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The prospect of pandemic influenza: Why should the optometrist be concerned about a public health problem?

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Abstract

BACKGROUND: Optometrists are uniquely placed in the health care field because they provide both services as well as goods to patients. In the event of an influenza pandemic, optometrists may be challenged with a host of issues, including impediments to clinical patient care, manufacture and delivery of ophthalmic devices, and maintaining business continuity and infection control.

OVERVIEW: This report reviews pandemic influenza, the effect of a pandemic event on business survival, and response measures for the primary eye care provider. The ethical and legal issues surrounding control of a pandemic influenza and the prospect of telemedicine as a form of social distancing are also discussed.

CONCLUSIONS: Knowledge of the pharmacologic and nonpharmacologic measures to control a pandemic influenza will help prepare the eye care provider for addressing challenges to patient care and business continuity in the face of a highly contagious disease. Understanding the legal and ethical issues that arise during a pandemic event will help optometrists make informed choices as health care professionals and as citizens.

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Nearly 90 years have passed since the devastating influenza outbreak of 1918. Worldwide, approximately 500 million people contracted the disease and nearly 50 million died over a 2-year period.[1] The re-emergence of a pandemic influenza is inevitable, but the timing and virulence of the next event cannot be predicted.

Recent emergence of atypical influenza strains and other deadly respiratory viruses has generated concern over the possibility of catastrophic losses from influenza in terms of both lives and dollars. This article reviews influenza as an infectious disease, the potential global devastation from influenza, steps to prevent the spread of the disease in the community and in primary eye care practices, and the ethical issues surrounding extreme measures that may be required to quickly control a deadly virus.

Framing a pandemic influenza as a public health disorder

Public health professionals use 3 criteria to determine if and when a particular disease qualifies as a "public health disorder": (1) high disease burden affecting many or most members of the population, (2) relatively rapid rate of increase in disease burden, and (3) a sense of fear resulting from the public's perception that characteristics of the disease are out of control or unknown.[2] A pandemic influenza meets each of these

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criteria because it would represent a global event, affecting a large percentage of the population with significant morbidity and mortality and would have the potential to elicit widespread panic. Increased disease burden, incidence, and societal fear undoubtedly render a pandemic influenza not only a public health problem but, potentially, a public health catastrophe.

Review of influenza and influenza virus

Influenza illness

The clinical definition of influenza illness can be simply defined as the presence of a cough, history of recent-onset fever (≥37.8°C), and symptoms of fatigue.[3] Definitive diagnosis of influenza is achieved by positive viral culture, test for direct detection of specific antigens or influenza RNA, or appreciable rise in serum antibody titers for influenza. Polymerase chain reaction is also available for identification of the influenza strain.[4] It is estimated that accurate diagnosis based on history and clinical findings approaches 70% when compared with virus isolation by cell culture,[5] which is the definitive standard.[6] Rapid, in-office diagnostic tests for influenza are available, some of which are waived from requirements under the Clinical Laboratory Improvement Amendments of 1988 and provide results in under 30 minutes, yielding reasonably good sensitivity (median, 70% to 75%) and excellent specificity (90% to 95%) compared with viral culture.[7] Cough and fever within 48 hours of the onset of symptoms appears to be the best predictor of seasonal influenza infection, with a positive predictive value of 79% in adults[8] and 83% in children older than 4.[9]

Infection in mammals, including humans, is confined primarily to tracheo-bronchial epithelial cells and depends on inhalation of infective airborne droplet nuclei.[10,11] The first replication cycle is completed in 4 to 6 hours, with extremely high titers of viral shed leading to explosive outbreaks of infection. Clinical features of an influenza infection in general depend on the virulence of the particular strain and include the abrupt onset of fever (38°C to 40°C), chills, cough, headache, muscle ache, sore throat, and other nonspecific symptoms, which can persist for 1 to 2 weeks.

Seasonal influenza is a deadly disease, and over the last decade, an average of 36,000 Americans each year have died from it.[12] Excess mortality from a pandemic of influenza has resulted from complications of the primary infection, including viral and bacterial pneumonia and pulmonary manifestations resulting from the release of inflammatory cytokines and other chemo-attractants by the host immune system, what is termed *cytokine storm*.[5] Cytokine storm may lead to acute respiratory distress syndrome (ARDS), a condition characterized by vessel dilatation, leukocyte influx, pulmonary necrosis and the destruction of tissue.[13] ARDS is believed to have accounted for up to one half of all deaths from the Spanish flu of 1918 to 1920,[14] although a dysfunctional and inadequate host immune response has recently been found to augment lethality of this virus in a primate model of pulmonary infection.[15] To date, the majority of human deaths related to H5N1 avian influenza have been caused by respiratory failure secondary to ARDS.[16]

Influenza is particularly devastating among the elderly (patients ≥65 years old). In examining influenza epidemics and pandemics in the United States since 1918, elderly patients had higher excess flu mortality rates than nonelderly patients with the exception of the 1918 to 1919 pandemic. The ratios of excess deaths of elderly versus nonelderly in some influenza seasons were as high as 131 to 1.[17]

Although major concerns about influenza revolve around respiratory problems (including death from respiratory failure), there are ocular components of the disease. Certain strains of influenza are marked by conjunctivitis as a presenting sign.[18,19] In another published study of influenza aboard a commercial airliner, half of the patients complained of photophobia.[20] The conjunctiva and other mucous membranes are recognized to be portals of entry of influenza virus for avian-to-human and human-to-human transmission in some cases.[18,21] During flu vaccinations in 2000, a small series of vaccines developed a purported adverse reaction to the vaccination (distinct from a true allergic reaction to the vaccine itself) that manifested as respiratory symptoms accompanied by a follicular conjunctivitis with hyperemia and discharge within 4 hours of receiving the vaccine.[22] A smaller number of cases were reported in subsequent years.[23]

Influenza viruses

Influenza viruses are segmented, enveloped RNA viruses belonging to the family *Orthomyxoviridae*.[5] They may be spherical, ovoid, or filamentous in shape and are composed of a lipid bilayer, derived from the plasma membrane of the host cell, with 2 spike-shaped surface proteins embedded within: hemagglutinin (HA) and neuraminidase (NA). Sixteen different HA antigens and 9 NA antigens have been identified, and these determine both the virulence and host susceptibility of any given virus subtype.[24] The different influenza subtypes are specified by the HA and NA alleles they carry (e.g., H1N1) and are based on antibody responses to each HA and NA antigen.

