens result in the well-known influenza-related phenomena: antigenic drift and antigenic shift.<sup>6</sup> Antigenic drift refers to a minor change in either antigen, without a change in the subtype. It occurs almost annually in both influenza A and B, leading to epidemics which are associated with high attack rates (up to 60% in selected populations). In the Northern Hemisphere, epidemics occur between December and April, while in the Southern Hemisphere they occur between May and September. A laboratory-based review of influenza isolates from clinical specimens over a five-year period at the King Faisal Specialist Hospital and Research Centre (KFSH&RC) showed that the vast majority of isolates were seen between November and February (unpublished observations, Dr. Sami Hajjar).

Antigenic shift occurs only with influenza A, and refers to a major change in either or both antigens, with a change in the subtype of the virus. As a result, a “new” virus emerges to which the overall population is susceptible, causing pandemics where millions of people may become infected.<sup>2,6</sup> In 1918, 21 million influenza-related deaths were recorded worldwide, most of which occurred in people with pre-existing illnesses. Pandemics occur at variable intervals of 10 or more years. The last pandemic of this century occurred in 1977.

Vaccination has been the mainstay of influenza prevention since the vaccines were introduced 50 years ago. Currently, licensed influenza vaccines are chemically inactivated, highly purified preparations of egg-grown virus, and are of two types: 1) whole virus vaccine, and 2) subunit “split” virus vaccines, the preparation of which involves chemical disruption of the lipid-containing viral envelope to remove the low level of systemic toxicity seen with the whole virus vaccine. These vaccines are multivalent, and are updated every year to include viruses that are antigenically similar to the strains of the three distinct groups of influenza viruses that are circulating worldwide. Based on surveillance of influenza strains from various parts of the world, the influenza vaccine formula recommended for the 1997-1998 influenza season by the World Health Organization (WHO) contains an A/Wuhan/359/95-like (H3N2) strain, an A/Bayern/7/95-like (H1N1) strain, and a B/Beijing/184/93-like strain.

The safety, immunogenicity and protective efficacy of influenza vaccines have been well documented.<sup>2-4,7-10</sup> Unlike earlier influenza vaccines, the local and systemic adverse reactions that are associated with current vaccines are minimal and infrequent. The protective efficacy of influenza vaccines ranges from 67% to 92% depending on the study population, intensity of exposure, the antigenic match-up of the vaccine and challenge viruses and other factors. Vaccination decreases the incidence of influenza, and is associated with significant reductions in use of healthcare services, absenteeism from work due to illness, hospitalizations for management of lower respiratory tract complications, and deaths among persons with underlying risk factors. Strategies for use of influenza vaccine focus on prevention of influenza in people at increased risk of complications and death from influenza, in potential

transmitters of infection to those at high risk, and in prevention of morbidity in otherwise healthy individuals. The Advisory Committee on Immunization Practices<sup>2</sup> recommends annual vaccination for the following groups: persons aged 65 years or older; persons under 65 years who may be at high risk of severe illness and/or complications of influenza, such as those with cardiac and lung disease, diabetes or other chronic metabolic disease, renal disease, hemoglobinopathies, immunosuppression; recipients of long-term aspirin therapy; pregnant women who will be in the third trimester during the influenza season; residents of nursing homes and chronic care facilities; persons working or living with high-risk individuals; and any individual who wants to reduce the chance of becoming ill with influenza. The safety and efficacy of influenza vaccine has not been evaluated in infants younger than six months, and thus is not recommended for this age group.

Despite these recommendations and increasing utilization of influenza vaccine, there is no doubt that many high-risk patients still do not receive annual vaccination.<sup>2,6,11,12</sup> This could be due to a number of reasons: 1) lack of awareness of the availability of a vaccine; 2) misconception about risk status and vaccine recommendations; 3) misconception about efficacy of the vaccine, for instance, a low protection rate during a season when the vaccine strains do not closely match the circulating virus may be construed as a general lack of efficacy, resulting in a negative effect on vaccine usage in subsequent years; 4) lack of financial resources to cover the cost of vaccine and its administration, particularly since such costs are incurred annually; 5) vaccines being in short supply, or not readily accessible; and 6) simple forgetfulness. The annual distribution of influenza vaccine during the period 1980 to 1993 increased from 33 to 146 doses per 1000 population and from 70 to 159 doses per 1000 population in Canada and the United States, respectively. In Saudi Arabia, only approximately 30,000 doses were distributed, and presumably administered, in 1996 (personal communication, manufacturers and distributors of influenza vaccine). This is a negligible number considering the Kingdom's population of 16 million. Live-attenuated influenza virus vaccines of types A and B that are administered by the nasal route have been shown to be safe and effective in the prevention of influenza, and are expected to be marketed in 1999. These vaccines offer a number of advantages over the current ones, including ease and convenience of administration, stimulation of a wide range of antibody response, rapidity of production, and cost-effectiveness.<sup>6</sup>

While there is a clear consensus that people at high risk of severe influenza must receive influenza vaccine, widespread vaccination of healthy adults and children remains debatable, solely on the basis of questionable cost-

effectiveness in such situations. Obviously, the economic benefits of vaccination in a particular population depend on many factors, including the severity and actual costs of influenza-associated illnesses, productivity of the study population, the attack rate, the cost of vaccine and its administration, and the effectiveness of the vaccine during each season. Nichol et al.<sup>7</sup> showed that influenza vaccination of healthy working adults in the United States results in considerable health-related and economic benefits. There are no studies that either demonstrate or refute the cost-effectiveness of mass influenza vaccination of young healthy subjects of other age groups, or from other social/economic backgrounds or countries.

However, there are unique circumstances in this country that warrant immediate attention, and impose specific requirements and challenges to influenza prevention and control. Hundreds of thousands of people from the Kingdom and countries all over the world gather in Mecca each year to perform Hajj, a pilgrimage prescribed for Muslims as a religious duty. This number has been increasing steadily, reaching up to 2 million people in 1996, with over 55% coming from outside the Kingdom. In this setting, a high population density, close proximity of people, and high attack rate of influenza are conducive to the fast spread of infection among a large number of people, many of whom are elderly or suffer from conditions that predispose them to severe illness and complications of influenza. An influenza outbreak in such conditions could have significant consequences due to many factors: direct economic costs of medical care; exhaustion of available medical services, with a resultant further increase in morbidity and mortality from influenza and its complications; and potential disruption of essential services due to illness of providers of such services. Additionally, even minor illnesses may prevent pilgrims from partaking in the sacramental activities of the Hajj, causing disappointment and distress, as they are unable to perform their religious duty. This would be particularly stressful to those having traveled long distances and for whom this opportunity was long awaited. The magnitude of the problem may be further exacerbated if the peak pilgrimage activity occurs during the influenza season, as will be the case for the coming several or more years.

Data on the epidemiology, type and illness severity of influenza, and vaccine efficacy in Saudi Arabia are lacking. Most influenza isolates from clinical specimens of patients seen at KFSH&RC in 1996 were antigenically closely related to virus strains contained in the vaccine for the last season, but the limitation of this data precludes any conclusions about vaccine efficacy in this country. As a result, recommendations for or against widespread immunization of healthy subjects in Saudi Arabia are merely conjectural at the present time. Studies are needed to determine the magnitude, severity, and health and

economic effects of influenza infection in the Kingdom. A particular emphasis and priority ought to be placed on studying the scope and effects of influenza infection on the pilgrims during Hajj. Such studies are an important and necessary requisite for design and implementation of strategies for effective prevention of influenza in the population of this country and in pilgrims coming from abroad.

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