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Influenza

Vaccine introduced in 1998

NOTIFIABLE

In some circumstances, advice in these guidelines may differ from that in the Summary of Product Characteristics (SmPC) of the vaccines. When this occurs, the recommendations in these guidelines, which are based on current expert advice from NIAC, should be followed.

Introduction

Influenza is an acute illness of the respiratory tract with systemic symptoms. It affects all age groups and is characterised by the abrupt onset of fever headache, myalgia, cough, sore throat and malaise. It is usually self-limited, with recovery in 2-7 days but it can be severe.

Influenza is caused by a highly infectious RNA virus that spreads rapidly, especially in institutions. There are three types of influenza virus, A, B and C. Types A and B cause most influenza illness.

Influenza outbreaks occur most years (Fig 11.1), with the extent and severity varying widely. In some outbreaks, influenza A and B viruses circulate simultaneously. Pandemics provide the most dramatic evidence of the impact of influenza, although outbreaks that occur between pandemics account for greater mortality and morbidity, albeit over a longer period of time. Since 2009, influenza A (H1N1 2009), influenza A (H3N2) and influenza B have been in circulation.

Influenza A viruses infect a wide range of animal and avian species, particularly waterfowl. They have two surface antigens- haemagglutinin (H) and neuraminidase (N). The viruses are divided into subtypes, based on their H and N content. Only H1, H2, H3, N1 and N2 have been implicated in widespread human infection. Periodic mutations of the

surface antigens occur. Minor changes, (antigenic drift) are seen from season to season, and are the reason why the vaccine composition changes each year. Major changes (antigenic shift) occur periodically and result in an immunologically distinct virus, facilitating pandemic spread with the potential for severe morbidity and high mortality. The most recent pandemic was in 2009/ 2010, caused by H1N1 (2009) virus. Most seasonal influenza is caused by Type A.

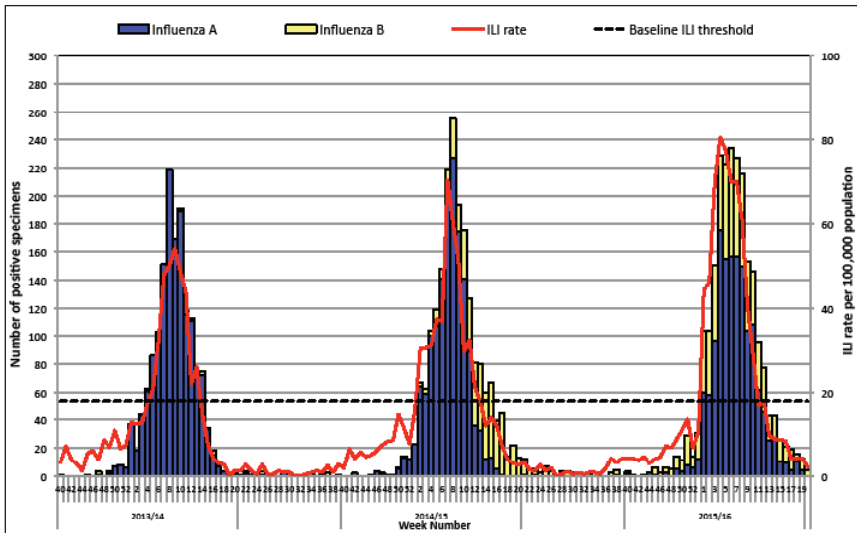
Influenza B viruses only infect humans and seals. This limited host range is likely to be the reason for the lack of Influenza B virus -caused pandemics. Mutations rarely occur in influenza B. Type B causes outbreaks every few years. The illness is generally less severe than that caused by Type A.

Influenza C is a common cause of mild upper respiratory tract illness. It infects humans and pigs. Lower respiratory tract complications and systemic illness are uncommon and occur mainly in children. Most people have acquired immunity by adulthood.

Influenza epidemics begin abruptly, reach a peak over a 2-3 week period, generally last for 2-3 months and often subside as rapidly as they began. Epidemics in temperate climates begin almost exclusively during late Autumn.

Figure 11.1 Influenza-like illness (ILI) sentinel GP consultation rates per 100,000 population, baseline ILI threshold rate, and number of positive influenza A and B specimens tested by the NVRL, by influenza week and season (2013 - 2015).

