Recommendations for Vaccination Against Seasonal Influenza in Adult High Risk Groups: South Asian Recommendations

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Abstract
Influenza is a global public health problem and concern especially in high risk people. Prevention plays a key role in avoiding complications of influenza related illnesses. Despite the existing prevalence of influenza, and documented importance of vaccination, the uptake of influenza vaccine is very poor. This document provide recommendations for influenza vaccination in high-risk individuals and help implement best practices in the South Asian region and improve coverage of influenza vaccination to achieve better outcomes in this population.

Introduction
Acute respiratory infection (ARI) is a global public health problem and India is no exception. It is one of the important causes of morbidity and mortality in India. Every year, about 43 million episodes of ARI occur in India,¹ of which influenza is one of the most important causes. According to the World Health Organization (WHO), every year in the world about 5–15 % population is affected with influenza with about 3 to 5 million cases of severe illness and 250,000 to 500,000 deaths.² A study in and around Delhi evaluating pattern of influenza viruses from 2007-2010 showed 17% positivity rate for influenza viruses among patients with influenza like illness,³ while a multisite surveillance data from September 2004 to December 2008 showed 4.43% positive cases among those with influenza-like illness (ILI) and severe acute respiratory infections (SARI).⁴

Influenza is a concern especially in high risk people including but not limited to elderly people, patients with co-morbid conditions and immunocompromised persons. Fortunately, it is a preventable disease. Prevention plays a key role in avoiding complications of influenza related illnesses. According to the World Health Organization (WHO),⁵ with the exception of clean drinking water, vaccines are the most effective intervention in reducing and preventing infectious diseases. The importance of vaccination and its’ enormous success is visible; smallpox has been eradicated globally while polio is on the verge of eradication. Vaccines are the best preventive measures to prevent the complications arising out of influenza.⁶ Despite the existing prevalence of influenza, and documented importance of vaccination, the uptake of vaccine is poor in India⁷,⁸ compared to other countries.⁹,¹⁰

The objective of this document was to outline the recommendations for influenza vaccination in high-risk individuals and help implement best practices in the South Asian region. It should also help improve coverage of influenza vaccination to achieve better outcomes in this population.

Influenza-Basics
Influenza is caused by three groups of viruses of the orthomyxoviridae family; type A (which undergoes antigenic shifts as well as drifts), type B (which undergoes antigenic drifts) and type C. Influenza “A” and “B” can cause significant illness and outbreaks and epidemics. The surface of the virions has antigens that evoke an immune response in the host. Two antigens on the cell surface include HA and NA. About 16 HA subtypes and 9 NA subtypes are known to exist. The strain of influenza virus is named based on the subtype of HA (Hemagglutinin) and NA (Neuraminidase ) surface proteins on the virus. Type “A” influenza viruses mutate easily and are common in India. Minor generic changes in the virus (antigenic shifts) result in the modification of the virus to a form which is closely related to the original. However, a major abrupt change in the genetic makeup of the virus can
occurred and is termed as antigenic shift which results in a new strain that is not recognized by the immune system and thus has a potential of causing large scale epidemics and pandemics. When human and avian viruses come in contact with animals such as pigs, there occurs an antigenic shift due to genetic reassortment and a new type of virus is generated. Antigenic drift occur slowly due to point mutation of HA and NA genes.

Influenza is a highly contagious disease and the risk of infection is increased by proximity of large numbers of individuals. The disease spreads through respiratory droplets, coughing, sneezing and touching respiratory droplets on persons or an object, then touching mucus membranes (e.g., mouth, nose, eyes) without washing hands. Influenza is most contagious during first 3-4 days of illness. Influenza is different from common cold. Fever in influenza is usually high grade and can continue up to 5 days. The other symptoms of the disease include headache, severe cough, severe tiredness, muscle aches and pain and runny or stuffy nose. Long term natural immunity against influenza is not possible since the virus continuously changes.

There have been several outbreaks in history with different strains such as H2N2, H3N8, H1N1, H2N2, H3N2 etc. Recently in 2015, was an outbreak of influenza in India which created fear among the public. A need was felt to prepare a document providing recommendations for the vaccination in high risk groups.

