INFLUENZA VACCINE

Introduction

Influenza continues to be a major threat to public health world wide because of its ability to spread rapidly through populations. Children are efficient transmitters of influenza viruses and those 5–9 years of age typically manifest the highest rates of infection and illness. However, severe morbidity and mortality are more common among elderly people and in specific high-risk groups. Although morbidity, mortality and affected risk groups appear to be similar all over the world, in many developing countries the disease burden and the socioeconomic impact of influenza are largely unknown. Whereas in temperate climates outbreaks are experienced mainly during the winter season, influenza occurs more unpredictably in tropical regions.

Influenza viruses can also cause pandemics, during which the rates of illness and mortality can rise dramatically. Recorded since the middle of the 18th century, new influenza A subtypes have caused major global outbreaks at unpredictable intervals. Of these pandemics, the "Spanish flu" in 1918 was the most severe, causing an estimated 20–40 million cases or more deaths worldwide. Less severe pandemics occurred in 1957 and 1968.

Virology

The influenza viruses are orthomyxo viruses. They are classified antigenically as types A, B or C, but only influenza A and B are clinically important in human disease. Influenza viruses possess 2 surface glycoprotein antigens, the haemagglutinin (H) which is involved in cell attachment during infection, and the neuraminidase (N) which facilitates the release of newly synthesized virus from the cell. The influenza A viruses can be segregated into subtypes based on differences in these surface antigens, whereas influenza B cannot be segregated into subtypes. Influenza viruses undergo frequent changes in their surface antigens. Immunity resulting from infection by one influenza virus does not protect fully against antigenic or genetic variants of the same subtype (influenza A viruses) or type (influenza B viruses). As a consequence, influenza outbreaks may occur every year. New influenza vaccines must be designed annually to match the circulating viruses which are expected to cause the next epidemic.

Mode of transmission

Influenza is very contagious. The virus is primarily spread from person to person by the aerosol route, via inhalation of droplets formed during coughing and sneezing, or by direct contact with articles contaminated with respiratory secretions. Inhaled virus particles initiate infection in the respiratory tract, although infection can also occur through the mucous membranes of the eyes, nose and mouth. The incubation period can range from 1 to 7 days but is commonly one to 7 days, during which time the virus replicates in the ciliated columnar epithelial cells of the upper and lower respiratory tract.

An infected person is contagious from 1 to 2 days before symptoms start until about day five of illness. Peak viral shedding occurs 1 to 3 days after the development of symptoms, diminishing to a low level by five days. Children shed more virus and remain infectious for considerably longer.

Clinical Features

Influenza is caused by a virus that attacks mainly the upper respiratory tract – the nose, throat and bronchi and rarely the lungs. The infection usually lasts for about a week. It is characterized by sudden onset of high fever, myalgia, headache, severe malaise, non-productive cough, sore throat, and rhinitis. Most people recover within 1 to 2 weeks without requiring any medical treatment. In the very young, the elderly and people suffering from medical conditions such as lung diseases, diabetes, cancer, kidney or heart problems, influenza poses a serious risk. In these people, the infection may lead to severe complications of underlying diseases, pneumonia and death.

Epidemiology

Global Situation

Influenza rapidly spreads around the world in seasonal epidemics and imposes a considerable economic burden in the form of hospital and other health care costs and lost productivity. Precise data on influenza morbidity and mortality are available mainly from industrialized countries.

In annual influenza epidemics, 5-15% of the population is affected with upper respiratory tract infections. Hospitalization and deaths mainly occur in high-risk groups (elderly, chronically ill). Although difficult to assess, these annual epidemics are thought to result in between 3-5 million cases of severe illness and between 250 000 and 500 000 deaths every year around the world. Most deaths currently associated with influenza in industrialized countries occur among the elderly over 65 years of age.

Much less is known about the impact of influenza in the developing world. However, influenza outbreaks in the tropics where viral transmission normally continues year-round tend to have high attack and case-fatality rates.

The annual incidence of influenza varies widely, depending on the virulence of circulating strains and the susceptibility of the population, which is affected by antigenic changes in the virus, vaccine match and vaccine coverage.

Sri Lankan situation

In Sri Lanka Influenza Like Illness (ILI) surveillance has been initiated since 2005 in 20 hospitals identified as sentinel surveillance sites for Avian/Pandemic influenza. They are expected to send at least 30 samples per month from patients with ILI attending OPD to the Medical Research Institute (MRI). MRI is the national influenza centre in Sri Lanka for human influenza surveillance.

Influenza vaccine

Vaccination is the principal measure for preventing influenza and reducing the impact of epidemics. Various types of influenza vaccines have been available and used for more than 60 years. They are safe and effective in preventing both mild and severe outcomes of influenza. Influenza vaccination can reduce both health-care costs and productivity losses associated with influenza illness.

Characteristics of the Influenza vaccine

Constant genetic changes in influenza viruses mean that the vaccines' virus composition must be adjusted annually to include the most recent circulating influenza A(H3N2), A(H1N1) and influenza B viruses.

There are two major types of vaccines available against influenza namely live attenuated and inactivated influenza vaccines.

Live attenuated influenza vaccine

A few countries have licensed live attenuated influenza vaccines for certain target groups. Until live attenuated vaccines are more widely available, they are not yet generally recommended for influenza prevention.