Source: HPSC



Transmission

Influenza is spread from person to person by aerosol, droplets or by contact with materials recently contaminated by respiratory secretions.

It is highly infectious,,especially in close contact environments such as homes for the elderly. It is contagious from 1- 2 days before to 4-5 days after symptom onset. Shedding can be more prolonged in young children and in the immunocompromised. Asymptomatic carriers may shed the virus.

Effects of influenza

Although infection may be asymptomatic in up to 75% of cases, influenza outbreaks result in significant morbidity. The incubation period is 1-4 days. Onset is sudden, with fever, rhinitis, cough, myalgia and headache. Pneumonia, either primary viral or secondary bacterial, can occur. Symptoms generally last for 3-5 days, and recovery is usually rapid.

The illness is more severe in the elderly, in those with chronic heart or lung disease, in children aged <4 years or with cerebral palsy and in pregnant women.

Eighty to 90% of reported deaths from influenza occur in the elderly, mainly from secondary bacterial pneumonia, but also from exacerbations of underlying disease e.g. chronic obstructive pulmonary disease or cardiac disease.

Influenza vaccines

Vaccines recommended by WHO are prepared each year, using virus strains similar to those considered most likely to circulate in the forthcoming season.

Three types of influenza vaccine are available:

- **Inactivated trivalent influenza vaccines (TIV)** contain antigens from two type A and one type B virus strains that have been cultured in eggs or in cell lines. The strains vary from season to season, depending on circulating viruses.

There are three types of TIVs - whole virus, split-virus (subvirion) and surface-antigen vaccines (one of which, Flud, is adjuvanted). The non-adjuvanted vaccines are of equivalent immunogenicity and effectiveness. The antibody response to Flud is increased when compared to vaccines without adjuvant, particularly in elderly subjects with low pre-immunisation titres and/or with underlying diseases (diabetes, cardiovascular and respiratory diseases).

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The whole-cell vaccines are more likely to induce febrile reactions in children.

- **Inactivated quadrivalent influenza vaccines (QIV)** contain antigens from two type A and two type B virus strains, that have been cultured in fertilised hens' eggs. The strains vary from season to season, depending on circulating viruses.

All parenteral TIV and QIV influenza vaccines are supplied in a prefilled syringe for IM injection.

- **Live attenuated quadrivalent influenza vaccine (LAIV)** containing antigens from two type A and two type B virus strains, cultured in eggs. The vaccine is provided as a nasal spray suspension.

Influenza vaccines provide seasonally variable protection of 40-90% against influenza in persons less than 65 years of age. Protective efficacy against infection is lower in the elderly. However influenza associated morbidity and mortality are significantly reduced in older people who have been vaccinated. Protection lasts about one year.

An up-to-date list of licensed vaccines can be accessed on the HPRAs website www.hpra.ie

A list of the currently available vaccines from the National Cold Chain Service can be found at www.immunisation.ie

The vaccines should be stored at +2 to +8°C. If a vaccine has been frozen it should not be used.

Dose and route of administration

Inactivated vaccine (TIV, QIV)

The dose is 0.5ml given by intramuscular injection into the anterolateral thigh or deltoid.

Live attenuated influenza vaccine (LAIV)

The dose is 0.2ml given by nasal spray – 0.1 ml into each nostril

LAIV immunisation must be given intranasally.

Children under 9 years of age and those in specific at risk groups require two doses of vaccine separated by 4 weeks. (Table 11.1).

Table 11.1 Dose of influenza vaccine

Age group	Dose
Children aged 6 months* to <9 years	Two doses, 4 weeks apart, if receiving influenza vaccine for the first time
Those aged 9 and older <ul style="list-style-type: none"> • post haematopoietic stem cell transplant • post solid organ transplant 	Two doses, 4 weeks apart, if receiving influenza vaccine for the first time post transplant
Cancer patients who receive the vaccine while on chemotherapy and who complete their treatment in the same season	Two doses 2 nd dose on completion of treatment at least 4 weeks after 1 st dose (regardless of influenza vaccination in previous seasons)
All others	One dose

*LAIV from 24 months

Influenza antibodies take from 10-14 days to reach protective levels following vaccination.

