

*Review Article*

## The H1N1 Influenza Pandemic: A Review of Recent Experience

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### Abstract

*The world has recently experienced a pandemic caused by a novel virus named H1N1. This antigenetically shifted virus spread to 213 countries through human to human transmission. In Bangladesh 899 cases were occurred. Therefore, a proper and clear insight is urgently required to prevent an outbreak in the future and make*

*preparations that may be planned well in advance. This review is an attempt to discuss the historical perspective of the swine flu virus, its epidemiology and route of transmission to better understand the various control measures that may be taken to fight the danger of another global pandemic.*

*Key words : H1N1, Pandemic*

### Introduction

The worldwide spread of a new deadly pathogen with sustained human-to-human transmission is one of the most concerned public health scenarios of today. As the first pandemic of the 21st century, the 2009 influenza A/H1N1 outbreak acts as an alert posed by emerging infectious diseases. As of 21 March 2010, worldwide more than 213 countries and overseas territories or communities have reported laboratory confirmed cases of pandemic influenza H1N1 2009, including at least 16931 deaths.<sup>1</sup> Influenza virus has the potential to cause widespread pandemics and it occurs when a new type of influenza strain appears in the human population, and spreads easily from person to person. The pandemic influenza is a new virus, and virtually everyone is susceptible to infection from it. It has affected a large number of countries globally, indicating that it is capable of causing large-scale pandemic destruction.<sup>2</sup> Bangladesh also could not escape from this recent occurrence.

### History

Influenza pandemics are unpredictable but recurring events that can have severe consequences on societies

worldwide. Since the 16th century, influenza pandemics have been described at intervals ranging between 10 and 50 years with varying severity and impact. Influenza virus is a common human pathogen that has caused serious respiratory illness and death over the past century. It was first described in the 1918 pandemic and made resurgence in April 2009 in the form of a triple-reassortant influenza A virus, which is composed of a combination of human, swine, and Eurasian avian strains.

In March of 2009 a novel strain of swine origin influenza A (H1N1) virus (S-OIV) was detected in Mexico. It has now spread to the rest of the world. With over 170,000 laboratory-confirmed cases worldwide, the World Health Organization (WHO) has declared a global pandemic.<sup>3,4</sup>

### *H1N1 influenza virus*

Many animal influenza viruses naturally infect and circulate among a variety of avian and mammalian species. Most of these animal influenza viruses do not normally infect humans. However, on occasion, certain animal viruses do infect humans. Such infections have most often occurred as sporadic or isolated infections or sometimes resulted in small clusters of human infections. An influenza pandemic occurs when an animal influenza virus to which most humans have no immunity acquires the ability to cause sustained chains of human-to-human transmission leading to community-wide outbreaks. Such a virus has the potential to spread worldwide, causing a pandemic. The development of an influenza pandemic can be considered the result of the transformation of an animal influenza virus into a human influenza

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**Table I**  
*The Influenza Pandemics occurred in the past*

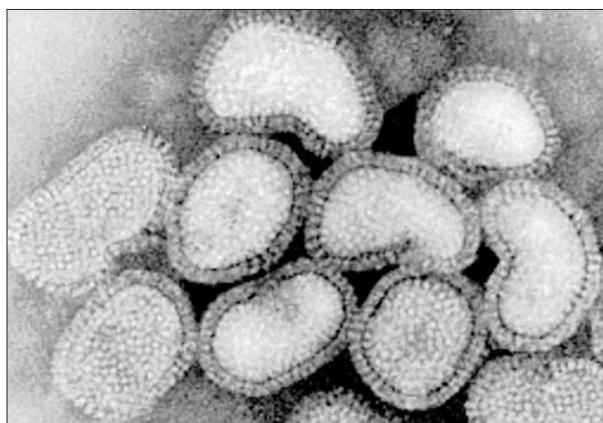
Common Name	Time Period Emergence	Area of Subtype	Influenza A Virus CFR	Estimated
"Spanish Flu"	1918-1919	Unclear	H1N1	2-3%
"Asian Flu"	1957-1958	Southern China	H2N2	<0.2%
"Hong Kong Flu"	1968-1969	Southern China	H3N2	<0.2%

