



Influenza

INFORMATION AND NEWS ON INFLUENZA

EDITORIAL

In February 1999 an important meeting, 'Fifty Years of Influenza Surveillance. A Challenge for the 21st Century', was held at the World Health Organization in Geneva, Switzerland. In this issue, Dr Lavanchy reports on the meeting. Approximately 250 participants from more than 80 countries attended the congress during which the status of influenza surveillance around the world was assessed, and the state of the art in the areas of molecular biology, epidemiology, prevention and treatment of the disease was reviewed.

Perspectives on the best management and control practices for influenza, taking into account the new technologies that are now available, were also presented. Several ESWI members gave presentations on the WHO surveillance network, diagnostic methods used in Europe and the preparation of inactivated vaccines.

The WHO's Influenza Pandemic Preparedness Plan, developed in close collaboration with ESWI, was formally presented. The Plan describes the stages of a pandemic and the associated actions to be taken. We hope that this document will help countries and public health authorities prepare National Contingency Influenza Pandemic Plans and provide harmonised responses in case of a pandemic or pandemic threat.

Five months earlier, a satellite symposium on 'Meeting the Challenge of Influenza' was held at the European Respiratory Society annual meeting.

The symposium considered the burden of the disease and ways to improve our control of influenza outbreaks. Proceedings of both the WHO and ERS meetings will be issued in due course.

New approaches to controlling influenza infection are also explored in this issue. On page 3, Dr Kilbourne presents the expected benefits of live vaccines but also points out potential problems. On page 6, Professor Osterhaus discusses the new neuraminidase inhibitors, their role in the early treatment of the disease and, under certain circumstances, their possible use for prophylaxis. However, these promising drugs should not be considered as alternatives to routine vaccination. Increasing immunisations with the current inactivated vaccines remains the best way to protect individuals at high risk and to control influenza outbreaks. Nevertheless, policies and recommendations for the control of influenza will have to be updated to avoid confusion in the medical profession and among the general public about the different and complementary roles of vaccines and antiviral agents for the control and management of the disease.

Preparations for the 'Options for the Control of Influenza IV' meeting are going well. The congress will take place in Hersonissos, Crete, Greece, from 23–28 September 2000. The meeting will be jointly chaired by Dr A Osterhaus, Dr N Cox and Dr A

Hampson. Eight hundred attendees are expected to gather on this picturesque island for what promises to be a stimulating and informative event. The meeting will provide an opportunity for scientists to present new data on influenza, from fields as diverse as molecular biology and macro-epidemiology, and to evaluate the experience and knowledge we have acquired during the 20th century before facing the challenges that await us in the next.

R. Snacken
Chair, ESWI

THE ESWI OFFICE HAS MOVED

Please note these new contact details:

ESWI Management, c/o Link Inc
Kapucinessenstraat 48
2000 Antwerp, Belgium
Tel: +32 3 232 93 4. Fax: +32 3 232 17 04
E-mail: eswi@ping.be

CONTENTS

- PAGE 1** – Editorial
- PAGE 2** – Influenza vaccine strains for the 1999–2000 season
- PAGE 3** – Live influenza virus vaccines: promise and problems
- PAGE 4** – Meeting the challenge of influenza
- PAGE 6** – The battle against influenza: antivirals versus vaccines
- PAGE 7** – WHO 50 years of influenza surveillance: a challenge for the 21st century
- PAGE 8** – Calendar of events

INFLUENZA VACCINE STRAINS FOR THE 1999–2000 SEASON

Introduction

In September 1998, the World Health Organization (WHO) made recommendations for the composition of influenza virus vaccines for use in the 1999 Southern Hemisphere influenza season (May–October) [1]. The process of formulating two WHO Recommendations each year (September for Southern Hemisphere; February for Northern Hemisphere) was a new venture for the WHO and it should ensure a more effective review of worldwide influenza activity than before. The following report is a summary of the data reviewed by the WHO in Geneva during the February 1999 meeting [2].

