Influenza A (H1N1) - A Globetrotting Virus

By Glenn Tzen M. Gloria, MD, RN

The World Health Organization (WHO) on its last official update on the 6th of July, 2009, has reported 94,512 laboratory confirmed cases of the Influenza A (H1N1) infection from 135 countries, 429 of which resulted to death. However, WHO announced that it will no longer issue the global tables showing the number of confirmed cases for all countries, as it is already extremely overwhelming to keep track of every suspected case with laboratory testing and resource-intensive, because of the rampant speed at which it has been spreading.

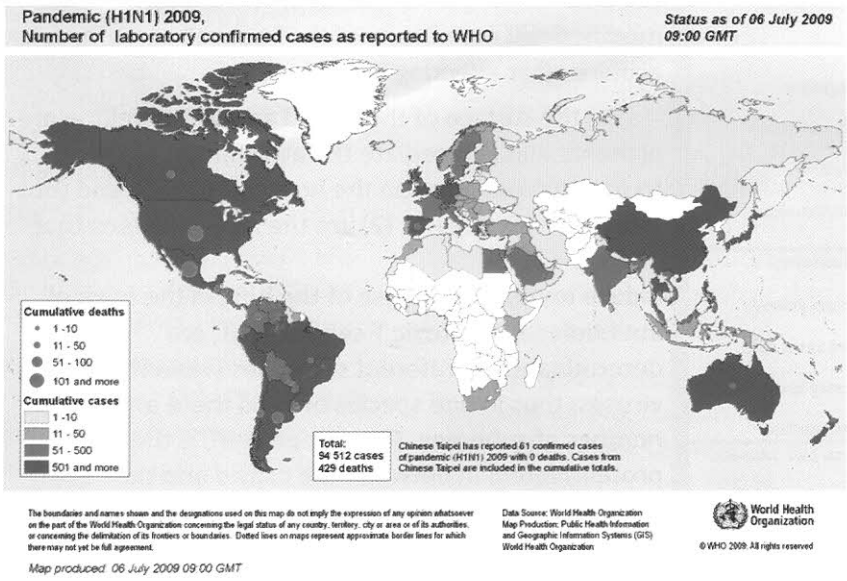

FIGURE 1. Map of the spread of pandemic (H1N1) 2009: number of laboratory confirmed cases and death as of 6th July, 2009 (from WHO website www.who.int)

The actual number of cases will be significantly higher, as only a small proportion of people with symptoms are being tested, and many more could have gone undetected, because of the mildness of symptoms in the majority of patients. Most people would recover readily at home without needing even medical treatment.

The outbreak that began in Mexico in early April, 2009 spread rapidly in other countries, escalating to a pandemic as WHO declared Phase 6 (Table 1) on June 11, 2009. It has taken less than six weeks to spread widely what the previous influenza pandemics took for more than six months. However, WHO considers the overall severity of the present influenza pandemic to be moderate, as reflected by most people recovering without the need for hospitalization, the similar pattern of illness to the seasonal influenza and the ability of the health care systems in most countries to cope up with the turn out of people seeking treatment.

Nonetheless, there is no room for complacency. As of this writing, the worldwide death toll has reached 822, almost double the figure since the last update of WHO, and cases continue to increase steeply. It is expected that with the advent of the cold months and the flue season, figures will rise up.

VIROLOGY 101

Here's a little background on the structure of viruses in general in order to understand why there is such concern regarding the pandemic spread of Influenza A (H1N1)

As agents of infectious diseases, viruses are quite distinct from other organisms. They lack the cellular organization of bacteria and other microorganisms. Instead of having a cell membrane, a cytoplasm and a nucleus, they consist mainly of two or, in the case of the Influenza virus, three parts: (1) all viruses have genome

PHASE	DESCRIPTION
PHASE 1	No animal influenza virus circulating among animals have been reported to cause infection in humans.
PHASE 2	An animal influenza virus circulating in domestic or wild animals is known to have caused infection in humans and is considered a specific potential pandemic threat.
PHASE 3	An animal or human-animal influenza reassortant virus has caused sporadic cases or small clusters of disease in people, but has not resulted in human-to-human transmission sufficient to sustain community-level outbreaks.
PHASE 4	Human-to-human transmission of an animal or human-animal influenza reassortant virus able to sustain community-level outbreaks has been verified.
PHASE 5	The same identified virus has caused sustained community level outbreaks in two or more countries in one WHO region.
PHASE 6	In addition to the criteria defined in Phase 5, the same virus has caused sustained community level outbreaks in at least one other country in another WHO region.
POST PEAK PERIOD	Levels of pandemic influenza in most countries with adequate surveillance have dropped below peak levels.
POST PANDEMIC PERIOD	Levels of influenza activity have returned to the levels seen for seasonal influenza in most countries with adequate surveillance

TABLE 1. WHO Pandemic Phase Descriptions (www.who.int)

that carry the genetic material made from either DNA or RNA; (2) all have a protein coat called capsid that protects these genes; and (3) some have an envelope made of lipid that surrounds them when they are outside a cell.

