



WORLD HEALTH ORGANIZATION

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Influenza

Report by the Secretariat

1. Influenza is a highly infectious disease caused by a very unstable virus. It rapidly spreads around the world in seasonal epidemics, affecting 10% to 20% of the total population. Such epidemics, and the significant morbidity and mortality they cause, are long-standing worldwide health problems. Although reporting is inadequate and estimates are based on data from developed countries, annual epidemics are thought to result in from three to five million cases of severe illness and from 250 000 to 500 000 deaths. Most deaths associated with influenza in industrialized countries are due to complications of underlying diseases in people with well defined risks, including age over 65 years, chronic cardiovascular, pulmonary, metabolic or renal disease, and immunosuppression.
2. Seasonal influenza epidemics also impose 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, estimates in 1986 put the cost of influenza epidemics to the economy at US\$ 5000 million per year.
3. Very little is known, however, about the public health significance of influenza in the tropical developing world, where viral transmission continues year-round and the disease is thought 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 the outbreak facilitated by WHO emphasized the increased likelihood of severe health consequences of influenza outbreaks in poorly nourished populations lacking access to well equipped health services.
4. Influenza vaccines, which have been available for more than 60 years, are safe and effective. WHO recommends annual immunization of at-risk persons as the best and most cost-effective strategy for reducing influenza-related morbidity and mortality.
5. The most important strains of human influenza virus are A and B. *Influenzavirus A* has several subtypes, of which two, H1N1 and H3N2, are currently of epidemiological significance. The instability of influenza viruses results in constant, permanent and usually small changes in their antigenic composition, a phenomenon known as antigenic drift, necessitating corresponding annual changes in the composition of influenza vaccines.
6. The greatest public health concern lies in the tendency of *Influenzavirus A* to change suddenly and markedly, either through mutation or through the exchange of influenza virus genes or through the transfer of whole virus between host species into novel, genetically distinct subtypes, in a process known as antigenic shift. The result is the sudden appearance of a new virus strain to which populations may have no immunity and against which no existing vaccine may confer protection. In

the past, such new strains have generated pandemics with high lethality and causing great social disruption. Based on historical patterns, influenza pandemics can be expected to occur, on average, three to four times each century when new viral strains emerge by antigenic shift and are readily transmitted from person to person. Thus, in the 20th century, the great influenza pandemic of 1918-1919, which caused an estimated 40 to 50 million deaths worldwide, was followed by pandemics in 1957-1958 and 1968-1969. The strains of *Influenzavirus A* implicated in those pandemics have been identified as H1N1, H2N2 and H3N2, respectively.

7. Experts agree that another influenza pandemic is inevitable and possibly imminent. Epidemiological models project that it is likely to result, in industrialized countries alone, in 57 to 132 million outpatient visits, 1.0 to 2.3 million admissions to hospital and 280 000 to 650 000 deaths in less than two years. In developing countries, where health care resources are already strained and the general population is frequently weakened by poor health and nutritional status, the impact is likely to be greatest.

8. The WHO influenza programme was established in 1947 with two main functions: to assist in planning for the possible recurrence of an influenza pandemic, and to devise control methods to limit the spread and severity of seasonal epidemics. These needs persist today and WHO's functions have been considerably strengthened and refined in line with advances in scientific knowledge. Information on circulating strains of influenza virus and epidemiological trends is gathered by an extensive network, administered by WHO since the programme's inception and currently comprising 112 national influenza centres in 83 countries and four WHO collaborating centres for reference and research on influenza.¹ National centres transfer representative viral isolates to the collaborating centres for immediate strain identification. Besides guiding the annual composition of recommended vaccines, the network operates as an early warning system for the emergence of influenza variants and novel strains. It was crucial to the early detection, investigation and containment of the outbreak of influenza in people in the Hong Kong Special Administrative Region of China in 1997 caused by an avian *Influenzavirus A*, subtype H5N1.

9. Despite the effectiveness of global surveillance of influenza viruses, national and international responses to influenza suffer several weaknesses, which could have particularly acute public health consequences in the event of a future pandemic. Recent consultations sponsored by WHO have identified the following needs and concerns.

(a) The occurrence, epidemiology, and disease and economic burden of influenza in developing countries needs to be better understood, particularly in the tropical developing world, where surveillance and control activities receive little support. As a result, the WHO surveillance network has important geographical gaps, and health administrations in countries with such deficiencies have little evidence on which to assess influenza as a health priority and, if necessary, to formulate appropriate policies for mitigating its effects.