Influenza activity

The first reports of influenza activity in the Northern Hemisphere were received in October and November 1998; by December outbreaks were occurring in Africa, Asia, Europe and North America. In Europe, the earliest influenza outbreaks occurred in the UK and Russia (December–January). The Northern Hemisphere activity was predominantly caused by influenza A (H3N2) viruses, although influenza B circulated widely and, in some countries, predominated. Few laboratory-confirmed cases of influenza A (H1N1) have been reported.

Virus characterisation

The majority of influenza A (H3N2) viruses were related antigenically to the vaccine strain, A/Sydney/5/97. A small number could be distinguished antigenically, but these viruses were heterogeneous and no representative variant could be found by antigenic and genetic analysis. Although few influenza A (H1N1) viruses were isolated, the majority were antigenically related to the A/Beijing/262/95 vaccine strain. Some resembled A/Bayern/7/95, the vaccine strain for the previous (1997–98) season and a small number of isolates were

antigenically distinguishable from both the above viruses. All recent influenza B viruses in Europe and the Americas resembled B/Beijing/184/93, the strain recommended by WHO for use in 1998–99 vaccines. Viruses resembling an earlier reference strain, B/Victoria/2/87 continued to co-circulate with B/Beijing/184/93-like viruses in Asia (Japan and Thailand). The reference strain for the B/Victoria/2/87-like viruses was B/Shangdong/7/97.

Vaccine studies

Current vaccines containing A/Sydney/5/97 (H3N2), A/Beijing/262/95 (H1N1) and B/Harbin/7/94 strains have been clinically evaluated in adults and the elderly and their postimmunisation antibodies have been tested against recent representative viruses.

For the A (H3N2) vaccine component, there were satisfactory antibody responses to A/Sydney/5/97-like viruses in approximately 93% of adult and 71% of elderly vaccinees. However, for a few recent variants, vaccine-induced antibodies were reduced in frequency and titre by up to twofold. The influenza A (H1N1) vaccine component stimulated satisfactory antibody responses to recent influenza A (H1N1) isolates in approximately 84% of adult and 69% of elderly vaccinees.

For the influenza B vaccine component, satisfactory antibody responses to recent B/Beijing/184/93-like strains were detected in the sera of approximately 88% of adult and 70% of elderly vaccinees. However, for viruses similar to B/Shangdong/7/97, the antibody titres were approximately 60% lower and the frequency of satisfactory responses was reduced to 50% in adults and 34% in the elderly. A trial vaccine containing B/Shangdong/7/97 (in place of B/Harbin/7/94) stimulated equivalent antibody responses to both B/Beijing/184/93-like and B/Shangdong/7/97-like strains.

Vaccine recommendations

The WHO recommended that the following strains are included in vaccines for the 1999–2000 season:

- an A/Sydney/5/97 (H3N2)-like virus
- an A/Beijing/262/95 (H1N1)-like virus
- a B/Beijing/184/93-like virus or a B/Shangdong/7/97-like virus.

The WHO also advised that in areas of Asia where both B/Beijing/184/93-like and B/Shangdong/7/97-like strains were circulating, and in nearby countries, a B/Shangdong/7/97-like strain would be most appropriate for use in 1999–2000 vaccines. For other areas (including Europe), a B/Beijing/184/93-like vaccine virus would be more closely related to the current influenza B virus isolates.

EU vaccine strains

The reference strains nominated by the WHO were accepted for vaccine production at a March meeting of the EU Committee for Proprietary Medicinal Products. For the influenza A vaccine components, the high-yielding reassortants X-127 (antigenically equivalent to A/Beijing/262/95), RESVIR-13 and IVR-108 (antigenically equivalent to A/Sydney/5/97) were accepted for use in EU vaccines. For the influenza B vaccine component, B/Yamanashi/166/98, a B/Beijing/184/93-like strain was selected.

J.M. Wood

National Institute for Biological
Standards and Control
Potters Bar, UK

References

1. Recommendation for the composition of influenza virus vaccines for use in 1999. *Wkly Epidemiol Rec* 1998; 73(40): 305–312.
2. Recommended composition of influenza virus vaccines for use in the 1999–2000 season. *Wkly Epidemiol Rec* 1999; 74(8): 57–64.

