INFLUENZA VACCINATION AND MANAGEMENT

SUMMARY

- **Morbidity and mortality related to influenza occur at a higher rate in people over 65 and those with underlying chronic medical conditions.**
- **Annual influenza vaccination of all older people is a cost-effective way of reducing influenza-related illness and deaths.**
- **Modern influenza vaccines are effective and safe.**
- **Lack of published data on the inhaled antiviral zanamivir limits its widespread use.**

INTRODUCTION

Epidemics of influenza occur during the winter months nearly every year and are responsible for approximately 20,000 deaths per year in the U.S.[1,2,3] Influenza viruses may cause global epidemics of disease known as pandemics during which rates of morbidity and mortality from influenza-related complications increase dramatically. Influenza viruses cause disease in all age groups. Rates of infection are highest among children but rates of serious morbidity and mortality are highest among persons aged >65yrs and persons of any age who have medical conditions that place them at high risk for complications from influenza.

Influenza vaccine is the primary method for preventing influenza and its more severe complications. Antiviral drugs for influenza are an adjunct to influenza vaccine for the control and prevention of influenza.

BIOLOGY OF INFLUENZA

Influenza A and B are the two types of influenza viruses that cause epidemic human disease.[1] Influenza A viruses are subdivided into subtypes on the basis of two surface antigens: haemaglutinin and neuraminidase. Both influenza A and B viruses undergo continual antigenic changes termed antigenic drift. The constant development of antigenic variants through antigenic drift is the virologic basis for seasonal epidemics and the reason for the incorporation of one or more new virus strains in each years influenza vaccine.[4,5]

Influenza A viruses also change through a process known as antigenic shift, giving rise to new subtypes at periodic intervals. Immunity to the surface antigens, especially haemaglutinin, reduces the likelihood of infection and lessens disease severity if infection occurs. However, antibody against one influenza strain confers

little or no protection against another strain. Antigenic shift can result in pandemics because there is no immunity to the new subtype.

CLINICAL SIGNS AND SYMPTOMS OF INFLUENZA

Uncomplicated influenza illness is characterised by the abrupt onset of constitutional and respiratory signs and symptoms (e.g. fever, myalgia, headache, malaise, sore throat, rhinitis and dry cough).[4,5] For most people the illness typically resolves after several days although malaise and cough may persist for a couple of weeks. In some people, influenza can exacerbate underlying medical conditions e.g. pulmonary or cardiac disease or lead to secondary bacterial pneumonia or primary influenza viral pneumonia.

Influenza is spread from person to person by direct contact, by droplet infection or by materials recently contaminated by nasopharyngeal secretions. It is highly contagious especially among institutionalised populations.

INFLUENZA VACCINE

The major public health measure for prevention of influenza has been the use of annual inactivated influenza vaccines. October through November is optimal time to vaccinate but the vaccine may be given any time during influenza season if cases are still occurring in the community.[6,7] Vaccination must be carried out annually because immunity wanes and because the vaccine is changed each year to incorporate the antigens of current and emerging influenza strains.[1,4,5,8] The World Health Organisation monitors influenza viruses throughout the world and makes recommendations each year about the strains to be included in vaccines for the forthcoming winter. Each years' Influenza vaccine contains three virus strains. The highly purified viruses are grown in embryonated hens eggs, chemically inactivated and then further treated and purified.

The effectiveness of influenza vaccine depends primarily on the age and immunocompetence of the vaccine recipient and the degree of similarity between the virus strains in the vaccine and those in circulation.[1] Studies on influenza vaccination in older people indicate that the vaccine is highly effective. The most comprehensive review showed cases of respiratory illness, pneumonia, hospitalisations (resulting from influenza related illness) and mortality to be reduced by over 50% in institutionalised elderly people.[9] Other observational studies have shown that the vaccine is equally effective in reducing mortality in older people living in the community and those not classed as medically at high risk.[10,11]

TARGET GROUPS FOR VACCINATION

The Immunisation Guidelines for Ireland recommend vaccination for the following groups who are at increased risk of complications from influenza:[4]

- Persons aged >65yrs
- Residents (any age) of nursing homes and other chronic-care facilities.
- Adults and children with chronic cardiac or pulmonary disorders.
- Adults and children with other chronic conditions such as diabetes mellitus, cancer, immunodeficiency, immunosuppression (due to underlying disease or therapy).