There are 3 genera of influenza viruses: A, B, and C, categorized by serologic response to their nonglycosylated internal proteins.[5] Humans are the natural hosts for influenza B and C, whereas wild birds are the natural hosts for type A viruses.[24] All 3 can cause human illness, but only type A and B have any public health significance. Although influenza A and B are responsible for most human illness, influenza A causes the most serious disease because of a heightened capacity for "antigenic variability" compared with influenza B,[25] a feature that allows the virus to escape, neutralizing antibodies produced by the human immune system.

It is generally believed that pathogenicity of seasonal influenza viruses develops over time, and virulent strains in any given flu season are strains that were pre-existing for several seasons and emerge as the predominant cause for worry.[24] The potential for increased pathogenicity arises when these lingering strains are introduced to new populations that do not have antibodies against them. Genetic analysis of some outbreaks suggests that global transport of viruses can achieve this.[26]

Theoretically, minor mutations could quickly create an exceptionally virulent strain. A study using animal models showed that a change in a single amino acid in a portion of the hemagglutinin protein increased the lethality of the mutated strain by 50,000-fold.[27] Fortunately, most mutations in flu virus' RNA do not result in changes in amino acid sequence, so the protein structure (and pathogenicity) remains unchanged.[26]

Epidemiology of influenza

Last's Dictionary of Epidemiology defines *epidemic* as "the occurrence in a community or region of cases of an illness, specific health-related behavior, or other health-related events clearly in excess of normal expectancy" and *pandemic* as "an epidemic occurring over a wide area and usually affecting a large proportion of the population."[28]

Epidemic and pandemic outbreaks of influenza differ markedly in scope when compared with the typical number of seasonal influenza cases that vary from year to year. In a typical season, flu will cause approximately 110,000 hospitalizations in the United States.[29] From October 2005 through May 2006, more than 17,000 laboratory-confirmed cases of influenza were reported in the United States.[30] In the event of a flu *pandemic*, it is estimated that about 30% of the United States population, or *100 million* people, could become ill,[31] with more than 200,000 deaths.[32] These shocking estimates are a by-product not only of the dramatic rate of infection but projections that the spread of infection will occur in 2 or 3 large waves, each lasting 6 to 8 weeks over the course of 1 to 2 years.[33]

With a pandemic influenza, even if sick individuals were isolated, and identification of contacts was 90% successful, the disease would be difficult to control, mostly because of the very short incubation period of the disease.[34]

Although much attention has been given to flu pandemics, it is worth noting that in the years between pandemics, the cumulative morbidity from influenza is greater than the expected toll during a pandemic.[24]

History of epidemic and pandemic influenza

The first historical report of a probable influenza epidemic occurred in 1173,[35] with scattered reports in the 15th and 16th centuries, and more numerous reports throughout the 17th through 20th centuries.[36]

The first influenza pandemic reported with relative certainty was in 1580.[37] Pandemic flu populates the historical record from 1700 forward in intervals ranging between 10 and 50 years, with no predictable periodicity or pattern[36,38]; total mortality from these episodes range from 300,000 (1729 to 1731) to more than 50 million (1918 to 1919).

The pandemic flu of 1918 to 1919 is regarded as one of the greatest health catastrophes in human history. Most deaths occurred in persons between the ages of 20 and 40, and by 1920, as many as 100 million people died.[39] Approximately 675,000 Americans died from the flu in 1918 and 1919 (about 5 times the typical flu-related mortality rate).[40] The emergence of this pandemic (caused by the H1N1 strain) in the army camps of Western Europe has been attributed to a convergence of overcrowding; proximity of pigs, horses, and bird markets; and the presence of many mutagenic gases deployed as part of combat operations during World War I.[41] Despite the high attack rate and virulence, most infections were subclinical, and more than 99% of those who contracted the virus survived despite the absence of antivirals, vaccines, and antibiotics.[42]

The next flu pandemic, from 1957 to 1958, originated in the Yunan Province of China and is commonly called the *Asian Flu*.[37] Transmission of this H2N2 virus occurred principally along the sea lanes, and the entire globe became affected within 6 months. More than 40% of the world's population became infected, with 25% having clinically typical disease, and most deaths occurring as a consequence of secondary bacterial pneumonia.[43] Total mortality is believed to have exceeded 1 million persons.[36] During 1968 and 1969, another strain emerged causing the "Hong Kong" influenza pandemic (H3N2), which also was caused by a direct genetic exchange (re-assortment event) between duck and human viral subtypes.[5] Worldwide mortality rates were lower compared with those of the Asian flu outbreak; still, as many as 750,000 people died. Descendents of the 1968 H3N2 virus cause the majority of influenza infections today.[44] It has been 38 years since the last flu pandemic; over the last 300 years, the longest recorded interval between pandemics is 39 years.[45]

Typical seasonal outbreaks or epidemics result from antigenic variation in previously circulating influenza A and B viruses as a consequence of cumulative and advantageous genetic mutations. The accumulation of mutational advantages is known as "antigenic drift." Such mutations allow the virus to elude detection by a previously exposed immune system.