The viral capsid is made up of identical protein subunits called capsomers. The arrangement of capsomers gives the viral shape its geometric symmetry, as icosahedral in which the capsomers form a closed quasi-spherical shell, or as helical in which the capsomers are stacked around the spiral genome forming a hollow tube. The envelope is the modified cell membrane of the host cell some viruses acquire after infecting it.

On the surface of the capsid and the envelope are proteins that (1) mediate the attachment of the virus to specific receptors on the host cell surface and thus infect specific organs; (2) are the main antigens that induce immune response of the host in the form of antibodies & cytotoxic T cells; and (3) are determinants of different serotypes (variants) among viruses, thus in one species of virus there are a number of subtypes. Another protein, is the matrix protein, found in between the capsid and the envelope, mediating the interactions between these two layers.

Viral infection occurs when a host organism is exposed to the virus. Only after entry inside the body the virus can gain access to susceptible cells. As they cannot survive on their own, viruses depend on the host cell's metabolic machineries in order to replicate, like a parasite benefiting from the host.

The viral life cycle (Figure 2) starts with: (1) the proteins on the surface of the viruses attaching to specific receptor proteins on the cell and are highly specific to the host or type of cells they infect. Once attached, a virus (2) penetrates inside the cell by allowing itself to be engulfed by the cell, and once inside (3) uncoats its capsid to release its viral genome. (4) The virus must then take control of the host cell's replication mechanisms for synthesis of its genome. After control is established and the environment is set for the virus to begin making copies of itself, replication occurs quickly. (5) After a

virus has assembled and made many copies of itself, it usually has exhausted the cell of its resources. The cell is now no longer useful to the virus, therefore it must find cells to infect. (6) The process by which virus progeny are released to find new hosts, is called shedding. This is the final stage in the viral life cycle. At this stage, the infected cells die and cause tissue damage.

THE ABC's, THE H's AND THE N's of INFLUENZA

The influenza virus is an RNA virus, and is a member of the Orthomyxoviridae (the term "myxo" refers to the virus' affinity to mucin of the respiratory tract). There are 3 genera of Influenza virus: Influenza A, Influenza B and Influenza C. These 3 are very similar in overall structure, but their antigenicity lies in the difference in the proteins of the capsid and matrix. Their genome, covered by a helical capsid, contains eight pieces of segmented RNA, each of which contains one or two genomes encoding for the capsid, matrix and envelope proteins. Sources of Influenza A are birds & mammals like pigs (swine), of Influenza C are swine, but all 3 types cause human infections. However, only Influenza A can cause wide-scale pandemics; Influenza B and C occur less commonly.

For Influenza B and C, there are no serotypes. But for Influenza A, viruses are further classified, based on the two viral envelope glycoprotein spikes hemagglutinin (HA or H) and neuraminidase (NA or N) (Figure 3). Sixteen H subtypes (or serotypes) and nine N subtypes of Influenza A virus have been identified. Hence the name Influenza A (H1N1). The function of the hemagglutinin is to bind to cell surface receptor to initiate infection, while the neuraminidase cleaves the cell membrane glycoprotein neuriminic acid to release progeny virus from infected cell; neurominidase also degrades the protective layer of mucus in the respiratory tract, enhancing the ability of the virus to infect the respiratory epithelium.

The type A virus is the most virulent among the three influenza types. Changes in the antigenicity of the H and N proteins (serotypes) as well as reassortment of the segments of the RNA genome contribute to the capacity of Influenza A virus to cause devastating pandemics. Known strains of Influenza A are: H1N1 which caused the Spanish Flu of 1918; H2N2 which caused the Asian Flu of 1957; H3N2 which caused the Hongkong Flu of 1968; and H5N1 the avian flu which is feared to pose as a pandemic threat. The seasonal flu that occurs every year during winter months is mainly serotypes A (H3N2), A (H1N1) and B.

The strain of the current pandemic is also Influenza A (H1N1) but it is believed to result from the reassortment of the genome segments from four strains (Figure 3): one found in humans, one endemic in birds and two from pigs, hence the name swine flu as it was called in its initial outbreak. This is a new strain that has never before caused infection in humans. Pandemics appear every 10-20 years, when the antigenicity of the virus has changed sufficiently that preexisting immunity of many people is no longer effective. As this is a new strain, with the advent of the colder months and the seasonal flu, it is feared that this pandemic flu would cause a more serious infection & fatalities, as people has not develop immunity against it, unlike the seasonal flu which occurs every year that many people have some immunity which helps limit infections.