Method

These recommendations are prepared based on the contribution from representatives of all specialties with an initiative from the Indian College of Physicians (ICP)-An academic wing of Association of Physicians of India (API) and Physician’s Research Foundation (PRF). The RSSDI, ISN, FOGSI, CSI actively participated in the meeting with senior representatives, The experts from India and Nepal deliberated on the issues in high risk people and prepared consolidated recommendations for high risk populations. The document is prepared based on the review of evidence available in respective therapy area and expert opinion in the absence of country specific data. The document is prepared to have recommendations for South Asian countries i.e. India, Nepal, Bangladesh and Sri Lanka. The document was reviewed and validated offline by the representatives from Sri Lanka and Bangladesh.

Influenza Vaccine

Through the collection of data from worldwide surveillance centers including Indian sub-continent, the WHO announces three most prevalent influenza strains and recommends the strains to vaccine manufacturers for incorporation in the next batch of vaccines. Northern hemisphere strains are announced in February and Southern hemisphere strains in September to cover the respective peaks of influenza in the particular region.

The WHO recommended strains for Southern hemisphere and Northern hemisphere for 2016-17 season:

It is recommended that trivalent vaccines for use in the 2016 influenza season (southern hemisphere winter) contain the following:
• an A/California/7/2009 (H1N1) pdm09-like virus;
• an A/Hong Kong/4801/2014 (H3N2)-like virus;
• a B/Phuket/3073/2013-like virus.

It is recommended that quadrivalent vaccines containing two influenza B viruses contain the above three viruses and a B/Phuket/3073/2013-like virus.

It is recommended that trivalent vaccines for use in the 2016-2017 influenza season (northern hemisphere winter) contain the following:
• an A/California/7/2009 (H1N1) pdm09-like virus;
• an A/Hong Kong/4801/2014 (H3N2)-like virus;
• a B/Phuket/3073/2013-like virus;
• an A/Perth/16/2009-like virus.

It is recommended that quadrivalent vaccines containing two influenza B viruses contain the above three viruses and a B/Phuket/3073/2013-like virus.

Whom to Vaccinate?

Ideally all individuals above 6 months of age should be vaccinated. However vaccination is particularly important for those individuals who are at higher risk for influenza-related complications which include the following:
• Children younger than 5, but especially children younger than 2 years old
• Adults 65 years of age and older
• Pregnant women (and women up to two weeks post partum)
• Health Care workers.
• Residents of nursing homes and other long-term care facilities
• Patients who have medical conditions including:
  • Asthma
  • Neurological and neurodevelopmental conditions [including disorders of the brain, spinal cord, peripheral nerve, and muscle such as cerebral palsy, epilepsy (seizure disorders), stroke, intellectual disability (mental retardation), moderate to severe developmental delay, muscular dystrophy, or spinal cord injury].
  • Chronic lung disease (such as chronic obstructive pulmonary disease [COPD] and cystic fibrosis)
  • Heart disease (such as congenital heart disease, congestive heart failure and coronary artery disease)
  • Blood disorders (such as sickle cell disease)
  • Endocrine disorders (such as diabetes mellitus)
  • Kidney disorders
  • Liver disorders
  • Metabolic disorders (e.g. Diabetes, inherited metabolic disorders and mitochondrial disorders)
  • Weakened immune system due to disease or medication (e.g. people with HIV/AIDS/cancer, or those on chronic steroids)
  • Individuals <19 years of age receiving long-term aspirin therapy
  • Morbidly obese people
• Adults who are high risk of infection with Influenza such as:
  • Pilgrims (Haj, Kumbh, Umrah etc)
  • Military (Army, Navy, Air-force)
  • Hostellers (Boarding schools, Universities, Medical colleges)
  • Prisoners
Recommended for 2-49 years of age.

Confirmed Influenza. 13 subunit vaccine in reducing laboratory of split virion is superior than the protein core. Vaccine effectiveness vaccine does not have the internal core proteins whereas subunit split-virion vaccine maintains the polymerases, and matrix proteins. A response is triggered by internal proteins such as nucleoprotein, subunit vaccine shows only antibody cellular and antibody response while remove the internal sub-viral core. Two sedimentation technique is used to disruption of membrane, differing disrupted with the use of a surfactant medium, and the virus membrane is grown in pathogen-free viruses are grown in pathogen-free (surface) vaccine.