Until recently, pandemic influenza was thought to result exclusively from the emergence of an entirely new influenza A virus subtype via genetic re-assortment of gene segments from distinct viruses within a common animal host. Such major and direct exchange of gene segments is known as *antigenic shift*. More recently, isolation of viral genes from tissue samples preserved from the 1918 pandemic suggest that key mutations within a pre-existing avian H1N1 subtype allowed for direct transmission from birds to humans and may, in fact, result in a pandemic influenza,[46] though

some have disputed this finding.[47] Influenza viruses tend to evolve more rapidly after the virus has crossed over into a novel host.[24]

Several important lessons may be drawn from the history of previous influenza A pandemics[5]: pandemics are unpredictable in time, severity, mortality, and pattern of spread; exponential rates of infection occur very quickly, typically in a matter of weeks; outbreaks have tended to appear in waves of increasing severity with dissemination of virus to areas remote from its geographic origin and within more immunologically vulnerable populations.

Because of the unpredictability of influenza, information is constantly changing, and the knowledge base is constantly growing. Numerous online resources exist for keeping up to date on the prospect of pandemic influenza. The official site of the Centers for Disease Control and Prevention (CDC) is *www.pandemicflu.gov*, and a monthly Pandemic Influenza Update, prepared by the CDC, can be viewed at *http://www.immunize.org/pandemic/*.

Transmissibility of the influenza virus

One essential concept used by epidemiologists to describe the transmissibility of an infectious agent is the value of R_o. R_o, or the reproductive ratio, is defined as the expected number of individuals infected by a single infected individual during that person's infectious period.[48] Calculations of R_o assume that no control measures are taken and that all members of the population are initially susceptible to infection. Larger values of R_o imply that the disease can be disseminated easily within the population. If R_o is greater than 1, then it is vital that measures be taken within the population to control spread. But if R_o is less than 1, the disease may be best contained by tracking down and sequestering the infective individual(s) rather than placing burdens (such as mass vaccination) across the entire population.[49] For a pandemic influenza, the R_o is estimated to be approximately 4 (as a frame of reference, malaria has an R_o of 1.6, and measles has an R_o of approximately 17).[48,50] Statistical models of R_o assume a homogenous population, and efforts have been made to refine the model to reflect the diversity of the U.S. population (e.g., age, sex, and vaccination status) to better identify more effective control measures for various subpopulations.[51]

Battling a pandemic influenza

In the event of a major influenza outbreak, methods to control the spread of illness are divided to into 2 categories: pharmacologic and nonpharmacologic.

Pharmacologic methods of influenza control

Pharmacologic methods include influenza vaccination and administration of antiviral medications (both therapeutically and prophylactically). Seasonal influenza vaccine contains 2 type A viruses and 1 type B virus, with changes in subtype composition based on international surveillance. Both inactivated virus (injected vaccine for patients older than 6 months, including those with chronic illness) and live attenuated virus (nasal spray for healthy patients between ages 5 and 49) are available.[52] Live attenuated virus may have greater potential for producing constitutional symptoms like headache, sore throat, and nausea and is contraindicated in immunocompromised patients and those with asthma, cystic fibrosis, and COPD.[53] Advisory Committee on Immunization Practices (ACIP) guidelines currently recommend that children between ages 6 months and 9 years who have not been previously vaccinated at any time receive 2 doses of vaccine initially.

Vaccination against influenza, particularly in response to an emerging pathogen that is spreading rapidly, can be problematic. First, the strain of virus must be isolated and vaccine produced in sufficient quantities for distribution. However, improved cell culture techniques in vaccine manufacture have decreased the preparation time compared with traditional egg-based technology.[54] Second, the ability to perform safety and efficacy testing in an environment of time constraints may be compromised. One need only recall the complications from the swine flu vaccine in 1976 to raise concerns over adverse effects of vaccination[55] (such as Guillain-Barré Syndrome, a debilitating neurologic condition with ocular effects that have been described elsewhere[56]). Third, distribution and allocation of vaccines both geographically and demographically will create difficult choices for policymakers.

Targeted vaccination of children before all other population groups appears to be more effective in minimizing spread of illness compared with randomly distributing a limited supply of vaccine (unless emergent strains were to disproportionately infect other age groups).[57,58] Vaccinating children could prevent about one third of secondary household cases of flu.[59,60] Vaccinating 80% of children and teenagers would yield nearly the equivalent effect of vaccinating 80% of the entire population in terms of numbers of cases prevented. However, vaccinating 80% of children would not be as effective in preventing the onset of an epidemic compared with vaccinating 80% of all people.[58] Other statistical models suggest that 80% vaccination of children could be up to 93% effective in containing a pandemic influenza, and 65% effective in preventing a pandemic influenza. Mortality and economic costs would also be reduced sharply.[61]

Several antiviral medications currently are available, and efficacy against influenza viruses has been well documented, although antivirals are not a substitute for vaccination but rather play an adjunctive role in prevention and containment. There are 2 current classes of antiviral influenza medications based on mechanism of action. One inhibits the active site of the neuraminidase (NA) enzyme (an enzyme vital to releasing progeny viruses inside the host) and the other inhibits the matrix protein M2 proton pump of

the influenza virus (a step required for viral uncoating inside the host cell).[62] M2 proton pump inhibitors include amantadine and rimantadine; both have been used in the treatment of influenza for more than 4 decades.[63] Neuraminidase inhibitors include oseltamivir and zanamivir. Both classes of anti-influenza medication appear to be effective in decreasing the severity of disease for those already infected (by up to 60%) as well as in preventing onset of influenza when used prophylactically (by up to 85%), although only oseltamivir is approved in the United States for prophylactic use.[62-64] Oseltamivir is most effective when administered within 48 hours of infection, and efficacy decreases rapidly by 60 hours postinfection. Oseltamivir (Tamiflu®; Roche Laboratories, Nutley, New Jersey) can be administered orally, whereas zanamivir (Relenza®; GlaxoSmithKline, Research Triangle Park, North Carolina) must be inhaled as a dry powder.[21]

There is evidence of drug resistance for both classes of antivirals (particularly amantadine), but the chance of the development of widespread resistance to neuraminidase inhibitors is considered to be low.[21,62] However, there is a distinct possibility that a particularly virulent strain just may not respond to pharmacologic therapy. Statistical models may be able to reveal the efficacy (or lack thereof) of any control measure within 2 weeks.[65] Because of these uncertainties, prophylactic use of antiviral medications remains controversial.