Source: WHO<sup>3</sup>

virus. At the genetic level, pandemic influenza viruses may arise through:

**Genetic reassortment:** a process in which genes from animal and human influenza viruses mix together to create a human-animal influenza reassortant virus;

**Genetic mutation:** a process in which genes in an animal influenza virus change allowing the virus to infect humans and transmit easily among them.



*H1N1 virus*

Source: google/images

Swine flu virus, a respiratory virus initially known to cause infection in pigs, belongs to the Orthomyxoviridae family of viruses that include influenza A, influenza B, influenza C and thogotoviruses. Swine flu virus generally circulates throughout the year, but the disease mostly occurs during the late fall and early winter season. The most commonly circulating strains of swine flu virus isolated from pigs in the United States are H1N1, H1N2, H3N2 and H3N1, which belong to the influenza A subtype. In the past, the Centers for Disease Control and Prevention (CDC) have received reports of approximately one human swine influenza virus infection every one to two years in the United States but a sustained pattern of human to-human transmission has been seen to occur only recently.<sup>2</sup>

The place of origin of the virus is unknown. This is a new influenza A (H1N1) virus that has never before circulated among humans. This virus is not related to previous or current human seasonal influenza viruses. H1N1pdm (also referred to as S-OIV) is a newly emergent human influenza A virus that is closely related to a number of currently circulating pig viruses in the 'classic North American' and 'Eurasian' swine influenza virus lineages. To reveal the early molecular epidemiology of the H1N1pdm, particularly its spatial patterning and evolutionary dynamics, an evolutionary analysis on available genome sequence data sampled globally was performed.<sup>5</sup> The pandemic (H1N1) 2009 influenza virus differs in its pathogenicity from seasonal influenza in two key aspects. First, as the majority of human population has little or no pre-existing immunity to the virus, the impact of the infection has been in a wider age range, in particular among children and young adults. Secondly, the virus can infect the lower respiratory tract and cause rapidly progressive pneumonia especially in children and young to middle-aged adults.<sup>6</sup>

#### **Mode of transmission**

The virus is transmitted from person-to-person as easily as the normal seasonal flu and can be passed to other people by inhalation of infectious droplets and droplet nuclei, by direct contact, and possibly, by indirect (fomite) contact, with self inoculation on to the upper respiratory tract or conjunctival mucosa<sup>7-9</sup>. There are no known instances of people getting infected by exposure to pigs or other animals. The incubation period appears to be approximately 2-3 days, but could range up to 7 day.<sup>6</sup>

#### **The global scenario**

A novel influenza A (H1N1) virus of swine origin emerged among people in Mexico during the spring of 2009 and spread with travelers worldwide, resulting in the first influenza pandemic since 1968. On April 23, several cases of severe respiratory illness laboratory

confirmed as swine-origin influenza A (H1N1) virus (S-OIV) infection were communicated to the PAHO.<sup>10</sup>

On April 21, 2009, CDC reported that two recent cases of febrile respiratory illness in children in southern California had been caused by infection with genetically similar swine influenza A (H1N1) viruses. Neither child had known contact with pigs, resulting in concern that human-to-human transmission might have occurred.<sup>11</sup> Within two months, the virus quickly spread globally.<sup>7</sup> By the time WHO declared a pandemic in June 2009, a total of 74 countries and territories had reported laboratory confirmed infections. To date, most countries in the world have confirmed infections from the new virus.<sup>1</sup>