Inactivated influenza vaccines

Inactivated vaccines are classified into several types, depending on whether they contain whole virus particles, partially disrupted virus particles (split. vaccines) or purified envelope antigens (subunit. vaccines). Some subunit vaccines have been combined with an adjuvant or delivery system.

Efficacious and safe inactivated vaccines remain the cornerstone of influenza prophylaxis in most countries. Unless stated otherwise, the data presented in this chapter relate to inactivated trivalent vaccines only.

Efficacy

It is recommended that elderly persons, and persons of any age who are considered at “high risk” for influenza-related complications due to underlying health conditions, should be vaccinated. Among the elderly, vaccination is thought to reduce influenza-related morbidity by 60% and influenza-related mortality by 70-80%. Among healthy adults the vaccine is very effective (70-90%) in terms of reducing influenza morbidity, and vaccination has been shown to have substantial health-related and economic benefits in this age group.

The effectiveness of influenza vaccine depends primarily on the age and immunocompetence of the vaccine recipient and the degree of similarity between the viruses in the vaccine and those in circulation.

Indication

Differences in health priorities as well as limitations of health budgets have so far restricted common use of influenza vaccine to high-risk groups in industrialized countries. However, even in these countries, a large proportion of the population at high risk for severe disease does not receive influenza vaccine. Based on data from industrialized countries, and listed in order of priority, the following groups of individuals may be targeted for influenza vaccination in order to reduce the incidence of severe illness and premature death.

- Residents of institutions for elderly people and the disabled.
- Elderly, non-institutionalized individuals with chronic heart or lung diseases, metabolic or renal disease, or immunodeficiencies.
- All individuals >6 months of age with chronic heart or lung diseases, metabolic or renal disease, or immunodeficiencies.
- Elderly individuals above a nationally defined age limit, irrespective of other risk factors.
- Other groups defined on the basis of national epidemiological data and capacities, such as contacts of high-risk people, pregnant women, healthcare workers and others with key functions in society, as well as children 6–23 months of age.

Dosage & Administration

Trivalent, inactivated influenza vaccines (TIVs) are administered IM into the deltoid muscle (vaccinees aged >1 year) or the antero-lateral aspect of the mid thigh (vaccinees aged between 6 and 12 months).

These vaccines should not be given to children aged <6 months; those aged 6–36 months should receive half the adult vaccine dose (0.25 ml). Children aged 3-9 years should receive the adult dose (0.5ml). Previously unvaccinated children aged <9 years should receive 2 doses, administered at least 1 month apart. A single dose (0.5ml) of the vaccine is appropriate for schoolchildren aged >9 years and healthy adults.

Inactivated influenza vaccines will not interfere with other concomitantly administered childhood vaccines. Immunity lasts about one year and the vaccine should be administered annually.

Storage

Influenza vaccine should be stored at a temperature between +2° C to +8° C and should not be frozen. At the end of each year, vaccine should be appropriately discarded to avoid inadvertent use of a product with incorrect formulation in the following year.

Cautions and contraindications

The following conditions are considered as absolute contraindications for the use of influenza vaccine.

- Persons with history of allergy to egg proteins
- Hypersensitivity to any component of the vaccine
- Previous allergic reaction to any influenza vaccine

Patients with a history of Guillain-Barré Syndrome (GBS) with an onset related in time to influenza vaccination may be at increased risk of again developing GBS if influenza vaccine is given. The risk should be weighed against the benefits to the individual patient of influenza vaccination.

Adverse Events

Influenza vaccines conforming to international standards of purity and potency have been used for many years and have an excellent safety record. They are largely free from systemic effects but may cause local tenderness or soreness at the injection site for 1-2 days. Transient systemic reactions such as fever, malaise and myalgias occur in a minority of vaccine recipients within 6–12 hours of vaccination. Split virus vaccines and subunit vaccines show reduced systemic reactogenicity in both children and adults, compared with whole virus preparations.

Usage of vaccine in specific circumstances

Pregnant women

It is recommended that influenza vaccine be offered in advance to women planning a pregnancy. Although the inactivated influenza vaccine is considered by many experts to be safe at any stage of pregnancy, others prefer to administer the influenza vaccine in the second trimester to avoid a coincidental association with spontaneous abortion. Practitioners should assess the risks for individual women.

planning a pregnancy. Although the inactivated influenza vaccine is considered by many experts to be safe at any stage of pregnancy, others prefer to administer the influenza vaccine in the second trimester to avoid a coincidental association with spontaneous abortion. Practitioners should assess the risks for individual women.

Travellers

People travelling who are at the risk groups should consider immunisation, depending on the season and their destination. In tropical countries influenza activity can occur throughout the year but is more likely during the monsoon, while in the northern hemisphere activity is commonest between the months of December and March.

Sources

Department of Health and Ageing, Australia, 2008. *The Australian Immunization Handbook,* 9th ed. Australia, p.184 – 194.

Heymann, DL, 2008. *Control of Communicable Diseases Manual*, 19th ed. American Public Health Association: Washington DC, p. 315 - 323.

Plotkin, SA, Orenstein, WA, 2008. *Vaccines*, Fifth Edition. Philadelphia: WB Saunders Company, p.805 – 839.

World Health Organization, 2005. Influenza vaccine: WHO Position Paper. *Weekly Epidemiological Record*, 80 (33), p.277-288. (www.who.int.wer)