Influenza immunisation

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SYNOPSIS

Many flu-like illnesses are not caused by influenza, however influenza is a significant cause of morbidity. Its complications include pneumonia, and increase mortality particularly during pandemics. Elderly people are particularly vulnerable and vaccination is recommended for everyone over 65 years old. The efficacy of the vaccines depends on how well they match the circulating strains of the virus. A systematic review suggests the efficacy for preventing infection may be as low as 24%. The vaccine may be more efficacious at preventing complications in the elderly. Neuraminidase inhibitors and ion channel inhibitors are not very effective treatments for influenza.

Index words: pneumonia, vaccines, amantadine, neuraminidase inhibitors.

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Introduction

Influenza is an infectious disease of humans, horses, pigs, and both wild and domesticated birds. It is highly infectious for humans and epidemics in European populations have been recorded since the early sixteenth century. Pandemics have occurred 3–5 times each century since 1700.[1]

Clinical features

Influenza is an acute viral respiratory infection characterised by febrile illness, myalgia, unproductive cough, headache, severe malaise, sore throat and rhinitis. The incubation period is 1–4 days. While the median duration of illness is three days, this may vary by viral serotype. Cough and malaise can persist for weeks. Complications include otitis media, pneumonia, bronchiolitis and exacerbations of chronic respiratory disease. Other consequences include febrile convulsions, Reye's syndrome and myocarditis.[2,3] The complications account for the considerable morbidity and mortality of influenza.

Virology

The viruses causing human influenza were discovered in the 1930s.[4] The virus has an RNA core, a protein shell and a lipid membrane. There are two glycoproteins on the membrane, a haemagglutinin (H) and a neuraminidase (N). The haemagglutinin assists viral entry into the cells of the respiratory epithelium while the neuraminidase also facilitates release of new virions from infected cells.

There are three serotypes of influenza virus (A, B and C) determined by the antigenic make-up of the core, but only serotypes A and B are of importance in human disease. Serotype A viruses are further characterised by serological identification of the H and N proteins. Since 1977 the commonly circulating A serotypes have been H1N1 and H3N2. There is further variation and individual strains are named after the place, serial number and year of first isolation, e.g. influenza A/Sydney/5/97 (H3N2).[2]

The virus has a marked capacity to mutate, undergoing antigenic drift, with incremental changes over time, and antigenic shift, where large changes occur over a short interval. For example, in 1957 the predominant influenza A virus changed from H1N1 to H2N2. Antigenic shifts were associated with the pandemics in 1919, 1957 and 1968.

Most new varieties appear to originate in southern China in ducks or pigs, and the high population numbers and densities in that region then promote rapid transmission to the rest of the world. A recent example of an antigenic shift is the A/Hong Kong/156/97 (H5N1) virus, and despite fears at the time of a pandemic this did not eventuate.[2]

Epidemiology

Defining a case of influenza is difficult without virological or serological testing, and clinical diagnosis is unreliable. Surveillance for influenza is based on laboratory data resulting in high specificity (cases identified tend to be true cases), and low sensitivity (many true cases are not identified). Surveillance data therefore do not tell us about the burden of disease.[5] Influenza possibly accounts for 13% of cases of respiratory tract infection, and 9% of the world's population may catch influenza each year. Infection peaks in winter, with a typical season lasting 6–8 weeks.[6]

Mortality and morbidity

Generally, the incidence of influenza is higher in children, the elderly, and those living in close proximity to each other. Influenza and pneumonia (of all types) are among the 10 leading causes of death, mostly in the elderly. In the USA estimates of 'excess' mortality due to 'pneumonia and influenza' have ranged from 1800 to 11 700 in the period 1979–92 (in a population of some 250 million). Interestingly, only A H3N2 'is regularly associated with excess mortality'.[7]

Complications of influenza are not evenly distributed over the population. High-risk population groups for mortality include the elderly and those with chronic morbidity.[5] The risk of hospitalisation varies according to age and pre-existing health status.[3] During pandemics the burden of disease can be very high indeed.[2]

Preventive strategies

Preventive strategies for influenza include immunisation and the use of antiviral agents.

Vaccines

Currently available influenza vaccines are inactivated split virus vaccines manufactured from virus stock grown in chick embryos. They are trivalent, containing two A types (H1N1 and H3N2) and one B type. They are standardised to contain 15 microgram of haemagglutinin of each virus and are given by deep subcutaneous injection (the National Health and Medical Research Council (NHMRC) recommends a 25 mm 23 gauge needle). Immunity to haemagglutinin appears to be a strong determinant of protection.[2]

The efficacy of influenza vaccine is determined by several factors[8], including:

- the immunogenicity of the vaccine
- the degree of match between vaccine and wild virus
- the age and health of recipient.

During ageing, primary T-cell dependent antibody responses decline, but secondary responses tend to be maintained. Some of this effect may be due to prior exposure to similar wild virus. Persons with chronic medical conditions tend to respond less well, leading to a problem of low response in nursing homes.[9] The vaccine prevents complications (death, hospitalisation) in recipients[4], but does not prevent transmission in aged-care settings.[7]

To be efficacious, vaccines have to be tailored to the circulating serotypes of the influenza virus. The World Health Organization (WHO) has established a system for predicting which serotypes will be in circulation. This surveillance system is based on 110 laboratories in 79 countries and four reference centres (London, Atlanta, Tokyo and Melbourne). Each year WHO recommends the composition of vaccine for the influenza season in each hemisphere. This recommendation is then considered by the Australian Influenza Vaccine Composition Committee, which decides on the composition of the vaccine to be used during the influenza season in Australia.