A case for the vaccination of other groups such as health care workers and working adults has been advanced.[1,12]

PERSONS WHO SHOULD NOT BE VACCINATED

Inactivated influenza vaccine should not be administered to persons known to have anaphylactic hypersensitivity to eggs or to other components of the influenza vaccine. Persons with acute febrile illness usually should not be vaccinated until their symptoms have abated. While there is no evidence that the inactivated vaccine causes damage to the fetus it is not recommended during pregnancy.[4,5]

ADVERSE EFFECTS OF VACCINES

Influenza vaccines are safe and associated with only minimal side-effects.[1,4,5,6] It should be emphasised to patients that inactivated influenza vaccine contains non-infectious killed viruses and cannot cause influenza and that respiratory disease after vaccination is coincidental and unrelated to vaccination. Asthma is thought not to be exacerbated by influenza vaccination. The most frequent side effect of vaccination is soreness and redness at the vaccination site. These local reactions are usually mild and normally subside within 48 hours of vaccination.

Systemic side effects such as fever, malaise, myalgia and headaches occur with the same frequency in those receiving a placebo as they do in vaccinated groups.[1]

Immediate reactions e.g., hives, angioedema, allergic asthma and systemic anaphylaxis rarely occur after influenza vaccination. These reactions probably result from hypersensitivity to some vaccine component most likely residual egg protein.

Guillian-Barre Syndrome (GBS) has been reported in association with influenza vaccination in 1976 to 1977 season.[13,14] However active surveillance in 1978 and retrospective studies in subsequent years have not demonstrated a causal link between GBS and influenza vaccine.

COST-EFFECTIVENESS

Economic evaluations in the USA based on studies comparing vaccinated and non-vaccinated populations have shown that annual influenza vaccination is a cost-

effective way of reducing morbidity and saving lives in people over 65.[15-18.] There have been no cost-effectiveness studies to date in Britain or Ireland.

ANTIVIRALS

The development of influenza neuraminidase inhibitors offer the possibility of actively treating influenza infection.[19] The only agent available prior to this, amantadine, was little used because of side-effects, emergence of resistance and the non-susceptibility of influenza B.[20,21] Neuraminidase is essential for the release of virus from infected cells and may also reduce the inactivation of virus by respiratory secretions.

A number of these drugs are in the course of development and one zanamivir, (Relenza®) has recently been launched in Ireland. There is little experience of its use outside clinical trials, so a cautious approach is warranted.

Zanamivir is licensed for use commencing within 48 hours of symptom onset, however in two of the largest published studies to date no significant benefit was shown in the subgroup where treatment was commenced after 30 hours.[22-24] In a third study the mean duration of symptoms at enrolment was 25 hours.[25] Patients with symptoms for longer than 36 hours at presentation were excluded from this study. It is likely that many patients will not present to their doctor and have the prescription dispensed within this time frame. Zanamivir is delivered by dry powder inhaler as it has poor oral bioavailability. This has the advantage of minimal systemic absorption and low risk of drug-drug interactions or side effects, but may make it more difficult to use for some patients (at least one trial used poor inhaler technique as an exclusion criterion, although no figures were given).[25]

The other difficulty is that the drug is specific to influenza (both A and B subtypes) and no benefit was shown for patients who were not subsequently proven to have influenza virus. In clinical trials only between 57% and 71% of subjects recruited were found to have laboratory confirmed influenza.[23-25] In the absence of a surveillance system in the community, these figures could be significantly lower.

Little if any benefit accrues to subjects who were not pyrexial (>37.8°C) at presentation.

While the duration of symptoms may be reduced in those treated early it remains to be proven whether zanamivir will reduce morbidity, hospitalisation and mortality among high-risk patients. It is not a substitute for vaccination.

Pending further experience and published trials it is reasonable to confine use of zanamivir to patients:

- presenting within 30 hours of onset of influenza symptoms, with pyrexia >37.8°C
- where there is no evidence of bacterial infection

- when influenza has been confirmed to be prevalent.

- The first dose of the drug must be readily available.

The absence of near patient testing or a formal surveillance system makes the rational use of this drug problematic, but it represents an exciting development in the management of viral illness. It will compete with an oral neuraminidase inhibitor, oseltamivir, which is awaiting approval worldwide.

COST OF 5 DAYS THERAPY (GMS SEPTEMBER 1999)

Preparation	**Cost**
Zanamivir (Relenza®) 10mg BD	**£15.32**

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