**Table II**  
*WHO pandemic phase description*

Phase	Description
Phase I	No animal influenza virus circulating among animals have been reported to cause human infections
Phase II	An animal influenza virus circulating in domesticated or wild animals is known to have caused human infections and is therefore considered a specific potential pandemic threats
Phase III	Animal or human-animal reassortant virus has caused sporadic cases or small clusters of diseases in people, but has not resulted in human-to-human transmission sufficient to sustain community-level outbreaks
Phase IV	Human-to-human transmission of an Animal or human-animal reassortant virus able to sustain community-level outbreaks has been verified
Phase V	The same identified virus has caused sustained community-level outbreaks in two or more countries in one WHO region
Phase VI	In addition to 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	Levels of influenza activity have returned to the levels seen for seasonal influenza in most countries with adequate surveillance

Source: WHO<sup>3</sup>

The H1N1 virus had caused significant outbreaks in most southern hemisphere countries between May and September 2009. As of early December 2009, it has been spreading in northern hemisphere countries. Overall pandemic influenza activity in the temperate northern hemisphere peaked between late October and late November 2009 and has continued to decline since.

In Europe, pandemic influenza virus transmission remains geographically widespread across parts of western, central, and southeastern Europe, however overall influenza activity continued to decline or remain low in most countries. The areas of most intense transmission currently include Poland, Austria, Estonia, Romania, Hungary, and Moldova; however, in all but Romania, ILI activity has declined significantly since peaking in November.

The most active areas of pandemic influenza virus transmission currently are in parts of Southeast Asia, West Africa, and in the tropical zone of the Americas. After a period of sustained pandemic influenza transmission in Thailand over the past two months, overall activity now appears to be decreasing. In West Africa, limited data suggests that active transmission of pandemic influenza virus persists without clear evidence of a peak in activity. In Central America and in the tropical zone of South America, an increasing trend of respiratory disease activity associated with circulation of pandemic influenza virus has been reported since early March 2010 in an increasing number of countries. Although pandemic influenza virus continues to be the predominant influenza virus circulating worldwide, seasonal influenza B viruses are predominate in East Asia, and have been increasingly detected at low levels across southeast and western Asia, eastern Africa, and in parts of Europe.

In Southeast Asia, pandemic influenza virus transmission has remained active and geographically widespread in Thailand since mid February 2010 and has been increasing since early March in Malaysia. In Thailand, the overall intensity of respiratory disease activity was reported to be low to moderate, and activity now appears to decreasing since mid March 2009; 10-22% of sentinel respiratory samples from patients with ILI tested positive for pandemic influenza during the most recent reporting week. In Malaysia, limited data suggests increasing detections of pandemic H1N1 cases over the past two weeks, although the extent and severity of illness is not

currently known. Low numbers of seasonal influenza B viruses continue to be isolated in Thailand and in other parts of Southeast Asia.

In Myanmar, respiratory disease activity may be declining after a period of increased activity associated with increased detection of pandemic H1N1 cases during February 2010. In South Asia, pandemic influenza virus transmission remains variable across the subcontinent. In Bangladesh, an increasing trend in respiratory disease activity and increasing detections of H1N1 cases has been reported since late February 2010; however, overall intensity of disease activity remains low. In India, although overall pandemic influenza activity remains low, pandemic H1N1 cases continue to be reported in Western India.<sup>1</sup>

The epidemiology of pandemic (H1N1) 2009 virus infection to date indicates that children and young adults have had the highest attack rates. A wide clinical spectrum of disease ranging from non-febrile, mild upper respiratory tract illness, febrile influenza like illness (ILI) to severe or even fatal complications, including rapidly progressive pneumonia has been described. Approximately 10-30% of hospitalized patients in some countries have required admission to intensive care units (ICU). Critically ill patients include those who experienced rapidly progressive lower respiratory tract disease, respiratory failure, and acute respiratory distress syndrome (ARDS) with refractory hypoxemia. On average, about 1/2 of hospitalized patients have had at least one or more underlying medical conditions. However, about 1/3 of patients with very severe illness admitted to ICU were previously healthy persons.