There are 2 kinds of available vaccines; the inactivated vaccine and the live attenuated vaccine. The former can be trivalent consisting of 2 influenza A strains and one influenza B strain, or quadrivalent with an additional Influenza B strain.

The trivalent vaccine protects against 2 types of influenza A strains (H1N1, H3N2) and one type of influenza B. Quadrivalent vaccine is not available in India and efforts should be done to introduce this vaccine in India as early as possible.

There are two types of trivalent vaccines: split virion and subunit (surface) vaccine.

In the split virion vaccine, influenza viruses are grown in pathogen-free medium, and the virus membrane is disrupted with the use of a surfactant while in the subunit vaccine, in addition to disruption of membrane, differing sedimentation technique is used to remove the internal sub-viral core. Two types of responses are needed from body to clear Influenza virus; cellular response and antibody response.

Split-virion vaccine shows both cellular and antibody response while subunit vaccine shows only antibody response. This is because the cellular response is triggered by internal proteins such as nucleoprotein, polymerases, and matrix proteins. Split-virion vaccine maintains the internal proteins whereas subunit vaccine does not have the internal protein core. Vaccine effectiveness of split virion is superior than the subunit vaccine in reducing laboratory confirmed Influenza. 13

Cell culture based and recombinant DNA influenza vaccines are available in certain regions and are likely to be available in our country soon. The advantages of these vaccines are a quick turnaround and a closer match with the likely circulating strains.

Which Vaccine?

There are two types of available vaccines: split virion and subunit vaccine. For the high risk group, especially in immunocompromized patients, live attenuated vaccine should not be used, instead, inactivated influenza vaccine is recommended. In pregnancy also, LAIV is contraindicated. Apart from these, there is no advantage of one over the other.

Nasal vaccine may be associated with adverse events such as runny nose, wheezing, headache, vomiting, cough, sore throat, malaise and fever while inactivated injectable vaccine may cause soreness, redness and swelling at the site of injection, fever and bodyaches. Usually these side effects are minor and not serious.

Nasal spray vaccine (LAIV) should not be used among the following:
- Children younger than 2 years
- Adults 50 years and older
- People with history of severe allergic reaction to any component of the vaccine or to a previous dose of any influenza vaccine
- People with egg allergy
- Children 2 years through 17 years of age who are receiving aspirin therapy or aspirin-containing therapy
- Pregnant women
- People with weakened immune system (immunosuppression)
- Children 2 years through 4 years who have asthma or who have had a history of wheezing in the past 12 months
- People who have taken influenza antiviral drugs within the previous 48 hours
- People who care for severely immunocompromized persons who require a protective environment (or otherwise avoid contact with those persons for 7 days after getting the nasal spray vaccine)

In addition, patients with asthma, previous history of a Guillain Bare syndrome, chronic conditions or having received vaccine in past 4 weeks must discuss taking vaccine with their physicians.

Nasal Versus Inactivated Vaccine

Nasal spray vaccine (LAIV) is recommended for 2-49 years of age.

What is the Appropriate Time for Vaccination in India?

The peak season for influenza in India is during the monsoon; so vaccine should be given pre-monsoon i.e. April-May and the second peak is seen in winter in northern states i.e. Jammu Kashmir, Himachal and Delhi during November-February. Tamil Nadu receives north-east monsoon, so the peak season there is November-February. Broadly, in areas with peak in winter, the vaccine should be given during September-October and for rest of the country where monsoon is the peak season for influenza, it should be given during April-May.

The vast majority of vaccines produced globally use egg-based manufacturing processes. This often requires 6 to 8 months in order to produce the hundreds of millions of doses available for the next influenza season. Therefore, for the vaccine to be readily available in India in April-May 2016, the vaccine developed from the strains notified in September 2015 for the Southern hemisphere would be effective. The vaccine developed from the strains notified in February 2016 would in turn be available for the November-February peak.

We strongly recommend continued surveillance from other areas of the country in order to obtain seasonality patterns for the whole of the country so that future recommendations can be based on more robust data.