Use of antiviral medications is not without risk. The frequency of adverse reactions varies from drug to drug, and manifestations include gastrointestinal discomfort and neuropsychiatric effects.[21] Recently, a warning was released detailing psychiatric disturbances (self-injury and delirium) with oseltamivir use in children.[66] Moreover, both oseltamivir and zanamivir are Pregnancy Category C agents, and their lactation safeties are unknown.[53] Oseltamivir dosage must be adjusted in patients with renal impairment (creatinine clearance of 10 to 30 mL/min versus a normal rate of about 140 mL/min).[67]

Nonpharmacologic methods of influenza control

Nonpharmacologic methods to control spread of influenza include heightened surveillance, social distancing, and planning for surge capacity.

Because emergence of new and destructive pathogens is so unpredictable, surveillance is the first line of defense in the broad-scale detection and containment of outbreaks.[68] Surveillance is performed at many levels, from the local community to global agencies. In addition to formal methods of surveillance by public health agencies at all levels of government, alternative forms of surveillance can provide early clues to the beginning of disease outbreaks. Sudden increases in "rumors" via Internet bulletin boards or cellular phone text messages were noted in the early stages of severe acute respiratory syndrome (SARS)[69] (a deadly respiratory infection that emerged from Asia in 2003 that is caused by a coronavirus and characterized by fever, diarrhea, and pneumonia[70]). Formal electronic communication between infection control professionals has enhanced surveillance efforts.[71]

Social distancing refers to physical separation of infectious and high-risk individuals from other susceptible individuals in the hope of controlling the spread of disease by reducing person-to-person contact. Social distancing on a global scale may entail curtailing air travel to prevent illnesses from "hopscotching" across large areas. For example, the 2003 outbreak of SARS originated in China and spread to Hong Kong and ultimately to 22 countries, in part, as a result of air travel.[72] Five international commercial airliners were linked to the spread of SARS from infected passengers to fellow passengers and airline crew.[73] A 1979 cluster of influenza A aboard a commercial aircraft was documented in which 72% of passengers had contracted the same viral strain.[20]

Efforts to limit air travel, however, would require the isolation of many larger airports[74] and consistent adherence to advice that symptomatic passengers postpone travel or seek medical advice if they have flu symptoms.[75] The decrease in airline travel after the September 11, 2001, attacks provided an opportunity to observe a change in the spread of influenza resulting from altered travel patterns. The influenza season that year was delayed and smaller presumably because fewer travelers translated into fewer opportunities to disseminate flu across the country.[76]

Mathematical models have been devised to predict the onset of peak incidence of influenza during an epidemic or pandemic as well as the role of air travel in spreading disease. Models suggest that air travel does add to the number of predicted cases of influenza across the nation, and such models can also help characterize an epidemic once it has started.[76] Another model suggests that if an influenza strain is highly transmissible (similar to the spread of SARS), a global outbreak could quickly spread if even a few infected individuals were allowed to travel to just 3 major destination cities. Isolating the top 2% most populous cities from the normal influx of visitors could cut the need to vaccinate by almost one half.[74]

Community-level social distancing would be aimed at decreasing person-to-person contact. This could include steps such as canceling large-scale events and encouraging workplace strategies to decrease person-to-person contact, such as working remotely from home, teleconferencing, and increasing physical distance of workstations.[77]

It is widely accepted that young children most easily transmit the virus. This is attributable to the observations that: (1) children experience a large number of contacts with other children in school or daycare, (2) children are assumed to be more susceptible because of lower immune status, and (3) children could be more infectious because they shed more virus and shed the virus for a longer time period compared with older individuals.[59] Modeling of social contacts suggests that teenagers may also substantially increase the spread of influenza.[78]

Table 1 Methods of protecting office staff and patients from exposure to respiratory infectious agents[89,146,147]

Administrative, work practice, and engineering controls
- Develop policies that encourage ill employees to stay home without fear of reprisal.
- Encourage home delivery of products (when feasible) to reduce the number of potentially sick patients who must visit your workplace.
- Perform systematic decontamination of work surfaces (eg, patient chairs, countertops, doorknobs, faucet handles) particularly after examining a sick patient.
- Provide resources that promote personal hygiene of employees and patients (including accessible supply of tissues, no-touch trash cans, hand soap, alcohol-based hand sanitizer and disposable towels).
- Encourage employees to receive the influenza vaccine or make it available to employees as an employee benefit.
- Educate employees on influenza risk factors, methods of protection, and proper behavior (e.g., cough etiquette).
- Consider use of telemedicine where appropriate during an outbreak.
- Install "sneeze guard" shields to slit-lamp biomicroscopes and other equipment where appropriate.

Personal protective equipment
- Use respiratory protection (N95 respirator) in situations of high likelihood of exposure to contagious patients (surgical masks may also be used when N95 respirators are unavailable); patients suspected of having influenza should also be provided with respiratory barrier protection (N95 respirator or place an adhesive surgical drape over the mouth and nostril area).

