REPORT OF CHIEF POLICY ADVISOR: INFLUENZA PANDEMIC

Background: The environmental scan done for the Strategic Planning Committee in early 2005 listed a potential influenza pandemic as a "wildcard" factor i.e., an unpredictable event of such gravity that it could influence dentistry and the American Dental Association to such a degree that "all planning bets are off." Still, some consideration can be given beforehand to the realization of such an occurrence—thinking ahead about the unthinkable.

There has been some public discussion about the imminent danger of a severe influenza pandemic originating from the Asian continent and the slaughter of millions of chickens and other birds in an attempt to prevent a pandemic from starting. Political leaders and health officials in several countries have addressed this issue, mostly decrying the lack of preparedness for such an event. The new Editor of our *Journal* made this the topic of his first editorial!

This report is written to provide information to assist the Board in understanding this important subject. The information discussed in this report was gathered from the web sites of US Department of Health and Human Services (HHS), the Centers for Disease Control and Prevention (CDC), the World Health Organization (WHO), the University of Minnesota Center for Infectious Disease Research and Policy (CIDRAP) and the writings of some individuals [Klempner, MS and Shapiro, DS (NEJM); Hatta M and Kawaoka Y (Trends in Microbiology); and Gensheimer KF, Fukuda K, Brammer L, Cox N, Patriarca PA, Strikes RA (Vaccine)]

A Pandemic: A pandemic is a world-wide epidemic. Pandemics usually occur following the emergence of a virulent infectious agent previously unknown for which there is no or insignificant immunity in humans. Efficient transfer of the infectious agent from humans-to-humans is an important characteristic of the agent if a pandemic is to get started. In the modern world, the ease with which people travel, especially from continent to continent, greatly facilitates the spread of disease and the speed at which it can be spread.

An influenza pandemic has a greater potential to cause rapid increases in death and illness than virtually any other natural health threat.

There have been three influenza pandemics in the 20th century, all of which spread world-wide within 1 year of their being identified:

- **1918-1919, Spanish flu:** more than 500,000 people died in the United States and 20-50 million people may have died around the world. Most people died within the first few days following infection and others died from complications soon after. Half of those who died were healthy, young adults. More combatants in World War I died from the flu than from combat.
- **1957-1958, Asian flu:** caused 70,000 deaths in the United States. This flu strain was identified in China late in February of 1957 and spread to the United States by June of that year.
- **1968-1969, Hong Kong flu:** caused about 34,000 deaths in the United States. It originated in Hong Kong in early 1968 and spread to the United States later that year. The strain of flu virus that caused this pandemic still circulates in the United States today.

Most of you have lived through an influenza pandemic. In addition, flu epidemics occur in the United States almost annually in the winter months and have been responsible for about 36,000 deaths each year during the 1990-1999 time period. There have also been three "flu scares" during the last quarter of the last century:

- **Swine flu scare, 1976**
- **Russian flu scare, 1977**

- **Avian flu scare, 1997 and 1999**

A severe pandemic, besides causing a large number of deaths, can raise havoc with medical capabilities, national and world economies, civil order and the ordinary conduct of daily living. Poor and developing countries will most probably suffer the most from a severe pandemic. Estimates of the number of deaths that could result from a severe influenza pandemic vary, with the highest estimates being up to 1.7 million deaths in the US and 177 million deaths across the world.

There are three theories about the emergence of viruses that are capable of causing a pandemic:

- **Genetic re-assortment between human and animal viruses:** a virus with a new protein configuration emerges from an animal that is susceptible to both human and animal viruses and is co-infected by both.
- **Direct transfer of viruses between animals and humans**
- **The re-emergence of viruses from unrecognized or unsuspected animal reservoirs**

A pandemic is characterized by several stages, not all of which occur simultaneously across the world:

- **Phase 0, Preparedness Level 0—**The inter-pandemic period
- **Phase 0, Preparedness Level 1**---The initial report of a new strain in humans
- **Phase 0, Preparedness Level 2**---Novel virus alert, human infection confirmed
- **Phase 0, Preparedness Level 3**---Human transmission confirmed
- **Phase 1**---Confirmation of onset of pandemic
- **Phase 2**---Regional and multi-regional epidemics
- **Phase 3**---The end of the first pandemic wave
- **Phase 4**---The second or later waves of the pandemic
- **Phase 5**---The end of the pandemic-back to phase 0

Influenza: Influenza viruses cause disease in all age groups. Rates of infection are highest among children, but the rate of serious illness is highest among individuals older than 65 and those with other medical conditions that put them at increased risk.