Contraindications for Influenza Vaccine

Following are the contraindications for influenza vaccination:
- Children less than 6 months of age
- Hypersensitivity to the active substance or any recipient in the vaccine
- History of chicken egg allergy or history of severe or life threatening hypersensitivity reaction to flu vaccine or any ingredients in the vaccine which includes gelatin, antibiotics or other ingredients
- If an individual has a history of egg allergy, he must discuss vaccination with the physician
- History of Guillain Barre Syndrome within 6 weeks of previous
influenza vaccination
Vaccination should be postponed in patients with acute febrile illness, or acute infection with fever. Vaccine should not be frozen, but stored under manufacturer recommended storage conditions.

Recommendations for Special Risk Population
In the following section, recommendations for the special population groups are given.

Diabetes Mellitus
Diabetes is associated with several immunological changes. Cell-mediated immunity appears to be the most affected, with alterations in immune cells including polymorphonuclear leukocytes, monocytes, and lymphocytes. Generally, infections in diabetes patients are more common and serious because of several pathological changes in diabetes patients including reduced T lymphocyte response, reduced neutrophil function, changes in humoral immunity, reduced antioxidant defense, lower secretion of inflammatory cytokines and hyperglycemia. Diabetes results in increased risk of infections and death associated with infectious disease. During influenza epidemics, there is 5-15% increase in the mortality among diabetes patients. Diabetic patients are six fold more likely to require hospitalization with complications of diabetes patients. Diabetic patients have similar benefits as elderly people. On the contrary, a study among West Virginia showed that medicare beneficiaries with diabetes without influenza vaccination had 1.7 times higher risk of death during subsequent influenza season compared with those who received vaccination.

Benefit of influenza vaccination in reducing mortality in diabetic patients above 65 years has been documented which supports the annual vaccination with inactivated influenza vaccine in community-dwelling elderly diabetics. Influenza vaccination is also significantly associated with lower mortality for diabetes mellitus.

Recommendations
- Every one with diabetes over the age of six month are strongly advised to maintain good glycemic control and to take influenza vaccination yearly for minimizing infective episodes, except who are allergic to eggs.
- Influenza immunization is strongly recommended yearly in all people with diabetes with renal failure, immunocompromised state due to concomitant illness and comorbidities, chronic respiratory diseases like bronchial asthma and COPD, smokers, poor hygienic conditions (like slum dwellers) and those who frequently travel to high risk areas.
- In younger persons with diabetes (18-50 years) counseling should be done about influenza vaccination. People with diabetes with long duration of disease and poor control have greater susceptibility to infection by Influenza virus hence should be vaccinated.
- Elderly people with diabetes above 50 years of age and with co-morbidities should be strongly motivated for mandatory vaccination against influenza.

Renal Disease
Renal failure is associated with alterations in the immune functions. The immunological changes in these patients include abnormal phagocytosis and B and T-cell response. Moreover, there are alterations in the chemotaxis mechanism and abnormalities in the functions of monocytes and macrophages. These changes along with frequent exposure to medical interventions increases the risk of frequency and severity of infections.

End-stage renal disease (ESRD) patients have high rates of infection-related complications. Patients receiving hemodialysis have higher risk of hospitalization for infection related complications such as bacteremia and pneumonia. End-stage renal disease (ESRD) patients have higher mortality rate compared to those with without ESRD and these patients visit healthcare providers more often than other chronic kidney disease patients providing opportunities for preventive healthcare. Moreover, immunosuppressive therapies also increase the risk of infections in chronic kidney disease patients. Benefits of influenza vaccination in dialysis patients are documented. Vaccination against influenza and pneumococcal disease has been shown to be associated with better survival in dialysis patients with an independent effect of both vaccines on mortality.