Because children (especially preschoolers) are thought to play a major role in spreading influenza in the community, some social distancing strategies are directed specifically at children, including closure of schools and daycare facilities. One study estimates more than 40% of secondary flu cases are attributable to exposure to a sick preschool child. The effectiveness of social distancing targeting children is demonstrated by a study showing that the proportion of sick children decreased sharply once winter school recess commenced. The entire profile of this epidemic changed abruptly as a result of interrupting the cycle of infection by sending children home for the holidays.[79] Such a strategy is not foolproof, however, because some benefits could be negated by increased spread of illness in the home or neighborhood when school is canceled. Even with school closures, preventing contact with *nonhousehold* children markedly increased the efficacy of social distancing.[78]

In the event of a pandemic outbreak of the flu, the multitude of persons expected to become ill will likely overwhelm hospitals and other health care facilities. This challenge of so-called "surge capacity" is a concern for clinic administrators and planners at the community public health level. Efforts are being made to increase surge capacity to meet the unprecedented demand for care anticipated during a pandemic. Measures include identification of temporary clinical care areas on the premises of health care facilities or makeshift patient wards in large structures (e.g., aircraft hangars, recreation centers, churches), predetermined procedures to facilitate and monitor home care, and caching of specific supplies.[80] Surge capacity also can be enhanced by restricting elective surgeries to free up beds and personnel.[81]

Benefits of using various pharmacologic and nonpharmacologic control measures would be (1) a lower total number of cases of illness (versus no interventions), (2) a dampening of the peak number of cases during each outbreak, and (3) spreading out the number of sick patients over a longer time interval.[79,82] Flattening and extending the pattern of an epidemic or pandemic will make the outbreak more manageable and less overwhelming at any given point in time.

Preventing influenza in the primary care setting

When sick patients are intermingled with well patients in common areas such as reception areas, examination rooms, clinical laboratory, and radiology departments, health care facilities provide an environment in which influenza can be transmitted from person to person or from inanimate objects. Aggressive measures to prevent the spread of influenza include use of hygiene/infection control procedures, protective equipment, and social distancing. Table 1 provides examples of these control measures, which can be implemented in the outpatient environment to decrease the risk of spreading respiratory infections, including influenza.

Typical influenza viruses can remain viable on nonporous inanimate surfaces for up to 48 hours.[83] Porous surfaces appear to make for a less hospitable environment for viruses, and viral titers decrease rapidly for surfaces such as cotton, polyester, and other plastics.[84] The influenza virus persists in a variety of environments with humidity between 35% and 49% at room temperature.[11] The virus may persist even longer and be more likely to cause infection if the humidity is decreased to between 20% and 30%.[11,85]

Disinfection of work surfaces and other objects patients might touch (eg, doorknobs and chair handles) is a prudent method of preventing spread of infectious agents. The United States Environmental Protection Agency has compiled a list of disinfectants registered and labeled to be effective against avian influenza virus. The list can be accessed online at *http://www.epa.gov/pesticides/factsheets/avian_flu_products.htm*.[86]

Interestingly, the influenza virus may be viable on contaminated hands for a mere 5 minutes, which is usually

sufficient time for self-inoculation.[11,83] Of course, frequent hand washing after patient contact is a prudent means of reducing the spread of any infectious material.[87] Furthermore, alcohol-based hand sanitizers are known to be effective virucides[88] and are more effective than hand washing against infective droplet nuclei.[89]

Use of respiratory protection has been a topic of ongoing debate. It is widely accepted that the spread of influenza occurs by airborne means, although the extent of transmission relative to direct contact with contaminated surfaces or other patients is unknown.[90] Theoretical models suggest increased replacement with fresh air in ventilation systems will decrease risk of influenza.[91] A sneeze can generate up to 40,000 small droplets, which travel upward of 100 meters per second and settle several meters from their origin. Particles that are smaller than 3 μm can remain suspended indefinitely.[90] Suspension or resuspension of particles can occur simply by opening and closing a hinged door, and sliding doors may reduce movement of infectious droplets.

Facemasks provide respiratory protection and are divided mainly into surgical masks and N-95 high-efficiency particulate air filtering respirators. Surgical masks are worn over the nose and mouth such as those worn in the operating room. N-95 respirators are masks designed to be 95% effective in filtering particles down to 0.3 μm in size and are used in a variety of occupational settings. Facemasks must be replaced frequently because the accumulation of moisture from breathing will decrease the ability to block the penetration of microbes.[92] Use of facemasks and covering the mouth when sneezing may have helped reduce transmission of SARS.[93]

Official recommendations for the use of respiratory protection are undergoing constant review. Recently, the National Institute of Occupational Safety and Health (NIOSH), an arm of the CDC, modified prior recommendations from 2004 and now advocates the use of N-95 respirators for workers engaged in activities with the high likelihood of generating infectious aerosols.[94] Other CDC guidance documents recommend the use of surgical masks in the event of a shortage of N-95 respirators. Surgical masks offer protection from larger aerosol droplets and are not as effective as the N-95 in protecting the wearer. If respiratory protection is worn, users must be trained in its proper use, including advice on proper fitting, maintenance and hygiene, re-use protocols and proper disposal of used respirators.[95] Despite recommendations for the use of respirators or surgical masks in caring for flu patients in the health care setting, the Department of Health and Human Services is stopping short of recommending their use by the general public unless they are caring for family members known to be ill from pandemic influenza.[96]

The CDC's recommendations for airline flight crews encourage giving sick passengers surgical masks to reduce dissemination of aerosol particles to others in the aircraft cabin.[97] Still, the government has not strongly advocated their use elsewhere by sick individuals nor have they encouraged production and stockpiling of respirators or surgical masks for use during a pandemic.[98] In addition, there is a stigma in most Western countries about wearing surgical face masks and respirators in public, and this may prove to be a barrier to their use.[99]

Hogg and Houston[89] have developed a simple mnemonic, MASKS, for basic precautions that can be taken in an outpatient setting:

M—masks for patients with cough and fever and for providers examining those patients.

A—alcohol hand gel for sanitation (for patients as well as office staff).

S—seating of potentially infectious individuals apart form others (recommended distance at least 1 M).

K—"kleening" (disinfecting) hard surfaces.

S—signs to guide patients and staff (e.g., to promote hand washing).

Such precautions are estimated to cost a typical office, seeing 30 patients daily, an average of about $2 per day to implement.

Can telemedicine play a role?