(b) Geographical gaps in influenza disease surveillance diminish global capacity to detect the emergence of influenza variants and novel strains. In view of the conditions that have surrounded the emergence of new viral subtypes in the past, both disease and virological surveillance is particularly important in areas where humans and epidemiologically important animal hosts, including poultry and pigs, live in close proximity.

¹ Located in Atlanta (Georgia, United States of America), London, Melbourne (Australia) and Tokyo.

(c) Some countries have made considerable progress in increasing immunization coverage, particularly when operational targets are set. However, knowledge about the benefits of influenza vaccines has not been translated into effective immunization programmes in most Member States. At present, only 50 countries, mainly in the industrialized world, have policies for influenza immunization and only 10% to 20% of people in high-risk groups are protected; coverage rates in developing countries are often negligible. In addition, immunization coverage of health care workers in direct contact with the elderly high-risk group is often low despite strong evidence of their role in contributing to outbreaks in institutions caring for the elderly and their own vulnerability to infection.

(d) At present, an estimated 1000 million people worldwide belong to the group considered at highest risk of suffering or dying from influenza-related complications. Prophylactic immunization is the best strategy for preventing excessive deaths and health care costs in this high-risk group. However, only nine countries have facilities for the production of influenza vaccine. In 2001, global vaccine production, which responds to market demand, totalled 250 million doses, an amount clearly inadequate for the protection of high-risk groups.

(e) No currently available vaccine confers protection against all emerging variants of even a single influenza virus subtype, much less several subtypes. As a result, influenza immunization must be repeated each year; vaccine formulation must be constantly adjusted, requiring annual licensing and registration; stockpiling of vaccine is not an option; and influenza vaccines continue to be comparatively expensive. Research on novel vaccines, application methods, and production technologies is needed to overcome these limitations.

10. Better vaccines are urgently needed. In May 2002, WHO convened a consultation of influenza experts, virologists, epidemiologists, and public health officials to agree the first Global agenda on influenza surveillance and control.¹ The agenda sets out 17 prioritized activities needed to reduce the burden of epidemics and to prepare the world for the next pandemic. It responds in particular to inadequacies caused by poor understanding of the impact of influenza in developing countries, the long time frame of six to eight months needed to manufacture influenza vaccines, inadequate vaccine coverage, and the need for surveillance activities to be more closely related to control. The agenda encourages collaboration among partners in the public and private sectors and sets out a strategy for better influenza surveillance and control. The 17 activities are designed to meet four main objectives: (i) to strengthen surveillance; (ii) to improve knowledge of the disease and economic burden of influenza; (iii) to increase usage of influenza vaccine, and (iv) to enhance pandemic preparedness through national and international action. Each priority activity is further defined through a series of recommended activities for researchers, industry, governments and WHO.

11. A few Member States are formulating national plans for pandemic preparedness, but only one country has completed a formal, legally sanctioned plan. The absence of such national plans, including projected needs for vaccines, antiviral drugs, and other essential supplies, hinders efforts to coordinate preparedness planning at the global level. As things stand, no country will have suitable vaccines at the start of a pandemic caused by the next viral antigenic shift. Given current manufacturing capacity and licensing and registration requirements, production of significant quantities of vaccine could not begin until six to eight months after the detection of a new virus, by which time the epidemic it caused is likely to have become pandemic. Annual reviews of current vaccine usage would help in assessing the magnitude of the gap between that and the needs projected in preparedness plans. Better use of

¹ Global agenda on influenza – adopted version. Part I. *Weekly Epidemiological Record* 2002; 77:179-182. Adoption of Global agenda on influenza – Part II. *Weekly Epidemiological Record* 2002; 77:191-195.

vaccines in seasonal epidemics will help to ensure that manufacturing capacity meets demand in a future pandemic.

12. WHO has issued Guidelines on the use of vaccines and antiviral agents during influenza pandemics¹ to support countries in making difficult decisions about priorities for distribution of finite quantities of supplies. In particular, antiviral agents, which reduce the duration and severity of symptoms and can be stockpiled in advance, are likely to assume a special importance in the early stage of a pandemic when vaccines are not available. However, issues of price and licensing need to be resolved, and questions about side-effects and the likelihood of rapid development of drug resistance need to be answered.

13. Plans for preparedness against a pandemic will, in turn, help to make the response to seasonal epidemics more rational and cost-effective as well as preventing numerous deaths. All countries need to be aware of the need to begin preparedness planning well in advance of a pandemic, as many essential activities take considerable time – such activities will also enhance general preparedness for other public health emergencies of infectious origin. To this end, WHO is elaborating a model preparedness plan, with defined roles for WHO and Member States before and during an influenza pandemic.