Influenza Viruses: The viruses that cause influenza are classified into two main types, **A** and **B.** Although both types regularly give rise to epidemics, only the Influenza A virus has the ability to cause pandemics. Influenza type A viruses are divided into subtypes based upon two surface proteins, hemagglutinin (HA) and neuramidinase (NA). There are 15 different HA subtypes and nine different NA subtypes. There are many combinations of HA and NA proteins possible, only a few of which are in general circulation among humans. Other subtypes are found in other species.

Influenza A subtypes are named according to their surface proteins. For example, the virus of concern endemic in Asian poultry is designated subtype H5N1---hemagglutinin type 5, neuraminidase type 1. The only subtypes of influenza type A that normally infects humans are H1N1, H1N2 and H3N2. Only type A, subtype H5 and 7 viruses infect birds. These viruses can be either highly pathogenic or low pathogenic for birds, the low pathogenic virus undetectable by the birds behavior. The relationship of the pathogenicity to risk of disease in humans in not known.

Influenza viruses change by antigenic drift or antigenic shift. Antigenic drift occurs through small changes in the virus that happen continuously. This process produces a new virus strain that may not be recognized by antibodies developed as a response to earlier strains so the new strain can cause infection. That’s why we need a new vaccination each year. Antigenic shift is a major, abrupt change in a viral strain that results in a new

virus subtype for which the population is immunologically naïve. If the new subtype that evolved is easily transmitted from person to person, a pandemic may occur. Influenza viruses are changing through both phenomena all the time.

Influenza viruses have eight separate gene segments. This segmented genome allows viruses from different species to mix and create a new influenza virus if viruses from two different species infect the same person or animal simultaneously. There is no evidence to date of genetic re-assortment between human and avian influenza virus genes.

Avian Influenza Infection In Humans: Although avian influenza A viruses do not usually infect humans, several instances of human infections and outbreaks of avian influenza have been reported since 1997. Most infections are thought to have resulted from direct contact with infected poultry or contaminated surfaces. Because of the concern for more widespread infection in humans, outbreaks of human illness associated with avian flu are closely monitored. Even though there has not been any sustained human-to-human transmission to date, the ability of influenza viruses to change and potentially gain the ability to spread among humans requires careful monitoring.

The Influenza A (H5N1) virus has become endemic in birds in Asia, particularly in domestic poultry. Infected poultry have been identified in eight Asian countries. In an attempt to control the spread of the H5N1 virus more than 100 million poultry have been killed. Although that virus has developed the ability to infect humans and cause severe disease (in 2004, 35 people were infected and of those, 23 died) the real fear is that efficient human-to-human transmission may be developed through exchange of genetic material with influenza viruses that are highly pathogenic and have the ability to spread in humans in species that are infected with both viruses at the same time, so-called “mixing vessels.” Pigs and humans and, perhaps, cats have been identified as potential mixing vessels for the avian influenza virus.

Preparation For An Influenza Pandemic: Past influenza pandemics have occurred with little warning. Means for identification of influenza viruses were either non-existent or were not used in a timely manner. The pandemic had already been established before its existence was known, with reliance on the occurrence of disease and patient symptomatology for identification. There was no “pandemic early warning system.” There was relatively little known about influenza and effective antibiotics were not available.

The situation is vastly different today:

- There are four WHO Collaborating Centers for Reference and Research on Influenza located on different continents that classify thousands of isolates each year.
- There are methods for identifying new viruses, including rapid genome sequencing.
- A large amount of knowledge is known about animal influenza viruses.
- Communications about events and the transportation of laboratory samples can be achieved rapidly.
- Among other countries that have joined the international surveillance program, China is an active participant.

