World Health Organization

Influenza

Fact Sheet N°211
Revised March 2003

Overview

Influenza is caused by a virus that attacks mainly the upper respiratory tract – the nose, throat and bronchi and rarely also the lungs. The infection usually lasts for about a week. It is characterized by sudden onset of high fever, myalgia, headache and severe malaise, non-productive cough, sore throat, and rhinitis. Most people recover within one to two 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.

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. In the United States of America, for example, recent estimates put the cost of influenza epidemics to the economy at US$ 71-167 billion per year.

In annual influenza epidemics 5-15% of the population are 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 three and five 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. For example, during an influenza outbreak in Madagascar in 2002, more than 27 000 cases were reported within three months and 800 deaths occurred despite rapid intervention. An investigation of this outbreak, coordinated by the World Health Organization (WHO), found that there were severe health consequences in poorly nourished populations with limited access to adequate health care (see ”Outbreak of influenza, Madagascar, July-August 2002”,Weekly Epidemiological Record,). It is not possible to extrapolate the exact annual burden of influenza in the tropics from data from such occasional and severe outbreaks.

The virus

The currently circulating influenza viruses that cause human disease are divided into two groups: A and B. Influenza A has 2 subtypes which are important for humans: A(H3N2) and A(H1N1), of which the former is currently associated with most deaths. Influenza viruses are defined by 2 different protein components, known as antigens, on the surface of the virus. They are spike-like features called haemagglutinin (H) and neuraminidase (N) components.

The genetic makeup of influenza viruses allows frequent minor genetic changes, known as antigenic drift, and these changes require annual reformulation of influenza vaccines.

Pandemic influenza

Three times in the last century, the influenza A viruses have undergone major genetic changes mainly in their H-component, resulting in global pandemics and large tolls in terms of both disease and deaths. The most infamous pandemic was “Spanish Flu” which affected large parts of the world population and is thought to have killed at least 40 million people in 1918-1919. More recently, two other influenza A pandemics occurred in 1957 (“Asian influenza”) and 1968 (“Hong Kong influenza”) and caused significant morbidity and mortality globally. In contrast to current influenza epidemics, these pandemics were associated with severe outcomes also among healthy younger persons, albeit not on such a dramatic scale as the “Spanish flu” where the death rate was highest among healthy young adults.

Most recently, limited outbreaks of a new influenza subtype A (H5N1) directly transmitted from birds to humans have occurred in Hong Kong Special Administrative Region of China in 1997 and 2003.

Transmission

The virus is easily passed from person to person through the air by droplets and small particles excreted when infected individuals cough or sneeze. The influenza virus enters the body through the nose or throat. It then takes between one and four days for the person to develop symptoms. Someone suffering from influenza can be infectious from the day before they develop symptoms until seven days afterwards.

Disease spreads very quickly among the population especially in crowded circumstances. Cold and dry weather enables the virus to survive longer outside the body than in other conditions and, as a consequence, seasonal epidemics in temperate areas appear in winter.

Diagnosis

Respiratory illness caused by influenza is difficult to distinguish from illness caused by other respiratory pathogens on the basis of symptoms alone. However, during laboratory-confirmed influenza outbreaks, the majority of persons seeking medical advice for upper respiratory tract infections are likely to be infected by influenza. Laboratory confirmation will be required between annual influenza epidemics. Rapid diagnostic tests have recently become available that can be used to detect influenza viruses within 30 minutes.

Despite the availability of rapid diagnostic tests, the collection of clinical specimens for viral culture remains critical to provide information regarding circulating influenza subtypes and strains. This is needed to guide decisions regarding influenza treatment and chemoprophylaxis and to formulate vaccine for the coming year.

Prevention: Influenza vaccines

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

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. Influenza vaccination can reduce both health-care costs and productivity losses associated with influenza illness.

All current inactivated influenza vaccines contain trace levels of egg protein and should not be used by individuals with egg protein allergies.

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.

The WHO's Global Influenza Surveillance Network writes the annual vaccine recipe. The network, a partnership of 112 National Influenza Centres in 83 countries, is responsible for monitoring the influenza viruses circulating in humans and rapidly identifying new strains. Based on information collected by the Network, WHO recommends annually a vaccine that targets the 3 most virulent strains in circulation.

Treatment and prophylaxis:Antiviral agents

For most people influenza is an upper respiratory tract infection that lasts several days and requires symptomatic treatment only. Within days, the person’s body will eliminate the virus. Antibiotics, such as penicillin, which are designed to kill bacteria, cannot attack the virus. Therefore antibiotics have no role in treating influenza in otherwise healthy people although they are used to treat complications.

Antiviral drugs for influenza are an important adjunct to influenza vaccine for the treatment and prevention of influenza. However, they are not a substitute for vaccination. For several years, four antiviral drugs that act by preventing influenza virus replication have been available. They differ in terms of their pharmacokinetics, side effects, routes of administration, target age groups, dosages, and costs.

When taken before infection or during early stage of the disease (within two days of illness onset), antivirals may help prevent infection, and if infection has already taken hold, their early administration may reduce the duration of symptoms by one to two days.

For several years, amantadine and rimantadine were the only antiviral drugs. However, whilst relatively inexpensive, these drugs are effective only against type A influenza, and may be associated with severe adverse effects (including delirium and seizures that occur mostly in elderly persons on higher doses). When used for prophylaxis of pandemic influenza at lower doses, such adverse events are far less likely. In addition, the virus tends to develop resistance to these drugs.

A new class of antivirals, the neuraminidase inhibitors, has been developed. Such drugs, zanamivir and oseltamivir, have fewer adverse side effects (although zanamivir may exacerbate asthma or other chronic lung diseases) and the virus less often develops resistance . However, these drugs are expensive and currently not available for use in many countries.

In severe influenza, admission to hospital, intensive care, antibiotic therapy to prevent secondary infection and breathing support may be required.

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