Recommendations
- All patients with chronic kidney disease (CKD) and all kidney transplant recipients should be advised to receive annual influenza vaccine.
- Household contacts and healthcare workers should also be vaccinated annually to decrease the transmission to highrisk CKD or post-transplant patients

Special Considerations in Renal Disease
- Dialysis: No difference in the serological response to influenza vaccines was noted in peritoneal dialysis (PD) and hemodialysis (HD) patients, with response rate of 66-77.3% versus 66-78.7% in PD and HD patients, respectively. The present evidence suggests that both PD and HD patients should receive the standard annual dose of the vaccine.
- Kidney Transplant: Inactivated influenza vaccine may be given to transplant recipients despite intensive immunosuppression. It is best to wait until the first 3–6 months after kidney transplantation, the period of intense immunosuppression, before attempting vaccination. However, inactivated influenza vaccination can be administered as early as one month after kidney transplant to time it before onset of the flu season.
Concerns about influenza vaccine triggering an immune response and increase the risk of acute rejections have not been substantiated in large scale studies that demonstrated no increase in acute rejection episodes when influenza vaccine was used. In large registry data, influenza vaccine use in transplant recipients was associated with lower rates of allograft loss and death. Use of adjuvanted Influenza vaccines has been shown to cause a rise in antiHLA antibodies but not acute rejection episodes.

**Respiratory Disease**

Chronic lung diseases including chronic obstructive pulmonary disease (COPD) and asthma are global health problems. Patients with chronic respiratory disease are at a higher risk of complications from influenza. About 8% of the 498 exacerbations in a north Indian setting were found to be related to influenza virus. For elderly persons with chronic lung disease, influenza is associated with significant adverse health effects.

Viral infections are common in COPD patients. In a study, 27% of chronic obstructive pulmonary disease (COPD) exacerbations were associated with respiratory viruses. Upper respiratory tract infection results in more severe exacerbation and takes longer time for recovery in patients with exacerbations of COPD.

The effectiveness of influenza vaccination in respiratory diseases is proved in clinical trials. A prospective clinical trial has shown that influenza vaccination is highly effective in prevention of acute respiratory infections and is associated with reduced outpatient visits and hospitalisations in patients with COPD. Another randomized controlled trial demonstrated that influenza vaccination is prevents influenza-related acute respiratory infections regardless of the severity of COPD.

In a retrospective study comparing outcomes of vaccination (three year data) versus no vaccination among elderly persons with chronic lung disease, influenza vaccination was associated with significant benefits including lesser medical consultations, reduced hospitalization rate, and reduced mortality. Vaccination was associated with a 52% reduction in hospitalization.

A population-based retrospective study showed influenza vaccination associated protection against acute asthma exacerbations in children after controlling for asthma severity.

**Recommendations**

- All patients with chronic respiratory diseases including bronchial asthma, COPD, bronchiectasis, interstitial lung disease and chronic smoker should receive annual influenza vaccination.
- Smoking may increase the risk of hospitalization in smokers and ex-smokers when infected by the influenza virus. Current smokers in a recent Spanish study were found to be twice at risk of hospitalization than non-smokers.

**Liver Disease**

Influenza A can be responsible for hepatic decompensation and hospitalization in patients with cirrhosis and patients waiting for liver transplantation. The patients might have more complications due to higher disease severity.

A case series from India suggested that swine influenza may be associated with sudden clinical deterioration and risk of death in cirrhotic patients making cirrhotic patients suitable candidates for yearly influenza vaccination. Several studies have evaluated impact of vaccination in liver cirrhosis and liver transplant recipients. A study evaluating interferon (IFN) gamma secretion response and hemagglutinin inhibition (HI) of antibody titer in patients with cirrhosis and control subjects suggest that patients with liver cirrhosis might benefit from influenza vaccination. Another study reported that cirrhotic patients including patients under treatment, and liver transplant recipients can receive benefit from influenza vaccination.

**Recommendations**

- Influenza vaccination is recommended for patients with chronic liver disease with cirrhosis (both compensated and decompensated cirrhosis). Annual vaccination is also recommended for Chronic Hepatitis (especially Hepatitis B and C) and alcoholics.