LIVE INFLUENZA VIRUS VACCINES: PROMISE AND PROBLEMS

Although live influenza virus vaccines (LIVV) are not new, having been used in one form or another for over half a century, none are licensed at present despite the success and acceptance of live virus vaccines for other diseases. To some extent this reflects the continuing availability and moderate success of inactivated virus vaccines (IVV), but also problems intrinsic in undertaking protection with a highly mutable and evolutionarily unstable virus. However, the last decade has witnessed the development of LIVV into which attenuating genes have been introduced by genetic reassortment. Reassortant viruses (developed initially by H.F. Maassab) incorporate genes for internal or non-structural viral proteins from a standard 'master strain' which confer cold-adapted (CA) and temperature sensitive (TS) characteristics to viruses bearing the haemagglutinin (HA) and neuraminidase (NA) glycoproteins of wild type viruses newly emerged in nature. It is principally through the HA and NA proteins that immunity is mediated.

The accruing evidence of the safety and efficacy of these vaccines in subjects of all ages, including infants, has resulted in their strong candidacy for licensure. This in turn has led to recent meetings in which their potential benefits as well as deficiencies have received serious consideration. One such meeting was held at the Center for Biologics Evaluation and Research of the Food and Drug Administration in Bethesda, Maryland, USA, in late November 1998, and another in Frankfurt, Germany, at the Paul Ehrlich Institute in December 1998, both with international attendance. The present brief review will reflect discussions at both these meetings as well as the author's evaluation of current evidence.

Is there a need for a live virus vaccine?

When appropriately matched to the virus strain circulating in nature, present

inactivated vaccines have proved to be safe and effective – but immunity is relatively brief and often narrowly specific. To the extent that they may simulate natural infection, LIVV may prove to be more broadly immunogenic and to induce more enduring immunity – perhaps through their capacity to stimulate local, and cell-mediated immunity more effectively. It is also the case that IVV are not optimally effective in the elderly and are relatively reactogenic in the very young. Present evidence is not definitive but suggests the possibility that age, per se, may not prove a barrier to immunisation with LIVV.

The promise of current live virus vaccines

(Present evidence of the value of LIVV with TS and CA attenuating mutations)

Transfer of attenuating mutations to a number of influenza A H3N2 and H1N1 strains, as well as to an influenza B strain, has been achieved to produce reassortant vaccines that have proved protective against either artificial or natural challenge. Most of these studies have been conducted in children, but successful adult immunisation has also been carried out. In sum, almost 20,000 adults and children have now received CA live virus vaccines in a number of studies without significant untoward effects or evidence of virus transmission. In these studies, evidence of reversion from the CA/TS phenotype, or transmission of virus from vaccinees has not been found, although reassortment between influenza A subtypes appears to occur at a high rate (25%) within individual vaccinees.

Potential problems

Superiority or equivalence to IVV still needs to be determined in more side-by-side comparisons of IVV and LIVV than have yet been done. Even though attenuated, LIVV comprise cyto-necrotising viruses which damage the

respiratory tract epithelium and thus could pave the way for secondary bacterial colonisation or infection, as does natural infection. Future studies must focus on this possibility.

Despite encouraging evidence for the genetic stability of LIVV, its viruses will be subject to the same evolutionary pressures as are wild viruses, leading to possible reversion, extragenic suppression, and reassortment with wild viruses and among vaccine viruses – the latter having already been demonstrated. The chances for reversion will be enhanced if LIVV are administered to the immunosuppressed, in whom protracted infection can occur. More information is needed on the genetic nature of virus shed after vaccination.

Will the attenuation and immunogenicity of each new vaccine need to be tested each year before use? (The addition of new HA and NA genes to the master strain core of attenuating genes may change these attributes.)

In epidemic situations, will LIVV prove to be a strategic resource because of ease of administration or a danger because of the possibility of premature acquisition and distribution of wild virus genes for the external proteins of the pandemic virus? There is a need to define the exact role of LIVV in influenza vaccination.