Despite the better environment today, it must be noted that:

- Prediction of the onset of an influenza pandemic remains impossible.
- Preparation of control measures, such as vaccine manufacturing, might take more time than is available after the agent has been identified and before the pandemic strikes.
- Stockpiling of anti-influenza drugs in quantities sufficient to treat whole populations worldwide is unrealistic.

- Many countries lack sufficient resources to adequately prepare for an influenza pandemic.
- The increased speed and volume of international travel, increased urbanization and the expansion of the population in many regions will limit the effectiveness of control measures.
- No pandemic preparation plan prepared in advance will be 100% relevant or best for whatever situation that occurs.
- The process and the issues to be confronted in developing a response to a critical pandemic may well be more important than the details of any plan, since they may be inapplicable to any specific pandemic.

Preparation for a possible pandemic involves two areas of activity:

- the assessment of the risk from new viruses after they have been identified
- management of the risk when the new virus can spread widely and cause serious disease. This does not imply the ability to prevent a pandemic, only to reduce the extent of the disease, reduce the impact of secondary catastrophes and to prevent public panic.

The US Department Of Health And Human Services Pandemic Influenza Preparedness And Response Plan: The Department's plan for effectively responding to an influenza pandemic contains elements specific to influenza and generally increasing preparedness for bioterrorism and other emerging infectious disease threats. The plan includes:

- assurance and expansion of influenza vaccine production
- increasing influenza vaccine use
- stockpiling influenza antiviral drugs in the Strategic National Stockpile (SNS)
- enhancing the US and global disease detection and surveillance infrastructure
- expanding influenza-related research
- supporting public health planning and laboratory capabilities
- improving health care system readiness at the community level

Vaccination is the primary strategy to reduce the impact of a pandemic, but the time currently required to develop a vaccine and the limited manufacturing capacity are barriers to an effective response. Early detection of a novel virus and generation of seed viruses for vaccine development is essential. Surveillance activities are being expanded, vaccine production capacity is being expanded through agreements with vaccine manufacturers and "candidate vaccines" are being developed in laboratories through artificial genetic re-assortment to categorize the potential pathogenicity of possible natural new viruses. Normally, the influenza vaccine produced each year is a tri-valent vaccine, giving the producers three chances of guessing the virus that will cause the particular year's epidemic. In the case of a pandemic, a mono-valent vaccine against the identified pathogen will be produced, increasing the production capabilities of vaccine manufacturers.

It is hoped that effective anti-viral medications (adamantines-- amantadine and rimantadine; and neuraminidases--osteltamivir and zanamavir) can "hold off" the spread of the pandemic through treatment of infected individuals and as a prophylactic agent in non-infected individuals until an effective vaccine is available. Infection control strategies to decrease the global and community spread of infection may reduce the number of people infected early in the pandemic awaiting the availability of vaccines. Travel restrictions or advisories, screening of persons arriving into the US from affected areas, closing schools and restricting public gatherings and quarantine of exposed persons may be employed to try to limit the spread of infections. The epidemiologic pattern of the pandemic will dictate the implementation of these control measures.

Impact On Dentistry: Dentistry and the ADA will suffer similar disruptions of ordinary business as experienced by the general community. Vigilance concerning patient behaviors may possible aid in the early detection of an influenza outbreak beyond that usually experienced, although one would expect the medical community to be the first to know, since patients would come to them when ill with flu-like symptoms, not the dentist.

In the event of a pandemic that hits the US, dentists may play an important role in controlling the disease, however. Dentists may be called upon to provide services similar to some of those they may perform related to a significant bioterrorism attack, namely vaccinations and the mass dispensing of medications, providing medical care, surveillance, etc.

The planning and integration of the primary response by dentists in the event of a bioterrorism attack should be of great value in preparing dentists to aid in the event of a severe influenza pandemic.

Dental offices most likely will have to modify their office procedures, intensifying infection control procedures in all areas of the office, not just the in the operatories, for example. Scheduling may have to change to accommodate the status of the disease locally, including closing of the office. Plans for covering emergencies during difficult times should be made. Since priority lists for distribution of vaccines and medication will be established in some areas, dentistry should strive to have dentists, their staffs and their families included in the highest level of priority.