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An Integrated Approach From Disease To Prevention

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Introduction

Seasonal influenza, more commonly referred to as "flu" is an acute viral infection caused by an influenza virus. The virus circulates worldwide and can affect anybody, in any age group. The clinical features and complications associated with the disease are highlighted in Table 1. There are 3 types of seasonal influenza viruses – A, B and C. Type A influenza viruses are further classified into subtypes according to the combinations of various virus surface proteins. Among many subtypes of influenza A viruses, influenza A (H1N1) and A (H3N2) subtypes are currently circulating amongst humans. WHO, with its partners, monitors influenza globally, recommends seasonal influenza vaccine compositions twice a year for the Northern and Southern hemispheres, and supports member states efforts to develop prevention and control strategies. WHO works to strengthen national and regional influenza diagnostic capacities including antiviral susceptibility monitoring, disease surveillance, outbreak responses, and increases vaccine coverage among high-risk group.

Epidemiology and Disease Burden

Annual epidemics of seasonal influenza with a peak during winter season are common in the temperate regions. In tropical regions, out breaks are largely irregular but occur throughout the year. Seasonal influenza is a serious public health problem that causes severe morbidity and mortality in high-risk population. People at high risk of getting influenza infection are mentioned in Table 2. An influenza epidemic can take an economic toll through lost workforce productivity and strain health services.

Influenza occurs globally with an annual attack rate estimated at 5–10% in adults and 20–30% in children [2]. A systematic review covering 30 years of seasonal influenza epidemiology in sub-Saharan Africa showed that on an average, influenza accounted for about 10% (range 1–25%) of all outpatient visits and for about 6.5% (range 0.6–15.6%) of hospital admissions for acute respiratory infections in children [3]. Over a period of 30 years between 1976 and 2006, estimates of flu-associated deaths in the United States range from a low of about 3,000 to a high of about 49,000 people. During a regular flu season, about 90 percent of deaths occur in people 65 years and older [4]. Country

Table 1: Influenza Clinical Features & Complication.
Clinical Features
• Incubation period 2 day (range 1-4 days)
• Severity of illness depends on prior experience with related variants
• Abrupt onset of fever
• Myalgia
• Sore throat
• Non productive cough
• Headache
Complications
• Secondary bacterial pneumonia
• Primary influenza viral pneumonia
• Reye syndrome
• Myocarditis
• Worsening of chronic bronchitis and other chronic pulmonary diseases.
• Death in 0.5–1 per 1,000 cases (mainly in ≥ 65yrs)

Table 2: People at high risk [1].
• Children younger than 5, especially younger than 2 years old
• Adults 65 years of age and older
• Pregnant women (and women up to two weeks post partum)
• Residents of nursing homes and other long-term care facilities
• People of any age with certain medical conditions, such as chronic heart, lung, • kidney, liver, blood or metabolic diseases (such as diabetes).
• People with weakened immune system due to disease or medication (such as people with HIV or AIDS, or cancer, or those on chronic steroids)
• People younger than 19 years of age who are receiving long-term aspirin therapy
• People who are morbidly obese (Body Mass Index, or BMI, of 40 or greater)

wise data showing percentage of respiratory specimens that tested positive for influenza is shown in Figure 1.

Illnesses can result in hospitalization and death mainly among high-risk groups (the very young, elderly or chronically ill). Worldwide, these annual epidemics are estimated to result in about 3 to 5 million cases of severe illness, and about 250 000 to 500 000 deaths [2]. In industrialized countries, most deaths associated with influenza occur among people aged 65 years or older. Epidemics can result in high levels of worker/ school absenteeism and productivity losses. Clinics and hospitals can be overwhelmed during peak illness periods.

The precise effects of seasonal influenza epidemics in developing countries are not known, but research estimates indicate that a large percent of child deaths associated with influenza occur in developing countries every year.