Is LIVV seen as a replacement for, a supplement to, or an alternative stratagem to IVV in influenza vaccination? Perhaps administration of IVV (or especially recombinant NA vaccines now in clinical trials) and LIVV in tandem will alleviate concern about reversion to virulence. Probably the exact role of LIVV and its definitive risks and benefits can be defined only after extensive use in the field.

E.D. Kilbourne

New York Medical College
Valhalla, New York, USA

MEETING THE CHALLENGE OF INFLUENZA

Delegates at the European Respiratory Society 1998 Annual Congress, held in Geneva, Switzerland, in September 1998, were invited to attend a symposium entitled 'Meeting the challenge of influenza', sponsored by F. Hoffmann-La Roche Ltd. Professor Michèle Aymard from Hospices Civils de Lyon, France, introduced the meeting. She pointed out that the annual impact of influenza, both on the individual and on society as a whole, is greatly underestimated by the public and it is important that awareness is raised. One hundred million people are infected with the influenza virus each year in the Northern Hemisphere and most of these patients are debilitated in some way. In addition, the number of deaths as a result of influenza is considerable, particularly for patients in high-risk groups. In patients with cardiovascular and pulmonary disease, the death toll during epidemics from influenza or pneumonia can be as high as 870 per 100,000 population.

Professor Aymard said that while vaccines represent one method of protection against the disease, there is a clear need for new drugs for prevention and treatment. An ideal antiviral for influenza should:

- be effective against both influenza A and influenza B
- be effective for both treatment and prophylaxis
- reduce viral load, clinical symptoms and time to recovery
- not impair the immune response
- act within hours and last for the treatment period only
- be easy to administer
- be stable in storage for several years.

Interestingly, the next speaker, Dr Daniel Lavanchy of the World Health Organization (WHO), underlined the significance of the death toll from

influenza by comparing it with the likelihood of dying in a road traffic accident – the estimated risk of death from either event is the same.

Influenza: a global challenge each year

Influenza is a global challenge and, consequently, Dr Lavanchy spoke of the need for a system of global information exchange all year, every year. Currently, global influenza activity is monitored through four WHO collaborating centres and national influenza activity is monitored through a network of 110 National Influenza Centres in 83 countries. Together these form the global influenza surveillance system – vital for the optimal control of influenza through appropriate selection of influenza strains that are to be incorporated into the annual vaccine composition, and particularly important when planning for a pandemic.

'Each year is an influenza year' became a recurrent theme throughout the symposium. Although pandemics occur every 10–40 years and have a heavy death toll, it is annual outbreaks that have the highest impact on society. They occur with predictable regularity every year and can be extremely intense, resulting in a cumulative impact exceeding that of a pandemic.

Explosive outbreaks during the winter months

Dr Karl Nicholson from Leicester Royal Infirmary, UK, presented an overview of how the virus exerts its effects. The virus is transmitted from person to person in virus-laden droplets expelled during coughing and sneezing. Just a few hours after infection, the virus begins to replicate at a very high rate throughout the respiratory tract, reaching a peak after about 2 days. The short incubation period (2–3 days), together with high viral titres in secretions, the lengthy period of

viral shedding and the relatively small amounts of virus necessary to initiate infection, explain the explosive nature of outbreaks of influenza in the community during the winter months.

Influenza is characterised by abrupt onset of various respiratory and systematic symptoms, such as fever, cough, sore throat, coryza, fatigue, headache and muscle aches. This combination of fever with other systemic and local symptoms during periods of influenza activity can be used to effectively diagnose the disease.

Most complications associated with influenza infection are respiratory, but infection can also affect many of the major organs, such as the muscles, brain and heart. For example, acute bronchitis can occur in 10–30% of otherwise healthy people, depending on the circulating viral strain. Further respiratory complications include croup, pneumonia, bronchiolitis, lung abscess and asthma. Certain complications of influenza are especially common or unique to particular groups, for example otitis media can occur in up to 35% of young children. Primary viral or secondary bacterial pneumonia has been identified in 5–38% of influenza patients during a number of studies. Pneumonia is a particularly serious complication in the elderly and the high mortality rate is partly caused by the short interval between onset of illness and death (more than one-third of patients die within 2 days of admission), which allows doctors very little time to treat the disease effectively.