One method of creating social distancing in the clinical environment is use of telemedicine. Telemedicine can take many forms, including telephone consultations with patients and remote consultations with specialists by electronic transfer of data. Conceptually, telemedicine could prove useful as a means of preventing spread of an influenza pandemic via 3 dimensions: remote examination of patients with flu-like symptoms, education of patients and providers, and provision of care to "well" patients with noninfectious health issues. Use of telemedicine in the assessment of infectious disease has previously helped evade large outbreaks. For example, online consultations, performed during an investigation of a cluster of acute gastrointestinal diseases, aided in early containment of cholera at a religious gathering in India.[100]

Telemedicine in eye care has been shown to be useful, valid, and cost effective for a number of years in managing both anterior and posterior segment eye disease.[101-104] In the context of social distancing, sending clinical data electronically to an ophthalmic specialist for online consultation could reduce the need for patients to visit another public gathering place (e.g., the specialist's clinic or hospital setting) and in turn may reduce patients' exposure to contagious individuals.

Global and local economic impact of a pandemic influenza

A pandemic influenza is predicted to severely affect the global economy as disruption of commerce and infrastructure occurs and world markets lose confidence in the economic outlook. It is estimated that a pandemic flu outbreak could result in a negative impact on the United States

economy of approximately $166 billion in lost productivity and direct medical costs.[105] Another study estimates that insurers could have to pay up to $155 billion in life insurance claims from flu-related deaths.[106] Globally, economic losses caused by a pandemic flu could reach $800 billion.[107] By comparison, the estimated economic toll of hurricane Katrina was about $140 billion.[108]

Workers compensation insurance could provide some relief from medical bills and disability if it could be proven that the illness arose out of and in the course of employment. A pandemic flu is not specifically a compensable work-related condition at this time, but state-by-state regulatory changes could provide a partial payment mechanism for health care costs if the situation arises.[32]

Outbreaks of disease can change societal goals and allocation of resources. During an epidemic of a disease, the goal may be to minimize death and disability; during a disease pandemic, the goal may shift to preserving basic functioning of society by devoting available resources to maintenance of critical infrastructure, such as law enforcement, emergency medical services and utilities.[109,110]

Major unsettling events—particularly ones with national or global implications—can adversely affect entire industries, and health care is not immune to such systemic shocks. Optometrists are relatively unique in the health care sector as service providers while also being a link in the chain of commerce. In the case of a pandemic flu, fear of contagion, logistical and transportation challenges, understaffing of utility companies, suppliers, and couriers, and a host of other problems can impede the ability to give or receive goods and services. As other companies experience employee absenteeism, a "domino effect" could arise causing a shortage of manufacturing and warehouse personnel as well as a shortage of drivers and couriers fearing contracting illness during one of many delivery stops.

Business interruption

Excessive business "downtime" caused by lack of staffing, interrupted utilities or consumer fear can wreak economic havoc on a small business. A study of disasters has shown that two thirds of businesses that do not open within 2 weeks after a catastrophe will file bankruptcy within 1 year.[111]

Businesses affected by acute natural disasters (e.g., earthquake and flood) suffer problems such as lack of employee and customer accessibility and shipping delays that contribute to business losses and impede recovery. As both demand (customer volume) and supply (employee productivity) decrease in the wake of disaster, business owners may find it difficult to recover. If particular neighborhoods or regions become branded as areas of higher risk, challenges to recovery become magnified.[112] The fear of SARS, for example, caused a dramatic downturn of activity in the "Chinatown" areas of numerous North American cities, such as Toronto, Boston, Los Angeles, and San Francisco.[113,114] Canada alone experienced economic losses of over $1 billion because of SARS even though there were fewer than 500 patients directly affected by the disease. Given the millions of cases predicted in a flu pandemic, the economic costs would be truly staggering.[114] Providers of services and goods whose markets are limited to a local level (optometrists, for example) are more vulnerable to delays in long-term recovery after disaster.[115]

Business continuity and recovery

Providers of services or goods must be ready for disruption in the normal flow of commerce. Governmental agencies and numerous risk management consultants recommend that businesses develop a continuity plan to identify risks that could disrupt business and to prepare for such disruptions in business activities arising from a pandemic influenza outbreak. Businesses often commit resources to ensuring life safety in the wake of disaster but are less likely to devote resources toward preserving business continuity.[115] Businesses that prepare for disasters beforehand will tend to survive and resume normal operations in better fashion than those that do not.[112]

A planning template for business continuity is shown in Table 2. This table summarizes the 10 business planning objectives outlined in the pandemic influenza guidance document prepared by the Ministry of Health of the Canadian Province of British Columbia; other frameworks are similarly organized.[32,77,116-118] By benchmarking with other service and hybrid service-product industries, doctors of optometry can gain insight into possible ways of mitigating problems associated with a pandemic; some examples of action items are also listed in Table 2.

Ethical and legal aspects of pandemic influenza

Trying to save lives during an extreme situation such as a pandemic will require difficult choices. Strategies to preserve public health often are characterized as "utilitarian" in nature, that is, the action is ethically right if it produces more utility (or well-being) for all people than any alternative action, or if it maximizes utility from available resources.[119] Others state more succinctly that "the good of the public is the supreme law."[120] Balanced against the concept of utility are 4 basic tenets of health ethics[121,122]:

- Respect for autonomy: concern about individual rights and freedom.
- Nonmaleficence: "first do no harm" to the individual.
- Beneficence: the intent to do good for someone, even if it could pose harm to the health care provider.
- Justice: fairness, impartiality in making and carrying out rules.