ACTION BY THE EXECUTIVE BOARD

14. The Executive Board is invited to consider both the information in this report and the following draft resolution:

The Executive Board,

Having considered the report on influenza,²

RECOMMENDS to the Fifty-sixth World Health Assembly the adoption of the following resolution:

The Fifty-sixth World Health Assembly,

Recalling resolutions WHA22.47 and WHA48.13;

Recognizing that influenza viruses are responsible for seasonal epidemics that sicken millions worldwide and cause fatal complications in up to one million people each year;

Further recognizing that many of these deaths could be prevented through increased use, particularly in people at high risk, of existing vaccines, which are safe and highly effective;

¹ WHO guidelines on the use of vaccines and antivirals during influenza pandemics. *Weekly Epidemiological Record*, in press. [See also www.who.int/influenza]

² Document EB111/10.

Welcoming the contribution of global influenza surveillance, coordinated by WHO, to the annual determination of the antigenic composition of influenza vaccines and to early recognition of conditions conducive to a pandemic, and the assistance provided by WHO to timely manufacturing of influenza vaccines;

Expressing concern that the health burden and economic impact of influenza in developing countries are poorly documented, and that recent evidence suggests higher rates of fatal complications associated with poor nutritional and health status and limited access to health services;

Further concerned by the general lack of national and global preparedness for a future influenza pandemic, particularly in view of the recurrence of such pandemics and the high mortality, social disruption and economic costs that they invariably cause and which may be exacerbated by rapid international travel, the recent worldwide increase in the size of at-risk populations and the development of resistance to first-line antiviral drugs;

Recognizing the need for improved vaccine formulations, increased manufacturing capacity for vaccines, more equitable access to antiviral drugs, and strengthened disease surveillance as part of national and global pandemic preparedness;

Noting that better use of vaccines for seasonal epidemics will help to ensure that manufacturing capacity meets demand in a future pandemic, and that pandemic preparedness plans will help to make the response to seasonal epidemics more rational and cost-effective as well as preventing numerous deaths;

Noting with satisfaction the consensus reached by the WHO Consultation on Global Priorities in Influenza Surveillance and Control (Geneva, May 2002) on the first Global agenda on influenza surveillance and control, which provides a plan for coordinated activities to improve preparedness for both seasonal epidemics and a future pandemic;

Further noting with satisfaction WHO's work on influenza pandemic preparedness planning and its intention to draw up a model plan,

1. URGES Member States:

- (1) where national influenza vaccination policies exist, to establish and implement strategies to increase vaccination coverage of all people at high risk, including the elderly and persons with underlying diseases, with the goal of attaining vaccination coverage of the elderly population of at least 50% by 2006 and 75% by 2010;
- (2) where no national influenza vaccination policy exists, to assess the disease burden and economic impact of annual influenza epidemics as a basis for framing and implementing influenza prevention policies within the context of other national health priorities;
- (3) to draw up and implement national plans for preparedness for influenza pandemics, giving particular attention to the need to ensure adequate supplies of

vaccine, antiviral agents, and other vital medicines, as outlined in the Global agenda on influenza surveillance and control;

(4) to contribute to heightened preparedness for epidemics and pandemics through strengthening of national surveillance and laboratory capacity and, where appropriate, increased support to national influenza centres;

(5) to support research and development on improved influenza vaccines, particularly concerning their suitability for use in developing countries, in order to obtain an influenza-vaccine formulation that confers long-lasting and broad protection against all influenza virus strains;

2. REQUESTS the Director-General:

(1) to continue to combat influenza by advocating new partnerships with organizations of the United Nations system, bilateral development agencies, nongovernmental organizations and the private sector;

(2) to continue to provide leadership in coordinating the prioritized activities for epidemic and pandemic preparedness set out in the Global agenda on influenza surveillance and control;

(3) to provide support to developing countries in assessing the disease burden and economic impact of influenza and in framing and implementing appropriate national policies for influenza prevention;

(4) to continue to strengthen global influenza surveillance as a crucial component of preparedness for seasonal epidemics and pandemics of influenza;

(5) to provide technical support to Member States in the preparation of national pandemic preparedness plans, including guidance on estimating the demand for vaccines and antiviral drugs;

(6) to search jointly with other international and national partners, including those in the private sector, for solutions to reduce the present global shortage of, and inequitable access to, influenza vaccines and antiviral drugs, both for epidemic and global pandemic situations;

(7) to keep the Executive Board and Health Assembly informed of progress.

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