Respiratory infections linked to asthma exacerbation

The important role of respiratory viruses in the exacerbation of asthma was reviewed by Dr Sebastian Johnston from Southampton General Hospital, UK. Acute asthma in schoolchildren is

associated with a respiratory virus infection in a staggering 80–85% of cases and in around 50% of cases in adults. Furthermore, virus infection is implicated in the majority of asthma deaths, most notably in very young and elderly patients.

Dr Johnston concluded that there is no doubt that influenza has a major impact on asthma exacerbation, especially during influenza outbreaks. Hence, any treatment developed to impact on influenza should have a profound benefit for asthmatics and non-asthmatics alike.

The costs associated with influenza, as described by Professor Thomas Szucs from the University of Milan, Italy, include direct healthcare costs, indirect costs such as lost productivity, and intangible costs such as the cost of pain, grief and social disruption. Estimates of lost productivity in Germany in 1995/96 were over US\$900 million. The cost to the individual of impaired quality of life and functional status can have important consequences, e.g. impaired performance and reduced reaction times may compromise health and safety at work and family activities can be severely disrupted.

The three pillars for the control of influenza: surveillance, prevention and antiviral treatment

Dr René Snacken from the Scientific Institute of Public Health – Louis Pasteur, Belgium, discussed current options for the control of influenza. He described surveillance, prevention and treatment as the three pillars for the control and management of influenza.

An international programme of surveillance has been set up by WHO to monitor influenza activity. This serves a number of purposes:

- virological monitoring allowing definition of composition of vaccines
- epidemiological monitoring

- guidance for differential diagnosis of influenza
- forewarning of influenza pandemics
- to inform general practitioners.

Vaccines currently play a major role in the prevention of influenza and vaccination is recommended for all high-risk groups, in whom it significantly reduces influenza-related complications and mortality. However, vaccine efficacy is variable and can be below 50% in the elderly. New approaches to vaccination are constantly being investigated in order to improve effectiveness. For example, a live intranasal vaccine is currently being tested in children.

Antiviral intervention – the earlier the better

There is a clear rationale for antiviral intervention in the management of influenza, which would directly attack the cause of the disease – the virus. As viral replication peaks early in the disease, the earlier an antiviral is given the better. The currently available antiviral drugs, rimantadine and amantadine, can be used for either prevention or treatment, but are only effective against influenza A infection and are associated with the rapid development of resistance and toxicity. Antivirals with a broad activity against influenza viruses and a good tolerability profile are therefore desirable.

Neuraminidase – a new target for influenza control

Dr Frederick Hayden from the University of Virginia, USA, discussed the latest concept for antiviral treatment of influenza. Neuraminidase, a protein found on the surface of the influenza virus and essential for viral replication in the body, has an active enzyme site that is highly conserved amongst all clinically relevant influenza strains and that provides an attractive target for antiviral intervention. The first neuraminidase inhibitor to be developed was Zanamivir. When given

by inhalation it has proven efficacy in treating naturally acquired influenza in adults. However, it has been administered via the inhaled and/or intranasal route because of its poor oral bioavailability.

An important goal is to produce an oral neuraminidase inhibitor that can be conveniently administered to all patient groups, that is readily absorbed and that is widely distributed throughout the respiratory tract. GS4104 is a compound that has been recently developed to meet these requirements. An ethyl ester prodrug, oral administration of GS4104 provides excellent levels of the parent compound GS4071, which is a potent and selective inhibitor of influenza A and B virus neuraminidases.