Recommended Composition by WHO

Influenza viruses circulate in all parts of the world. Type C influenza cases occur much less frequently than A and B. That is why only influenza A and B viruses are included in seasonal influenza vaccines. The influenza vaccine is manufactured by viral propagation in embryonated eggs or appropriate cell cultures. Primarily, the antigenic characteristics of circulating influenza viruses obtained within the WHO Global Influenza Surveillance and Response System (GISRS). GISRS is a global public health laboratory network coordinated by WHO, currently consisting of 141 National Influenza Centres (NICs) in 111 Member States, 6 WHO Collaborating Centers for Influenza (CCs), 4 WHO Essential Regulatory Laboratories (ERLs) and 12 WHO H5 Reference Laboratories. Twice in a year, the vaccine's antigenic composition is reworked so as to provide optimal vaccine efficacy against prevailing strains in both the northern and southern hemispheres.

These WHO recommendations provide a guide to national public health authorities and vaccine manufacturers for the development and production of influenza vaccines for the next influenza season (Figure 2). In contrast to many other vaccines, the viruses in influenza vaccines have to be updated frequently because circulating influenza viruses continuously evolve. As it takes approximately 6-8 months to produce influenza vaccines, recommendations are made in September for the following influenza season in the southern hemisphere and in February for the following influenza season in the northern hemisphere.

Types of Vaccines

Influenza viruses circulate in all parts of the world. Type C influenza cases occur much less frequently than A and B. That is why only influenza A and B viruses are included in seasonal influenza vaccines. Presently, two types of season flu vaccines are available i) Trivalent inactivated vaccines (TIV) and ii) live attenuated influenza vaccines (LAIV).

Inactivated vaccines are licensed for children < 2 years of age, persons aged ≥ 50 years and for pregnant women. Non-pregnant women aged 2–49 years may receive either inactivated or live vaccine.

Immunization Schedules

TIV: It is administered intramuscularly except for intradermal formulations. Pediatric dose is recommended for children aged 6–35 months. In case of children who are less than 9 years of age and have not received vaccine previously, 2 injections to be administered at least 4 weeks apart. Single dose is recommended