Fast transmission of Influenza is due to three main ways: (1) inhalation of respiratory droplets from infected people's coughing, sneezing and spitting; (2) direct transmission of infected mucus secretions to other people's eyes, nose or mouth; and (3) direct personal contact such as hand-shake, then hand to mouth. The virus can persist outside the body, in inanimate objects such as doorknobs and table surfaces for longer periods.

Once the virus has been inhaled through the respiratory tract, the virus bind its hemaglutinin with the neurominic acid on the surface of epithelial cells of the nose, throat and lungs. The virus then enters the cell in vesicles

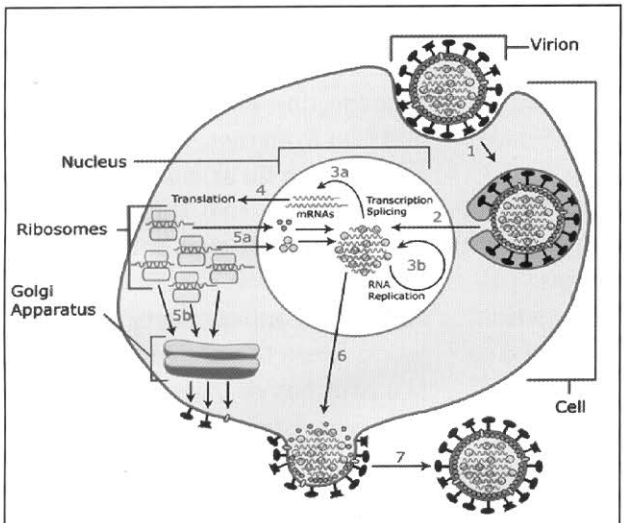

FIGURE 2. Influenza Virus Life Cycle
(from www.en.wikipedia.org/wiki/Inluenza)

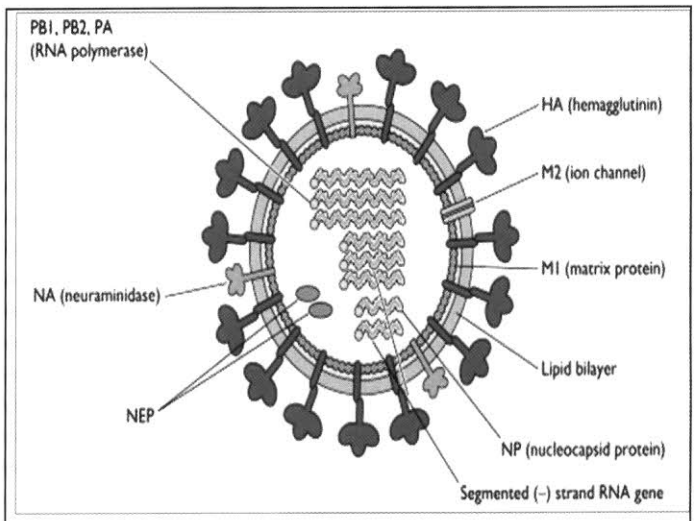

FIGURE 3. Influenza A structure
(from VIROLOGY BLOG website www.virology.ws)