Dr Hayden presented data from an experimental challenge study involving 80 volunteers who were treated with GS4104 28 hours after an intranasal experimental influenza A virus infection. A significant reduction in the amount of viral shedding was noted and both duration of viral shedding and duration of symptoms were reduced almost by half in the active drug arms compared with placebo. In another study where oral GS4104 was given before experimental infection, virus shedding and infection was prevented. The drug was generally well tolerated. Phase III clinical trials of GS4104 involving more than 2,500 patients in the treatment and prevention of influenza have recently been completed.

In drawing the symposium to a close, Dr Tom Schaberg from the Chest Clinic Unterstedt, Germany, commented that the encouraging data on neuraminidase inhibitors that had been presented should provide a major step forward in the management of the disease. "We are looking forward to learning more about this exciting new concept for the control of influenza", he concluded.

B. Francis

Medical Writer, Chester, UK

THE BATTLE AGAINST INFLUENZA: ANTIVIRALS VERSUS VACCINES

With the advent of a new generation of antiviral agents for the treatment of influenza in the form of neuraminidase inhibitors, current influenza control strategies will need to be re-evaluated. Clinical trials have demonstrated that these new agents do not suffer from the major drawbacks associated with the use of amantadine and rimantidine.

Neuraminidase inhibitors are effective against both influenza A and B viruses, cause fewer or no side effects and are less prone to the development of drug-resistant viruses than other currently available agents. They are most effective when used before or soon after infection and have been shown to reduce both the duration and severity of the disease.

Current control measures

At present, control of influenza is almost exclusively based on the use of vaccines aimed at preventing influenza caused by the virus strains most likely to circulate in the next influenza season. Vaccination is particularly recommended for those at high risk of developing severe influenza or its complications, such as individuals with chronic respiratory disease, chronic heart or kidney disease, diabetes, immunocompromised individuals and those aged over 65. Annual vaccination has been shown to be effective in preventing influenza and its complications in these risk groups, and is cost effective for high- and low-risk groups alike.

In most countries where national influenza vaccination campaigns have been introduced, vaccine coverage has increased dramatically over the last decade. The relative ease of administration and the safety of influenza vaccines have facilitated the implementation of such campaigns, which are now well established in most industrialised countries.

Caution should be exercised in introducing the new generation of antivirals

to the public, in order to avoid creating the false impression that antiviral agents might, in any way, be able to replace vaccination, which will undoubtedly remain the major cornerstone in the battle against influenza. In particular, the overall effect of the new antivirals' therapeutic potential in combating influenza may well be less than that of preventive vaccination as it is generally practised today.

Caution should be exercised in introducing the new generation of antivirals to the public, in order to avoid creating the false impression that antiviral agents might . . . be able to replace vaccination . . .

Close collaboration and consultation between, on the one hand, companies marketing influenza vaccines and, on the other, those marketing antivirals will therefore be absolutely essential. It is important that a clear and uniform message indicating the complementary roles of vaccines and antivirals is delivered.

Advantages of antivirals

The additional role that neuraminidase inhibitors may be able to play in the battle against influenza can be considered in a number of respects. First, they may be used in the early treatment of influenza during the annually emerging epidemics. Individuals who, for whatever reason, have not been vaccinated before the influenza season will benefit particularly from early treatment.

The relatively fast action of the antivirals compared with that of vaccines may favour their use in individuals who have possibly been exposed during epidemics. Since influenza vaccines are

not always fully protective, the use of antivirals during these epidemics may also be considered in vaccinated high-risk individuals as soon as they develop the first signs of influenza-like illness. Neuraminidase inhibitors should be recommended in high-risk individuals for the rare occasions when circulating influenza strains exhibit a significant mismatch with those represented in the vaccine.

Prophylactic role

In addition to their therapeutic application, the new antivirals may also be used as a preventive measure during the annually recurring influenza seasons. When the risk of exposure is high, non-vaccinated and, to a lesser extent, vaccinated individuals belonging to the risk groups may benefit from the prophylactic use of antivirals.

Prophylaxis in these groups will become even more important in the rare case of an antigenic mismatch with the circulating vaccine strains. It must be recognised that the prophylactic use of antivirals will then have to continue for extended periods of time, preferably for the entire period of virus circulation or for as long as the risk of exposure continues. Cost-benefit analyses can be carried out as soon as the price of the new antivirals is known.