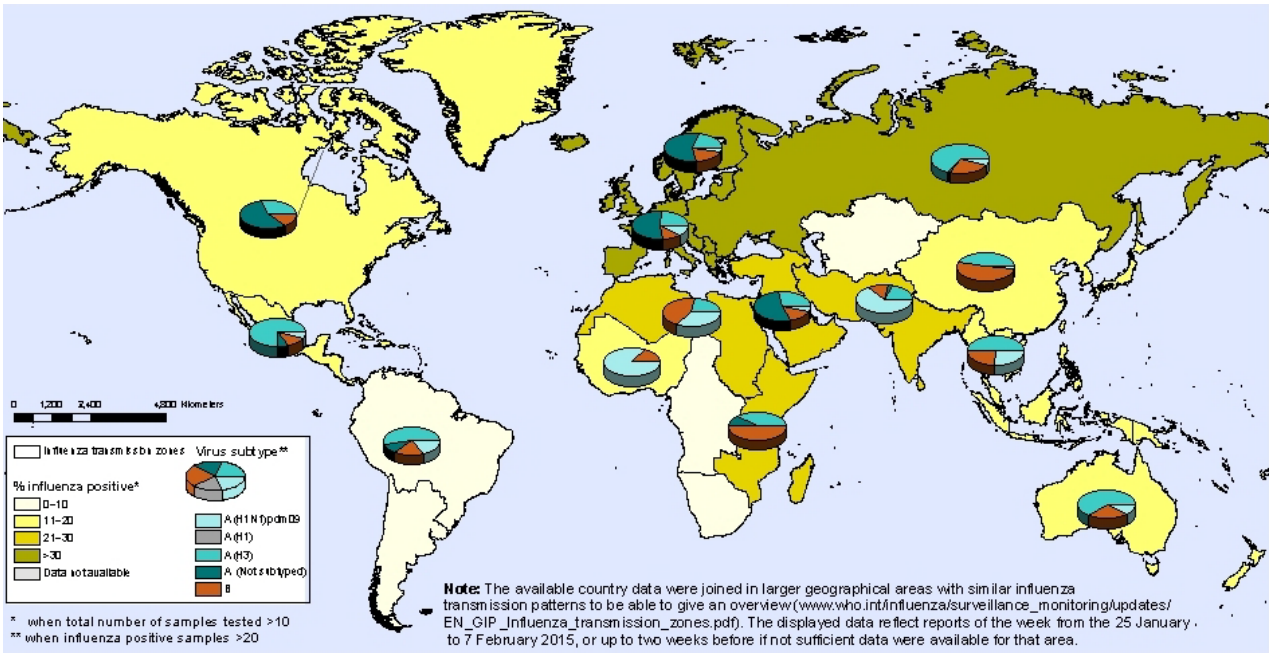

Figure 1: Percentage of respiratory specimens that tested positive for influenza (WHO, 20th Feb 2015).