The re-emergence of a pandemic influenza is inevitable, but the timing and virulence of the next event cannot be predicted. Expenditures for preparedness and treatment of

Table 2 Ten objectives for business pandemic planning[77,111,116,117]

Objectives	Examples of steps to meet objectives in the optometric practice
1. Get organized.	Assemble staff and outside resources (e.g., local business or professional organizations) for assistance in gathering information on a pandemic flu.
2. Assess risks.	Identify potential challenges to continuing business if there were a catastrophic outbreak of flu (e.g., loss of utility service, in-office banking, telecommunications, shipping/receiving courier service).
3. Protect employee health.	Promote proper hand washing, regularly clean common surfaces (e.g., doorknobs), remind staff of proper cough etiquette. Stockpile personal protective equipment, disinfectants and cleaners, cache emergency supply of food and water in appropriate quantities. Use social distancing techniques when possible (move employees out of public areas for tasks not critical to face-to-face contact with patients).
4. Prepare employee policies.	Develop pandemic flu work policies (including cancellation of vacations, approval of overtime), use direct deposit for payroll (assume banks may also be experiencing staff shortages).
5. Plan for business continuity.	Develop means to handle increased patient orders placed over the phone or online (and delivery of orders). Stock critical supplies vital to patient care (e.g., pharmaceuticals) because of expected shipping delays and decreased inventory from vendors. In the event of major fuel shortages, develop a plan to help employees get to work.
6. Prepare for supply and service interruptions.	Identify multiple vendors for core products (consider geographically diverse vendors [e.g., optical laboratories and contact lens distributors] in the event certain regions experience greater interruption than other areas). Keep in-office inventory of commonly prescribed products and/or make cooperative arrangements with other offices to share inventories of diversified products (e.g., Brand X stocked in one office and Brand Y in another office and exchanging product as needed). Develop emergency product substitution rules.
7. Prepare to fill vacancies.	Cross-train employees and reallocate employees where needed; streamline hiring process.
8. Inform employees.	Keep employees apprised of any locally anticipated pandemic influenza outbreaks and activation of new workplace policies in response to flu. Keep up-to-date contact lists for all employees, including next-of-kin. Respond to rumors with facts.
9. Inform other stakeholders.	Keep patients apprised of changes in hours or services or systematic delays in shipping. Develop "talking points" to reassure patients that the office is not "more sick" because the office is using protective equipment (e.g., masks). Respond to rumors with facts.
10. Prepare a pandemic influenza management plan.	Document any office policy changes made in preparation for, or response to, a pandemic flu.

an unpredictable event such as a pandemic flu must be balanced against the "opportunity costs" of not spending those dollars for other public goods (e.g., cancer research and treatment, homeland security, and highway safety).

Acquisition of "hard" medical assets like hospital beds and ventilators will have value in preparation for the management of multiple potential medical disasters, including an influenza pandemic; the political climate for such an argument may be particularly ripe as a result of the bioterrorist attacks of 2001. Hard assets, however, also are associated with high costs. In the event of a pandemic, the demand for intensive care unit beds and ventilators could be more than twice the current capacity. Patients with severe forms of acute respiratory failure (as is found with severe cases of influenza) will likely die without the aid of ventilators.[123] With respect to scarce, intensive and expensive medical interventions like mechanical ventilators, use of objective medical criteria like SOFA (Sequential Organ Failure Assessment) score has been advocated for triage to determine which acute care patients are most and least likely to benefit from respiratory support and provides a more or less objective and relatively accurate, utilitarian calculus for allocation of resources.[124,125]

Current stockpiles of antiviral medications in the United States are quite limited. As of last year, the United States had only enough oseltamivir to treat 1% to 2% of the population.[126] Vaccines and drugs are or will be manufactured at various locations around the world, and difficulties will be faced in meeting the surge in demand. In an attempt to save their own citizens, governments might suspend routine trading practices and limit the export of pharmaceuticals to other countries including the United States.[127,128]

The United States recently has announced intentions to purchase more oseltamivir, but supplies would still be woefully inadequate to treat all who would need it in the event of an influenza pandemic.[127] From a cost-benefit perspective, stockpiling oseltamivir is cost effective as long as there is a pandemic once very 80 years.[129]

The genetic variability of influenza viruses impedes pre-emptive production of the most effective vaccine. Production of novel antiviral medications cannot begin until the unique genetic features of the offending pathogen are identified. This is not to say, however, that likely candidates for novel and highly virulent infection cannot be identified in advance and that production of vaccine and medicines with at least *some* probabilistic efficacy cannot proceed, as has been seen with development of neutralizing antibody responses in human subjects given a prototype H5N1 vaccine.[130] An influenza vaccination, however, is far more cost effective than antiviral treatment or prohylaxis.[105,131]

There is substantial evidence that dilution of a vaccine provides at least some measure of protection,[132-134] even for the experimental H5N1 vaccine,[130] although antibody titers definitely rise with increasing dosage to levels deemed to give adequate (>50% of the vaccinated population) immunity. Given the crisis of a virulent influenza pandemic, however, it may be that diluting the available vaccine to at least *partially but equally* immunize a much larger percentage of the population would preserve social trust and be most ethically defensible by maximizing equitable distribution of risk.

Ezekiel Emanuel, a bioethicist with the National Institutes of Health, observes that "(d)eciding who should take priority for scarce influenza vaccine in a pandemic entails decisions about minimizing bad outcomes."[135] A compendium of several viewpoints on who should receive priority for influenza vaccine is shown in Table 3.[136] These guidelines weigh several, sometimes competing, ethical considerations, including the need for preservation of infrastructure and public order (law enforcement), provision of a healthy pool of health care providers tending to the ill, and protection of the more vulnerable members of society.

National Vaccine Advisory Committee/Advisory Committee on Immunization Policy (NVAC/ACIP) criteria have been labeled as a utilitarian "save-the-most-lives" approach to allocating vaccine.[135] The *life-cycle principle* system places higher value on younger lives because they have a greater number of potential years remaining. The *investment refinement of life-cycle principle* places higher value on the young but also prioritizes those who have invested more assets (time, energy, and money) into the development of ideas, hopes, and dreams that have not yet been realized; thus, the life of a 20-year-old individual is assigned higher value than the life of a 2-year-old individual. Emanuel implores decision makers to "reject the traditional public health approach to 'minimize mortality or infectious incidence': no one does—or should—just count numbers of dead bodies to determine which course of action is better."[135] However, it is not at all clear from such analysis how decision makers are to evaluate the relative moral worth of the ideas, hopes, and dreams of members of 1 age group as against those of another.