**Elderly**

Influenza is associated with significant morbidity and mortality in patients with chronic disease such as congestive heart failure. A retrospective study has shown that influenza activity is an independent significant factor for higher hospitalization for heart failure. Similarly, influenza infection may increase the risk of atrial fibrillation by activating systemic inflammatory responses and sympathetic tone. The risk was shown to be 18% higher in patients influenza infection. A study evaluating risk of influenza on heart attacks by examining autopsy-proven coronary deaths proved that influenza epidemics were associated with increased deaths due to coronary disease. The increased risk of heart related problems in patients with influenza may be related susceptibility to thrombosis due to several biochemical, cellular, and hemostatic changes. The risk of atrial fibrillation was reduced in patients receiving influenza vaccination. Another case-control study suggested that influenza vaccination in patients with chronic coronary heart disease may reduce the risk of myocardial infarction. The data suggest that influenza vaccination may reduce the risk of sudden death and acute myocardial infarction. The results of the FLU Vaccination Acute Coronary Syndromes (FLUVACS) study suggested that influenza vaccination may reduce mortality and ischemic event risk in patients with infarction and those recovering from angioplasty during influenza season possibly due to beneficial immune responses.

**Recommendations**

- Influenza vaccination is recommended for patients with atherosclerotic heart disease, congenital heart failure, and congenital heart disease.
- Patients with valvular heart disease should also receive annual influenza vaccination.
Trivalent seasonal influenza vaccination in elderly people results in significant reduction in the all-cause mortality and pneumonia-related mortality as well as hospitalization rate. The vaccination in elderly is also a cost saving measure. A cost effectiveness study evaluating impact of vaccination between 65 to 74 years of age over the six consecutive years showed 36%, 18% and 40% reduction in hospitalization for pneumonia/influenza, hospitalization for all respiratory conditions and mortality respectively with cost savings. Savings for each individual vaccinated were more than threefold of vaccination cost. A meta-analysis has also proved beneficial effects of vaccination in elderly in terms of reduction in influenza-like illness, hospitalization for pneumonia and influenza and mortality.

**Recommendations**
- Influenza vaccine is recommended in patients above 50 years of age
- Currently in India the high dose vaccine is not available. Available trivalent inactivated vaccine may be given to elderly people

**Pregnancy**

Pregnant women are at high risk of complications for influenza related hospitalizations and complications and as such constitute a high priority for influenza vaccination as well as prompt antiviral therapy when sick with influenza. In a recent Indian study, 50 out of 266 pregnant patients with acute respiratory infection had influenza as the causative agent with significant morbidity and mortality. In a randomized clinical trial Zaman et al showed 63% reduction in proven influenza illness with inactivated influenza vaccination in infants up to six months of age and also reduction in febrile respiratory illnesses in mothers as well as infants. The vaccine can even be given in the first trimester of pregnancy. A retrospective analysis of 5 year data showed that influenza vaccination was not associated with rise in major congenital malformations and was in fact associated with reduction in the overall stillbirth rate. Chambers et al after evaluation of vaccination records from 2009–12 influenza seasons demonstrated no significant increase in major birth defects or spontaneous abortion, or small for gestational age infants after vaccination.

Unfortunately, the update of the vaccination is very poor.

**Recommendations**
- Influenza vaccination should be given to all pregnant women
- Influenza vaccine can be given in any trimester of pregnancy
- LAIV is contraindicated in pregnancy

**Healthcare Workers**

A systematic review and meta-analysis has shown that health care workers have significantly higher risk of influenza compared to non-healthcare professionals. Despite this, the vaccination rate among healthcare workers is low. A randomized clinical trial has demonstrated effectiveness of influenza vaccine in preventing influenza infection in health care professionals. Vaccination can reduce days of work loss and febrile respiratory illness. Another randomized, placebo controlled double blind clinical trial demonstrated 28% reduction in the respiratory infection related absenteeism among pediatric health care providers. The efficacy of influenza vaccine in prevention of influenza like illness and decreasing illness related absence in healthcare workers has also been demonstrated in tropical settings.

**Recommendations**
- Influenza vaccine is recommended in all healthcare workers with direct or indirect interaction with patients or hospital staff. It should include hospital staff as well as office staff i.e. house keeping personnel, laundry personnel, receptionists etc
- Seniors in the hospital should act as role models to increase acceptance rate of vaccination

In case of inadequate vaccine supply, following prioritization is recommended

1. Those who are in close, prolonged contact and repeated contact with high risk patients should be vaccinated first
2. Close but not in prolonged or repeated contact with high risk patients, those work with high risk patients, perform the essential patient care functions and HCP who are in contact with patients not at risk should be given second priority and lastly

**Neurological Disorders, Obesity and Autoimmune Diseases**

Similar to the increased risk of heart diseases, patients with influenza may have higher risk of stroke due to susceptibility to thrombosis. The data suggest that influenza vaccination can decrease the risk of acute neurovascular event particularly stroke.