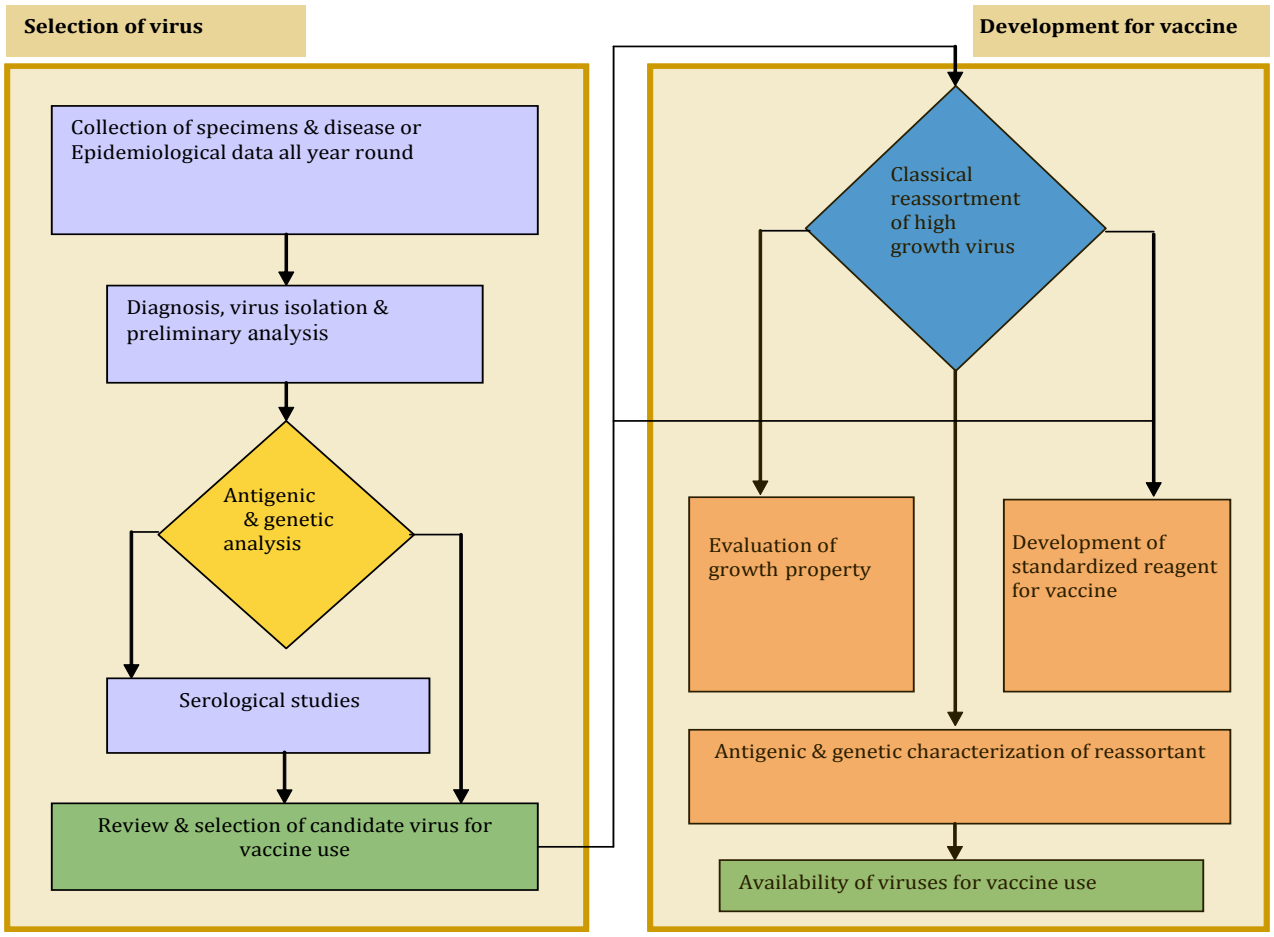

Figure 2: Process of seasonal Influenza vaccine virus selection and development.

for children aged ≥ 9 years and healthy adults.

LAIV: Only a single dose is given as nasal spray. However, children aged 2–8 years who are previously unvaccinated, should receive 2 doses, at least 4 weeks apart.

Annual vaccination (or re-vaccination, if the vaccine strains are identical) is recommended, particularly for high-risk groups (Table 3).

Effectiveness of Vaccine

How well the influenza vaccine works can range widely from season to season. Influenza vaccine effectiveness (VE) can also vary from year to year and among different age and risk groups. Among healthy adults, influenza vaccine can provide reasonable protection. However among the elderly, influenza vaccine may be less effective in preventing illness but may reduce severity of disease and incidence of complications and death.

Both pregnant women and their newborn will be protected if vaccine is administered during pregnancy. A study in Bangladesh showed that maternal immunization with influenza vaccine had significant clinical effectiveness, with a reduction of 63% in laboratory-proven influenza illnesses in infants up to 6 months of age and reduction of 29% and 36% in rates of respiratory illnesses with fever in infants and mothers, respectively [5]. In another study, influenza vaccine given to pregnant women was 91.5% effective in preventing hospitalization of their infants for influenza in the first 6 months of life [6]. Also, a study published in 1993 suggested an active transport of influenza specific maternal IgG across the placenta during pregnancy. Significantly higher GMT of antibodies against influenza vaccine strains were demonstrated among TIV vaccinated pregnant women compared to controls (tetanus toxoid vaccine recipients) as well as among infants of TIV vaccine recipients versus control group infants [7]. Thus, it can be concluded that maternal influenza immunization is an important strategy with substantial benefits for both mother and infants.

Most studies suggest that antibody responses to influenza vaccination are decreased in older adults. A large randomized placebo-controlled trial conducted among community-dwelling persons aged ≥ 60 years reported a vaccine efficacy of 58% (95% CI = 26% – 77%) against serologically confirmed clinical influenza illness during a season when the vaccine strains were considered to be well-matched to circulating strains [8]. When the vaccine strains closely match the circulating influenza viruses, efficacy rates in individuals younger than 65 years of age typically range from 70% to 90% [9, 10].

Table 3: Recommendations in different population.	
Pregnant women	• Highest priority for immunization. • Immunization with TIV at any stage of pregnancy.
Children aged <6 months	• Not eligible to receive currently licensed influenza vaccines. • Should be protected through vaccination of their mothers during pregnancy. • Ensure vaccination of close contacts to limit transmission of influenza viruses to the young infant.
Children aged 6–23 months	• High burden of severe disease in this group. • In this influenza-naïve population prevention is challenging, as effective immunization requires 2 doses and is highly dependent on vaccine strains matching the circulating influenza viruses. • Future availability of adjuvanted or live-attenuated vaccines will yield additional benefits and potentially reduce the need for 2 doses of influenza vaccine in this age group.
Children aged 2–5 year	• Children aged 2–5 have a high burden of disease, but less than those aged <2 years. • LAIV provides broader and higher levels of protection in this age group. • Respond better to vaccination with TIV than children <23 months.
Elderly persons (≥ 65 years of age)	• Have the highest risk of mortality from influenza. • Persons with specific chronic diseases are at high risk for severe influenza and continue to be an appropriate target group. • In some settings, indigenous populations may be considered a priority for influenza vaccination due to increased risk of infection and higher than average rates of predisposing chronic conditions.
Health-care workers	• Important priority group for influenza vaccination to maintain health-care services during influenza epidemics. • Help to reduce spread of influenza to vulnerable patient groups.
International travelers	• Travelers belonging to any of the aforementioned risk groups, influenza vaccination should be a part of the routine immunization programme.