Finally, during a possible future influenza pandemic, in view of their broad reactivity against influenza virus neuraminidase subtypes and the expected lack of sufficient quantities of vaccine, the new antivirals will undoubtedly have an essential role to play in reducing the number of victims.

A. Osterhaus, J. de Jong
WHO National Influenza Centre
Rotterdam, The Netherlands

WHO 50 YEARS OF INFLUENZA SURVEILLANCE: A CHALLENGE FOR THE 21ST CENTURY

To mark the 50th anniversary of the influenza surveillance network, the World Health Organization (WHO) held an international meeting in Geneva, Switzerland, from 17–19 February 1999. The meeting provided a unique opportunity – both to review past successes and to present the policies and strategies currently in place to prevent and control influenza. The invited audience represented a unique body of experience, knowledge and insight into the national and international issues that surround influenza.

The meeting opened with a look back at the achievements of the past 50 years and an examination of those areas where work is still needed. Key issues in setting up and maintaining the WHO's complex surveillance network for over half a century were reviewed. The 50th anniversary meeting was instrumental in increasing awareness of influenza as a disease. In the past, the subject of influenza, though close to the hearts of those directly involved, perhaps suffered from the 'preaching to the converted' syndrome. However, it has now been recognised as a subject of real public health importance.

A review of influenza surveillance networks on all continents, developments in antiviral treatments and influenza vaccines, and the lessons learnt from the Hong Kong incident in 1998, were among the topics covered during the meeting. Data and information on surveillance programmes were presented from Africa, the Americas, Asia, Europe, and Oceania. All speakers referred to previous pandemics and the associated high mortality rates for communities throughout the world, but they also acknowledged that, in the 20th century, overall mortality levels are higher during interpandemic periods than for individual pandemic events.

Future actions

The meeting elaborated on seven interconnected themes for future focus. It is important to:

Improve links between laboratory and disease surveillance to increase sampling and analysis of specimens and to produce a more rapid exchange of isolates for strain characterisation and confirmation of influenza infection.

Improve animal surveillance and encourage closer liaison between scientists monitoring the circulation of influenza strains and infections in animals and humans. More domesticated animals, changes in husbandry methods and people living closer together all create an environment in which the potential risk for a new influenza pandemic virus is increased.

Establish a direct presence in countries that do not yet have national influenza centres, particularly in Africa, South-East Asia and South America. Assist these countries to mobilise their knowledge and enthusiasm to produce an effective surveillance network, and establish a disease prioritisation system which will allow decision-makers to plan services on the basis of evidence.

Strengthen existing structures which have become weakened over time and no longer meet acceptable standards of influenza surveillance.

Disseminate high quality information, recognised as coming from a reputable source, using tools such as FluNet.

Stimulate research, to provide the technical basis and necessary authority for discussing prevention and control issues.

Build links to areas of government outside the public health sector, and to the private sector and civil society. Global co-ordination is the only way forward and we cannot talk about effective prevention and control measures if health

ministries are unable to make their case to other parts of government or to regulate the private sector.

WHO pandemic plan

The WHO released its influenza pandemic plan during the meeting. An electronic version will be posted on the World Wide Web and a printed version will also be available. It was reiterated that each country should establish a pandemic planning committee and produce a national pandemic plan. The committee should include representatives from the medical, scientific and veterinary communities and other national representatives. It was recommended that a national plan should identify the additional resources required in the event of a pandemic. Facilities for co-ordinating national and international activities should be set up.

To conclude, all those participating in global influenza surveillance should *act globally – not locally*. Effective influenza surveillance requires international teamwork supported by national public health strategies and institutions which undertake work in diagnosis, prevention and control, surveillance and research. The WHO global influenza surveillance system makes a small contribution, but it has had enormous global impact. This knowledge should encourage those countries not yet fully committed to influenza surveillance, prevention and control to become more committed and therefore more effective. For those countries that are already committed, this knowledge should ensure that they react more quickly and become more assertive in the face of new threats to human health from influenza.