Influenza vaccine effectiveness

Influenza vaccination appears to have 70–90% strain-specific effectiveness in healthy adults for 1–3 years[4] when vaccine and circulating strains are well matched. Vaccination of healthy adults is associated with reduced absenteeism and reduced demand on healthcare resources.[3] Vaccine effectiveness does not rapidly wane, however there is considerable antigenic drift from year to year in the circulating strains of influenza virus, so there is a need to immunise each year to cover the circulating virus. The timing of immunisation is not critical, provided the vaccine is the current strain and is given more than two weeks before the expected exposure to risk.

In elderly people the protection conferred against influenza is lower at about 30–60%, but protection against complications and death is higher.[4] The efficacy of influenza vaccine for preventing hospitalisation and pneumonia in the elderly is around 50–60%.[3]

In the military, respiratory disease is the second highest cause of morbidity and the sixth highest cause of reduced productivity. In the British Army in 1996–97, 40% of this respiratory disease was due to influenza, particularly in new recruits. This problem led to a Cochrane evaluation of influenza vaccine[10,2], which found 10 acceptable trials that showed a reduction of 29% in 'influenza cases' (95% CI* 12–42%), and a saving in time off work of 0.4 working days. Sixteen acceptable trials showed a vaccine efficacy for a clinical case definition of 24% (95% CI 15–32%), and for a serological and clinical case definition of 68% (95% CI 49–79%). Mismatches between vaccine and circulating strains appeared to explain most of the lack of efficacy. The review concluded that 'the results of this study seem to discourage the utilisation of vaccination against influenza in healthy adults as a public health measure.'[10]

Adverse events

Around 10–65% of influenza vaccine recipients report pain at the injection site, and occasionally more generalised myalgias. Local and systemic reactions, usually fever, malaise and myalgia, occur rarely. They are usually mild, maybe of 1–2 days duration.[4] Immediate hypersensitivity reactions, ranging from urticaria to anaphylaxis, are rare and are probably caused by hypersensitivity to egg protein. Guillain-Barré syndrome has been reported after influenza immunisation, first being noted with the 1976 vaccine. Analysis of adverse events with subsequent vaccines shows a much lower increase in risk (an increase of about 1–2 cases per million recipients above background), but these results are not statistically significant and are at the limits of epidemiological methods. Whether Guillain-Barré syndrome is caused by influenza vaccination has not been established.[11,3]

Contraindications

Influenza vaccine should not be given to people with anaphylactic hypersensitivity to eggs or hypersensitivity to any influenza vaccine component. Vaccination should be deferred in people with a current acute febrile illness (>38.5°C) and caution should be exercised if there is a history of Guillain-Barré syndrome.[3,11]

Drugs

The ion channel inhibitors (amantadine and rimantadine) and neuraminidase inhibitors (zanamivir and oseltamivir) have some effectiveness in influenza treatment and prophylaxis. Amantadine and rimantadine both interfere with the replication of type A influenza virus, but have no action on type B viruses. Neuraminidase inhibitors inhibit the entry of viruses into cells and the exit of virus particles from cells. They are active against types A and B.[2] None of these drugs is widely used in Australia and, while their use may be of value in individual cases, they confer little public health benefit.[2]

* CI confidence interval

Costs and benefits

Influenza is expensive to the community. The cost of influenza in the USA has been estimated to be US$1–3 billion in direct costs per year, and US$10–15 billion in indirect costs, mostly due to time off work.[6]

In the USA a demonstration project was carried out between 1989 and 1992 to determine the costs to Medicare (the US health insurance program for the elderly) of immunising the elderly against influenza.[12] This concluded that immunisation of persons over 65 years of age was likely to be cost-effective.

Recommendations for the use of vaccine

In the USA, the Advisory Committee on Immunization Practices recommends that 50–65 year-olds should receive vaccine because 24–32% have chronic medical conditions which confer a higher risk of influenza-related hospitalisation and death. Immunisation coverage of high-risk individuals under 65 years old is not high and the Advisory Committee on Immunization Practices considers that an age-based strategy will achieve higher levels of immunisation of at-risk individuals than a 'high-risk' strategy.[3] This is not currently recommended in Australia, but the Australian Technical Advisory Group on Immunisation is reconsidering its recommendations to the NHMRC on influenza immunisation, including the issue of immunising everyone 50 years of age and older.

The vaccine should be offered to patients a few months before the influenza season, which in most of Australia usually starts between June and September. The NHMRC currently recommends that annual influenza vaccination, with a vaccine registered for use in the current season, be offered to the following groups[11]:

- everyone 65 years of age and older
- Aboriginal and Torres Strait Islander people 50 years of age and older
- people six months of age and older with chronic illnesses requiring regular medical follow-up or hospitalisation in the previous year
- people six months of age and older with chronic illnesses of the pulmonary or circulatory systems (except asthma)
- residents of nursing homes or long-term care facilities
- children and teenagers aged six months to 18 years on long-term aspirin therapy (because aspirin treatment puts them at risk of Reye's syndrome if they develop a fever)
- healthcare and other workers providing care to the high-risk groups above.

Other groups for whom influenza immunisation should be considered include pregnant women, overseas travellers and persons infected with HIV.

Commonwealth-funded vaccine is available for:

- those 65 years of age and older
- Aboriginal and Torres Strait Islander people 50 years of age and older
- Aboriginal and Torres Strait Islander people with chronic medical conditions.

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Conflict of interest: none declared

Self-test questions

The following statements are either true or false (answers on page 23)

1. Influenza vaccine has an efficacy of 98% in protecting people against influenza.
2. Influenza vaccine contains a live virus so is contraindicated in people infected with HIV.

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