Pharmacologic countermeasures for a pandemic flu carry risks. Previous public health emergencies have created the need for compulsory enforcement of public health measures but also raise legal and ethical questions. Is it fair, for example, to require compulsory vaccinations? Some may argue that exposing a person to the risk of adverse effect of a hastily concocted vaccine in a pandemic situation is an unfair proposition. One publication speaks against exposing someone to the unknown because "(d)ue to the preventive nature of vaccines, in contrast to therapeutic treatment of existing disease, it is difficult to determine with confidence if an unvaccinated person will in fact contract disease."[137] Still, case law, such as *Jacobson v. Massachusetts* affirms the government's right to require people to be vaccinated depending on the circumstances of the day, and the courts generally have acted in deference to public health officials in determining when vaccinations are compulsory.[138]

What has been articulated less clearly in the current environment is the "duty to care" of health care providers in the event of an outbreak that poses significant risk to the health and life of those providers.[122] In the face of this risk, the underlying principle of beneficence dictates that doctors have a duty to care for patients in time of need, even if doing so would endanger the doctor's own well-being. The CDC has declared that the issue of duty to care is of central importance in pandemic planning and response.[139] However, the historical and ethical obligation of health care providers to care for the sick must be balanced against the limited number of professionals available to treat patients now and in the future, the medical necessity of services rendered by particular specialties, and the individual doctor's rights to life and health.[140]

Can an employee be forced to get a flu shot?

Healthy workers who receive influenza vaccine have 43% fewer sick days than those who are not vaccinated.[141] Discussion of the efficacy of influenza vaccinations will naturally lead to questions about whether workers (including health care workers) ought to receive, or be forced to receive, a flu vaccination. For instance, can employees be compelled to receive vaccinations as a condition of continued employment for the protection of business continuity at the doctor's practice?

A common form of employment is "at-will" employment. At will is defined as "the right of employers to fire employees for any reason, or for no reason at all" so long as they do not discriminate, violate public policy, or conflict with written or implied promises made concerning length of employment or grounds for termination.[142]

Is refusal to receive a vaccination grounds for termination of employment? The case law presents 1 related ruling, *Virginia Mason Hospital v. Washington State Nurses Association,* which opined that a hospital cannot force its nurses

Table 3 Priorities of distribution of vaccine[136]

Tier	NVAC and ACIP recommendations	Life-cycle principle*	Investment refinement of life-cycle principle including public order**
1.	Vaccine production and distribution workers	Vaccine production and distribution workers	Vaccine production and distribution workers
	Frontline health care workers	Frontline health care workers	Frontline health care workers
	Patients 6 months to 64 years old with ≥2 high-risk conditions or history of hospitalization for pneumonia or influenza		
	Pregnant women		
	Household contacts of severely immunocompromised people		
	Household contacts of children ≤6 months of age		
	Public health and emergency response workers		
	Key government workers		
2.	Healthy people ≥65 years old	Healthy 6-month-olds	People 13 to 40 years old with <2 high-risk conditions, with priority to key government leaders; public health, military, police and fire workers; utility and transportation workers; telecommunications and IT workers; funeral directors
	People 6 months to 64 years with 1 or more high-risk conditions	Healthy 1-year-olds	
	Healthy children 6 months to 23 months old	Healthy 2-year-olds	
	Other public health workers, emergency responders, public safety workers (police and fire), utility workers, transportation workers, telecommunications and IT workers	Healthy 3-year-olds	
			People 7 to 12 years old and 41 to 50 years old with <2 high-risk conditions with priority as above
			People 6 months to 6 years old and 51 to 64 years old with <2 high-risk conditions, with priority as above
			People ≥65 years old with <2 high-risk conditions
3.	Other decision makers in government	People with life-limiting morbidities or disabilities, prioritized according to expected life years	People 6 months to 64 years old with ≥2 high-risk conditions
	Funeral directors		
4.	Healthy people 2 to 64 years old		People ≥65 years old with ≥2 high-risk conditions

NVAC = National Vaccine Advisory Committee; ACIP = Advisory Committee on Immunization Policy.

Note: Tiers determine priority ranking for the distribution of vaccine if limited in supply (Tier 1 is assigned highest priority)

Subtiers marked by italics establish who gets priority within the tier (starting from the top of the tier) if limited vaccine cannot cover everyone in the tier; priority may occur within subtier as well.

Children 6 months to 13 years would not receive vaccine if they can be effectively confined to home or otherwise isolated.

* The "life-cycle principle" system places higher value on younger lives because they have a greater number of potential years of life remaining (see text for details).

** The "investment refinement of life-cycle principle" places higher value on the young but also prioritizes those who have invested more assets (time, energy, and money) into development of ideas, hopes, and dreams that have not yet been realized (see text for details).

to receive flu vaccinations, although the ruling involves issues of collective bargaining by the nurses union and not at-will employees *per se*.[143] Recent case law, such as *Dore v. Arnold Worldwide*, does affirm the right of employers to terminate at-will employees without any cause or prior notice given.[144] Whether a doctor (as employer) could mandate an influenza vaccination for office staff as a condition of continued employment is not completely certain at this time.

The American College of Occupational and Environmental Medicine has stated its opposition to mandatory influenza vaccination for health care workers in part because the coercive nature of mandated directives may harm the employer-employee relationship. However, it does state that its position may be modified if mandatory vaccination were in response to pandemic influenza as opposed to seasonal influenza.[145]

Conclusion

The onset of a pandemic influenza is a virtual certainty; what remains uncertain is when and how catastrophic the

outbreak will be. Meanwhile, one is left to wonder whether forewarnings by epidemiologists and business consultants alike will serve as an adequate call to action. As optometrists, our very livelihood may depend on it. Potentially dangerous flu strains are brewing, and now is the opportunity to assess our vulnerabilities as individuals, families, communities, nations, and health care professionals.

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