D. Lavanchy
Department of Communicable
Disease Surveillance and Response
WHO, Geneva, Switzerland

CALENDAR OF EVENTS – 1999

DATE/VENUE	TITLE	ORGANISER
16–18 May 1999 Gent, Belgium	ESVV Symposium on Animal Influenza Viruses	Dr Kristien Van Reeth Laboratory of Virology Faculty of Veterinary Medicine Gent University, Salisburylaan 133 9820 Merelbeke Belgium Fax: +32 9 264 7495
4–7 July 1999 Birmingham, UK	21st International Congress of Chemotherapy	Gardiner-Caldwell Communications Ltd Victoria Mill Windmill Street Macclesfield Cheshire SK11 7HQ UK Tel: +44 1625 664000 Fax: +44 1625 610260
3–5 August 1999 Melbourne, Australia	Macfarlane Burnet Centenary Conference on Virology	Melbourne Convention Centre 114 Flinders Street Melbourne, VIC 3000 Australia Tel: +61 3 9654 2288 Fax: +61 3 9654 8195
9–13 August 1999 Sydney, Australia	11th International Congress of Virology	IUMS, Congress Secretariat GPO Box 128 Sydney, NSW 2001 Australia Tel: +61 3 961 0043
2–5 September 1999 Budapest, Hungary	3rd Congress of the European Society for Clinical Virology	Dr Sytske Welling European Society for Clinical Virology Laboratorium voor Medische Microbiologie Hanzeplein 1 Groningen, NL-9713 GZ The Netherlands Tel: +31 50 363 3514 Fax: +31 50 363 3528
9–13 October 1999 Madrid, Spain	9th Annual Congress of the European Respiratory Society	Mrs Rosine Fieve European Respiratory Society Boulevard de Grancy 1 1006 Lausanne Switzerland Tel: +41 21 613 0202 Fax: +41 21 617 2865

INFLUENZA BULLETIN

The *Influenza* bulletin is published for the European Scientific Working Group on Influenza by Gardiner-Caldwell Communications Ltd. The opinions expressed in this publication should not be construed as those of the publisher or sponsors.

Consult full prescribing information on any drugs or devices discussed.



Gardiner-Caldwell Communications Ltd
Victoria Mill, Windmill Street, Macclesfield, Cheshire SK11 7HQ, UK
©1999 Gardiner-Caldwell Communications Limited

The organisations supporting ESWI include: Chiron Vaccines,
F. Hoffmann-La Roche Ltd, Glaxo Wellcome, Medeva Pharma Ltd,
Pasteur Mérieux MSD, SmithKline Beecham Biologicals and Solvay Pharmaceuticals.

EDITORIAL BOARD

Professor C. Hannoun
Mont Rouge, France

Dr K.G. Nicholson
Leicester, UK

Dr A.M. Palache
Weesp, The Netherlands

Dr R. Snacken
Brussels, Belgium

ESWI MEMBERS

Professor F. Ambrosch
Vienna, Austria

Dr I. Donatelli
Rome, Italy

Professor L.R. Haaheim
Bergen, Norway

Dr K.G. Nicholson
Leicester, UK

Professor A.D.M.E. Osterhaus
Rotterdam, The Netherlands

Professor O. Ruuskanen
Turku, Finland

Dr R. Snacken
Brussels, Belgium

Dr T. Szucs
Zurich, Switzerland

Professor S. van der Werf
Paris, France

Dr J.M. Watson
London, UK

Dr J.M. Wood
Potters Bar, UK

SENIOR MEMBERS

Professor C. Hannoun
Mont Rouge, France

Professor G.J. Ligthart
Amsterdam, The Netherlands

Professor C. Scholtissek
Giessen, Germany

Dr B. Tůmová
Prague, Czech Republic

ADVISERS

Dr A.P. Kendal
Atlanta, USA

Dr D. Lavanchy
Geneva, Switzerland

Dr A.M. Palache
Weesp, The Netherlands