Safety of Vaccines

Transient adverse events at injection site can occur frequently (> 1/100), due to inactivated vaccines. Fever, malaise, myalgia, and other systemic adverse events may affect persons without previous exposure to the influenza vaccine antigens, such as young children. Clinical study analyzing the safety of influenza vaccination in pregnancy found no significant adverse reactions, and no fetal, perinatal, or infant complications among offspring's of vaccinated women [5]. During a few seasons, inactivated vaccine have been linked with increase of Guillain-Barré syndrome (GBS) especially in older adults. However the increase was trivial and estimated at approximately 1 additional case per 1 million persons vaccinated [11]. An increased risk of narcolepsy was found in children aged 4-18 years, following vaccination with Pandemrix, a monovalent ASO3 adjuvanted pandemic A/H1N1 2009 influenza vaccine that was used in several European countries during the H1N1 influenza pandemic. This risk was initially found in Finland, and then some other European countries also detected an association. (Risk of narcolepsy in children and young people receiving AS03 adjuvanted pandemic A/H1N1 2009 influenza vaccine: retrospective analysis [12]. Following this, the European Medicines Agency changed the indication for use of Pandemrix vaccine in people aged under 20 to those for whom seasonal trivalent vaccine was not available and for whom prevention of A/H1N1 2009 influenza was considered necessary [13].

Live vaccines are generally considered safe; however, running nose, nasal congestion and low grade fever are common associated adverse events. Medically significant wheezing was increased in children aged with < 2 yrs when compared with children of 2-5 yrs [14]. A study with live vaccine on 130, 000 children aged 3-15 yrs did not report any serious adverse event [15]. Contraindications for live vaccines include asthma, anaphylactic reactions to eggs, patients aged < 18 years on long-term aspirin therapy, and advanced immunosuppression.

Prevention

Safe and effective vaccines are available and have been used for more than 60 years. Vaccination is the most effective way to prevent the disease and/or severe outcomes. Vaccination is especially important for people at higher risk of serious influenza complications, and for people who live with or care for high risk individuals.

Influenza vaccination is most effective when circulating viruses are well-matched with vaccine viruses. Influenza viruses are constantly changing, and the WHO Global Influenza Surveillance and Response System (GISRS) – a partnership of National Influenza Centres around the world –monitors the influenza viruses circulating in humans. For many years, WHO have updated its recommendation on vaccine composition biannually that targets the 3 (trivalent) most representative virus types in circulation (two subtypes of influenza A viruses and one B virus). Starting with the 2013-2014 northern hemisphere influenza season, quadrivalent vaccine composition has been recommended with a second influenza B virus in addition to the viruses in the conventional trivalent vaccines. Quadrivalent influenza vaccines are expected to provide wider protection against influenza B virus infections.

By taking preventing actions in day-to-day routine, one could stop the spread of the disease. Mainly, in case of flu like illness, stay home for at least 24 hours after your fever is gone except to get medical care or for other necessities. Cover your nose and mouth with a tissue when you cough or sneeze, regularly wash your hands with soap and water, avoid touching your eyes, nose and mouth, and try to avoid close contact with sick people as this is the most common way of transmitting infection. Finally, if you

would like to keep yourself away from influenza or any such kind of infection, you should try to prevent it rather than waiting to cure it, which may or may not be in your hand.

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