Inactivated influenza vaccine (TIV, QIV) may be given at the same time, but at a different site, as any other vaccine (except PCV see Precautions below).

Live attenuated influenza vaccine can be given at the same time as other live or inactivated vaccines.

Indications

Inactivated Trivalent influenza vaccines (TIV):

Non-adjuvanted: active immunisation of adults and children from 6 months of age for the prevention of influenza disease caused by the two influenza A virus subtypes and one influenza B virus subtype contained in the vaccine. Adjuvanted (Fluad): active immunisation against influenza in the elderly (65 years of age and over), especially for those with an increased risk of associated complications.

Quadrivalent influenza vaccines (QIV):

Active immunisation of adults and children from 3 years of age for the prevention of influenza disease caused by the two influenza A virus subtypes and the two influenza B virus types contained in the vaccine.

Live attenuated quadrivalent influenza vaccine (LAIV):

Prophylaxis of influenza in children and adolescents from 24 months to less than 18 years of age.

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LAIV should NOT be used below 24 months of age because of safety concerns regarding increased rates of hospitalisation and wheezing in this population

Annual influenza vaccination is strongly recommended for those in the at risk groups and all health care workers.

Influenza vaccination is strongly recommended for:

1. Those aged 6 months and older who are at increased risk of influenza-related complications:
 - a) People aged 50 years or older.
 - b) People with chronic illness requiring regular medical follow-up e.g. chronic heart disease (including acute coronary syndrome), chronic liver disease, chronic neurological disease (including multiple sclerosis and hereditary and degenerative disorders of the central nervous system), chronic renal failure, chronic respiratory disease (including chronic obstructive pulmonary disease, cystic fibrosis, moderate or severe asthma, and bronchopulmonary dysplasia), diabetes mellitus, haemoglobinopathies.
 - c) Patients with immunosuppression due to disease or treatment, including asplenia or hyposplenism and all cancer patients.
 - d) Patients with any condition that can compromise respiratory function (e.g. spinal cord injury, seizure disorder, or other neuromuscular disorder) especially those attending special schools/ day centres.
 - e) Children and adults with Down syndrome.
 - f) Children with moderate to severe neurodevelopmental disorders such as cerebral palsy and intellectual disability.
 - g) Children on long-term aspirin therapy (because of the risk of Reye's syndrome).
 - h) People with morbid obesity i.e. Body mass index ≥ 40 .
 - i) Residents of nursing homes, old people's homes, and other long stay facilities where rapid spread is likely to follow introduction of infection.
2. Those likely to transmit influenza to a person at high risk for influenza complications (see 1 above)
 - a) Health Care Workers, both for their own protection and for the protection of patients who may have a suboptimal response to influenza vaccinations (see Chapter 4).

- b) Household contacts of at-risk persons.
 - c) Out-of-home care givers to at-risk persons.
3. All pregnant women at any stage of pregnancy (inactivated influenza vaccine only). Pregnancy increases the risk of complications from influenza because of the alterations in heart rate, lung capacity, and immunological function. It is estimated that immunisation could prevent 1-2 hospitalisations per 1,000 pregnant women. Because inactivated influenza virus vaccine is not a live vaccine it is very safe in pregnancy.
 4. People who have close, regular contact with pigs, poultry or water fowl.

Anyone (aged 6 months and older) who wishes to reduce their risk of infection may choose to have the seasonal influenza vaccine.

Note: if travelling to the southern hemisphere refer to Chapter 5.

The ideal time for vaccination is before the influenza season, i.e. from September to October but the vaccine may be given until the end of April.

Contraindications

Inactivated influenza vaccine (TIV, QIV)

- Anaphylaxis following a previous dose of influenza vaccine or any of its constituents (other than ovalbumin – see precautions)

Live attenuated influenza vaccine

- Anaphylaxis following a previous dose of influenza vaccine or any of its constituents (including ovalbumin)
- Concomitant use of aspirin
- Significant immunosuppression (see Chapter 3).
- Children and adolescents with severe asthma or active wheezing corresponding to the British Thoracic Society BTS/ Sign Asthma Guideline Step 5
- Children who have taken influenza antiviral medications within the previous 48 hours
- Pregnancy
- Egg allergy (due to insufficient data)
- Persons who care for severely immunosuppressed persons should not receive LAIV, or should avoid contact with persons for 2 weeks after receipt.