**Recommendations**
- Vaccination should be recommended in all patients with chronic vascular disease
- Patients with history of stroke or transient ischemic attacks should receive an annual influenza vaccination
- Patients with diabetes mellitus or with a combination of risk factors that further increases risk of stroke should receive vaccination
- Obese patients should be considered priority group for influenza vaccination
- Patients with rheumatoid arthritis, systemic lupus erythematosus and Sjogren’s syndrome should be considered for annual influenza vaccination

**Immunocompromised, Cancers and Blood Disorders**

Influenza can result in severe complications in HIV infections patients leading to increased risk of hospitalisation and death. Influenza vaccination is is well tolerated in these patients, but the response is lower compared to immunocompetent people.

Cancer and treatment both result in immunosuppression. In a small study among lung cancer patients level of response to influenza vaccination was not affected by systemic steroid therapy or recent chemotherapy. A Cochrane analysis concluded that influenza vaccination is safe in adult patients with cancer on chemotherapy. The available evidence is in favour of vaccination. Annual influenza vaccine is useful to prevent influenza in immunocompromised patients.
Recommendations

- Annual vaccination for HIV-infected individuals with inactivated vaccine is recommended.
- Severely impaired antibody responses are observed in HIV-infected individuals with CD4+ T-lymphocyte counts <100 x 10^6/l. Annual vaccination of HIV-infected individuals with CD4+ T-lymphocyte counts exceeding 100 x 10^6/l seems to be worthwhile, although it may not be expected to render the same level of protection against influenza as in non-infected individuals.
- Annual influenza vaccination is recommended in cancer and solid organ transplant (SOT) recipients.
- Donors and recipients of solid organ transplant should be updated regarding vaccination.
- Post organ transplant, it is advisable to postpone influenza vaccination for the first two months, but in the event of an outbreak in the community, injectable vaccine can be given after one month of transplant. Live vaccines are not advised in this group of patients.
- Vaccine should be given prior to the immunosuppressive therapy if possible. Live vaccines if needed should be given at least four weeks before immunosuppression and should be avoided two weeks prior to immunosuppression. Inactivated vaccines can be given two weeks or more prior to immunosuppression.
- Annual vaccine with inactivated influenza vaccine is recommended for all immunocompromized patients aged six months after the immune-suppressive therapy except those who are unlikely to respond (e.g., those receiving intensive chemotherapy or those who have received anti B cell antibody in last six months). Live influenza vaccine should not be given to these patients.
- Households members of immunosuppressed members should preferably given the inactivated vaccine, especially for hematopoietic stem cell transplant recipients within two months after transplant, or for those with subacute combined immune-deficiency.
- Patients aged six months and more with hematological malignancy or solid tumor except those receiving anti B cell antibodies or intensive chemotherapy for induction or consolidation of leukemia should receive influenza vaccine every year.
- Acute leukemia patients on chemotherapy should not receive the vaccine. Before chemotherapy, they can receive the vaccine.
- Hematopoietic stem cell transplantation (HSCT) donor should be advocated regarding vaccination whereas recipient if not already immunocompromized should be advocated vaccination more than four weeks before immunosuppression in case of live vaccine and more than two weeks in case of inactivated vaccine.
- After HSCT, one dose should be given six months after the HSCT and if there is a community outbreak of influenza, it can be given four months after. In children, two doses should be given as per recommendations.
- In patients of chronic inflammatory diseases on immunosuppressive therapy, inactivated vaccine should be administered while planning to give immunosuppressive therapy. A live attenuated vaccine should be avoided for these patients.
- Patients with aplasia and sickle cell disease should be given the annual injectable vaccine and not the live attenuated vaccine.