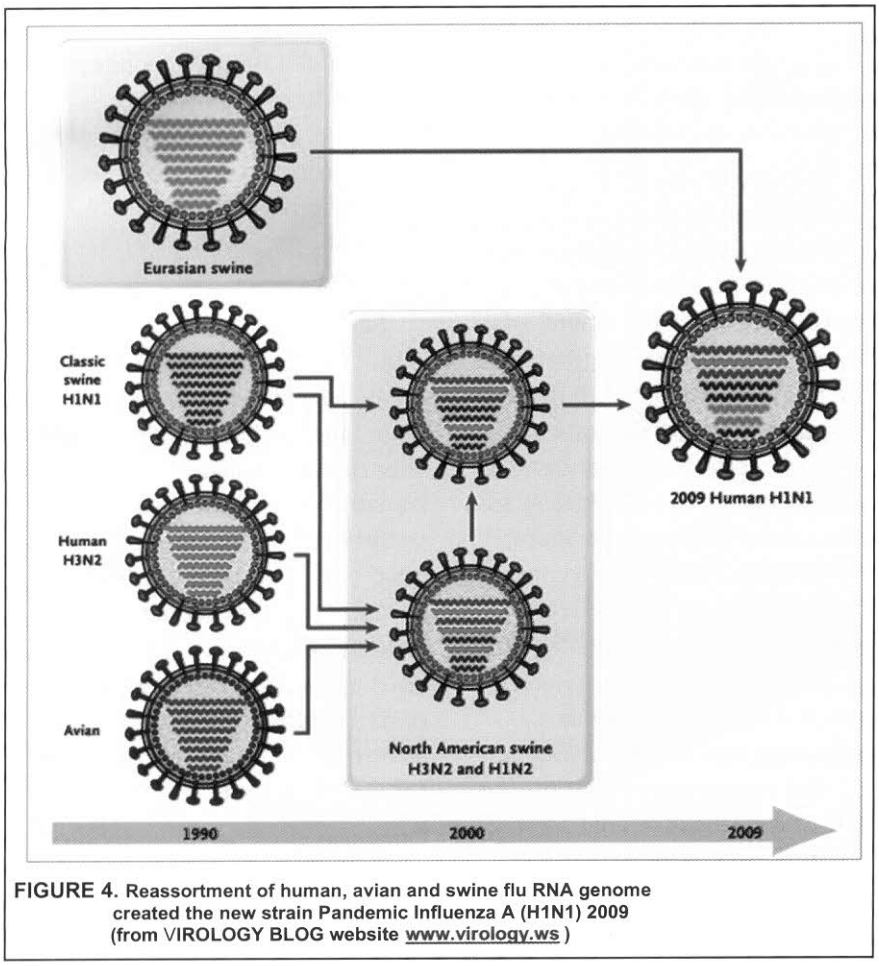

FIGURE 4. Reassortment of human, avian and swine flu RNA genome created the new strain Pandemic Influenza A (H1N1) 2009
(from VIROLOGY BLOG website www.virology.ws)

and uncoats within an endosome. The eight genome segments are transcribed into eight mRNAs which are translated into viral proteins in the cytoplasm. Progeny RNA genomes are synthesized in the nucleus. Assembly takes place in the cytoplasm and the progeny viruses are released from the cell by modifying the cell membrane to become their envelope as the neurominidase cleaves the neurominic acid on the cell surface. (Figure 2)

The infection is primarily limited to the respiratory tract because the proteases that cleave the hemagglutinin are located in this area. Symptoms of influenza can start one to two days after infection. Common symptoms include chills, fever, headache, myalgia and fatigue are the result of the huge amounts of proinflammatory cytokines and chemokines circulating in the blood. There is necrosis of the superficial layers of the respiratory epithelium. Pneumonia can complicate influenza.

With this new strain, children and young people are more likely to be more susceptible. At its

early course, the virus is behaving with moderate severity as if testing its powers. Cases of severe illness tend to occur in people with existing medical conditions and for reasons that are not yet understood, deaths are occuring in perfectly healthy young people. But as it will evolve later on into a more virulent strain, the clinical picture will remarkably change.

SPREADING GLOBAL VIGILANCE AND SOLIDARITY AGAINST THE SPREADING PANDEMIC

Multitude of lives were lost in previous influenza pandemics. Dealing with such loss puts strain in people's morale and results to social disruption. Lessons learned from those experiences prepares us for the present situation, as the global community defends its people from the impending battle.

The modern technologies we have today put us at an even more advantage. Communication speeds up dissemination of information across borders. Scientific investigations keeps us up to date

International concerted effort to curb the aftermath of this pandemic is underway. As the spread is already inevitable, strategic mitigation measures should be undertaken, like close monitoring of unusual clustering of severe respiratory illness, investigating increased absenteeism at workplaces and schools, public information drives geared towards personal hygiene and proper behavior to disrupt spread of infection like hand-washing, covering on mouth and nose when sneezing or coughing among other things, and promptly identifying the warning signs from people that needs urgent medical attention. Clinical trials for the new A (H1N1) flu vaccine has already began as the current flu vaccine in the market is ineffective against this new strain.

We at the medical and allied health frontline need to keep fit for the coming waves of people seeking treatment. Utilizing the clinical knowledge we have learned and updating our knowledge baseline can help us to cope up with the demands of the rising figures at the health care settings.

In her speech made during the high-level meeting on Influenza A (H1N1) in Mexico last 2nd of July, 2009, Dr. Margaret Chan, Director-General of World Health Organization, summed up that vigilance, collaboration and solidarity give us the upper hand in building the world's collective defenses against a threat common to all.

The world spreads unified consensus amidst the spreading pandemic: the health and lives of people are valuable. Lets take care of each other.

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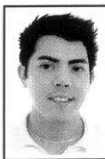

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Dr. Glenn Tzen M. Gloria is a Nurse and Physician. He is currently involved in Nursing Education, especially in Microbiology and Parasitology