In a small number of people receiving Ipilimumab or combination checkpoint inhibitor therapy, fatal immune related adverse events (irAEs) occurred after receipt of an influenza vaccination. The theoretical risk that any event that stimulates the immune system could trigger the onset of irAEs means a possible role of influenza vaccination cannot be discounted.

There are currently no international consensus statements on the use of influenza vaccines in people receiving combination immune checkpoint inhibitor treatment.

Until further evidence emerges, patients on combination checkpoint inhibitors (e.g. ipilimumab plus nivolumab) should not receive any influenza vaccines, because of a potential association with immune-related adverse reactions.

Precautions

Inactivated influenza vaccine (TIV, QIV)

- Acute severe febrile illness, defer until recovery.
- Egg allergy: Those with confirmed egg anaphylaxis or egg allergy can be given an influenza vaccine with an ovalbumin content <0.1 micrograms per dose, see Table 11.2. Vaccines with ovalbumin content equal to or more than 0.1 micrograms per dose or where content is not stated should not be used in egg-allergic individuals.

Table 11.2 Inactivated influenza vaccination of those with egg allergy

History	Recommendation
Non-anaphylactic egg allergy without severe asthma (BTS/ SIGN <4)	Seasonal influenza vaccine with ovalbumin content <0.1 micrograms per dose, in primary care, with observation for 60 minutes
Egg anaphylaxis or egg allergy and severe asthma (BTS/ SIGN ≥4)	Refer to hospital specialist for vaccination with seasonal influenza vaccine with ovalbumin content <0.1 micrograms per dose. Skin testing is <u>not</u> necessary and vaccine should be given as a single dose with observation for 60 minutes

- In children aged 12-23 months of age for whom influenza vaccine is recommended, it should be separated from PCV vaccine by at least 1 week. This is because of a slightly increased risk of febrile convulsions if the vaccines are given at the same time in this age group.

Live attenuated influenza vaccine

- Acute severe febrile illness, defer until recovery.

Adverse reactions

Inactivated influenza vaccines (TIV, QIV)

Local: Injection site pain and swelling are very common.

General: Fever, fatigue, myalgia, and irritability in young children are very common. Drowsiness, sweating and arthralgia are common.

A higher incidence of mild post-immunisation reactions has been reported with Fludac compared to non-adjuvanted influenza vaccines.

Very rare: Immediate allergic reactions.

Very rare reports of Guillain-Barré syndrome have been observed in the post-marketing setting following influenza vaccination. The risk of GBS following influenza infection is several times greater than that following influenza vaccination.

Injectable influenza vaccines are inactivated (non-live) and cannot cause influenza.

Live attenuated quadrivalent influenza vaccine (LAIV):

Local: Very common or common: Nasal congestion/rhinorrhoea, decreased appetite, malaise, pyrexia, headache and myalgia.

Very rare: Immediate allergic reactions. Very rare reports of Guillain-Barré syndrome have been observed in the post-marketing setting following influenza vaccination. The risk of GBS following influenza infection is significantly greater than that following influenza vaccination.

Prophylactic use of antiviral medication

If considering using antiviral medication check the HPSC website to ascertain if influenza is circulating and only use antivirals if this is confirmed.

Antivirals such as neuraminidase inhibitors can be used for treatment and prophylactic purposes during influenza outbreaks.

Indications for prophylaxis include:

- Non immunised persons in 'at risk' groups, including health-care workers, for 2 weeks while the vaccine takes effect.
- Control of influenza outbreaks in a closed setting such as institutions with high-risk individuals.
- Protection of immunocompromised children who may not respond to vaccine.

Influenza surveillance

The Health Protection Surveillance Centre in partnership with the Irish College of General Practitioners (ICGP) and the National Virus Reference Laboratory (NVRL) have established a network of 60 computerised sentinel practices who report on a weekly basis the number of patients seen with influenza-like illness. Virological confirmation by the NVRL is required to identify that influenza is the causative virus, with classification of type and sub-type.

Throughout the inter-season period weekly reports on clinical data, fortnightly reports on virological data and weekly or fortnightly surveillance reports are produced. Reports of worldwide influenza activity are also provided as part of the overall monitoring of influenza activity.

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