Other High Risk Populations (Hajj, Kumbh Mela, Umrah, Military, Army, Air Force, Hostellers, Prisoners and Other High Risk Situations Conditions like Corporates, Manufacturing Units, Miners, Frequent Air Travelers, etc.)

Military personnel are at higher risk of developing influenza and military camps carry the risk of disease outbreak. Similarly, students staying in hostels are also at higher risk of influenza outbreak. Influenza vaccination of Singapore’s Armed Forces resulted in moderate to high degree of protection against influenza A(H1N1)pdm09 and influenza B.

Recommendations

- Any industry can host immunization camps in their organization to benefit their workers. Vaccination of workers /employees for Influenza substantially reduces influenza like illness and absenteeism in all types of industries. Thus annual influenza vaccination is beneficial in these settings.
- In case of epidemics, if travel is must, vaccination should be taken before traveling.
- Military, paramilitary and emergency personnel are prone to outbreaks of respiratory illnesses including influenza for variety of reasons. They are at risk particularly in crowded places such as recruitment camps. Influenza is one of the few infectious diseases that is able to disrupt military operations quickly. Seasonal influenza varies from year to year and since its impact is dependent on antigenic evolution, it is largely unpredictable.
- Military land forces are typically most at risk of influenza when crowded into camps, particularly recruit camps.
- Air forces have been particularly concerned with influenza, not because they are more susceptible than other military groups, but because large numbers of flight personnel can suddenly become sick and unable to fly during an influenza outbreak within a short time. Flight personnel often undertake international travel extensively, thereby increasing the risk of early introduction of new influenza viruses into air force installations.
- Naval forces have to deal with the particular problem of ship board influenza epidemics given the crowded conditions on board most warships.
- Therefore annual Influenza vaccination is recommended to the armed forces personnel from Army, Navy or Air-force.
- Hostellers, boarding school and medical colleges: Mass immunization is very effective in increasing the uptake of vaccination and success rate. Hostellers comprise a large, susceptible segment of the population and...
regularly have a high attack rate. It is recommended to immunize the hostellers annually with Influenza vaccine.

- It is important to immunize the prison staff rather than the residents. Staff with influenza like illness should stay home and remain home for seven days after symptoms subside.
- In airline personnel - In case ill, it is important to immunize.
- Uptake in India is dismal.
- Periodic training of the staff.
- Access to vaccination is key to minimize risk of pandemic influenza. Vaccine should be made available at any time especially in high risk areas.
- Multiple vaccines given in single visit, reduction of financial barriers and use of all possible means to create awareness are some of the useful measures to improve the uptake rates of influenza.
- Vaccine reminders through cellular companies as a part of corporate social responsibility can be considered.

Other General Recommendation

- Importance of hand washing and cough etiquette should be emphasized to all.

Poor Influenza Vaccine Uptake in India

Vaccine uptake in India is dismal even among the high risk population including healthcare workers,8 COPD,29 diabetics,74 and pregnant females67 in India is dismal.

Recommendations for Improving the Implementation of Influenza Vaccination

Following are general recommendations for improving access to influenza vaccination.

- Efforts should be made to create and maintain disease specific registries for systemic tracking and reminders for vaccination.
- Periodic training of the staff accompanied by ongoing assessment of immunization rate and workflow with close follow up is essential.
- Quality assurance and standards of care should be maintained.
- Clinics using vaccination should try to maintain the records to assess the efficacy of vaccines and occurrence of complications.
- Awareness among patients as well as physicians should be improved for improving vaccination uptake rate.
- Along with the vaccine recommendation, the patients should also be educated about the risk of the illness and its complications which can be prevented by vaccination.
- Access to vaccination is key to minimize risk of pandemic influenza. Vaccine should be made available at any time especially in high risk areas.
- Haji & Umrah- Severe crowding, shared accommodation, reduced personal hygiene, and environmental pollution at Haji & Umrah may collectively lead to increased transmission of respiratory viruses, notably influenza. The Centre for Disease Control and Saudi Government recommend that international pilgrims be vaccinated against seasonal influenza before arriving in the country. The group endorses this recommendation. It is strongly recommended that even in other large gatherings like Kumbh mela the pilgrims should get an Influenza vaccination prior to travelling to the religious shrines.

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