The case fatality rate (CFR) of pandemic H1N1 was initially estimated to be about 0.4%. However, the recent estimate is significantly lower than the initial estimate. Moreover, CFR appears to be different between countries. The Global Influenza Surveillance Network (GISN) continues monitoring the global circulation of influenza viruses, including pandemic, seasonal and other influenza viruses infecting, or with the potential to infect, humans including seasonal influenza.<sup>1</sup>

### **Bangladesh situation**

First case of Influenza A H1N1 (Swine Flu) was identified in Bangladesh on 18th June 2009. Since then Eight Hundred and ninety-nine (899) cases have been identified (as of 29-03-10). Six laboratory confirmed

patients have died.<sup>12</sup> It is mentioned earlier that an increasing trend in respiratory disease activity and increasing detections of H1N1 cases has been reported for about a month.<sup>1</sup>

### **Clinical management of H1N1 influenza**

Presentation of H1N1 influenza can vary from asymptomatic condition through various stages to serious complicated illness. Signs of the pandemic influenza are flu-like; the most commonly reported symptoms have included cough, fever, sore throat, muscle aches, malaise, and headache. Some patients have experienced gastrointestinal symptoms (nausea, vomiting, and/or diarrhoea).<sup>13</sup>

### **Case Definitions<sup>13,14</sup>**

#### **Category A: Uncomplicated influenza/ Influenza like illness**

- ILI symptoms include: fever, cough, sore throat, running nose, headache, muscle pain, and malaise, but no shortness of breath and no dyspnoea. Patients may present with some or all of these symptoms.
- Gastrointestinal illness may also be present, such as diarrhoea and/or vomiting, especially in children, but without evidence of dehydration. AND not in risk group

#### **Category B: Uncomplicated influenza/ Influenza like illness (ILI)**

Influenza like illness symptoms (as above)

AND in risk group

Risk group includes:

Infants and children (<5 years)

Elderly (> 65 years)

Pregnant women

Patients with chronic co-morbid conditions such as cardiovascular, renal, respiratory or liver disease, diabetes mellitus

Those with immunosuppression related to malignancy, chemo-therapy, organ transplant recipient, HIV infection etc

Obesity defined as a BMI >30

#### **Category C : Complicated or severe pandemic influenza/ severe acute respiratory illness (SARI)**

Beginning symptoms of ILI

Presenting with shortness of breath, dyspnoea, tachypnea, hypoxia)

And/or radiological signs of pneumonia),  
 Central nervous system (CNS) findings (e.g. encephalopathy),  
 Severe dehydration,  
 Renal failure,  
 Multi-organ dysfunction/failure,  
 Sepsis syndrome

Other complications can include musculoskeletal system (rhabdomyolysis) and cardiac (myocarditis) dysfunction.

- Any other condition or clinical presentation requiring hospital admission for clinical management.
- Any of the 'danger signs' of disease progression listed below.

#### *Signs and symptoms of progressive disease 'Danger signs'*

Patients who present initially with uncomplicated influenza may progress to more severe disease. Progression can be rapid (i.e. within 24 hours). The following are some of the indicators of progression, which would necessitate an urgent review of patient management:

- Symptoms and signs suggesting oxygen impairment or cardiopulmonary insufficiency:
    - Shortness of breath (with activity or at rest), difficulty in breathing, cyanosis haemoptysis, chest pain, and low blood pressure;
    - In children, fast or laboured breathing/ chest indrawing/stridor; and
    - Hypoxia (<90% on air), as indicated by pulse oximetry.
  - Symptoms and signs suggesting CNS complications:
    - Altered mental status (such as unconsciousness, confusion, drowsiness, or difficult to awaken
    - recurring or persistent convulsions (seizures),
    - severe weakness, or paralysis.
  - Evidence of invasive secondary bacterial infection
- Sepsis or organ specific infections
- Severe dehydration,

#### *Diagnosis*

Laboratory diagnosis of pandemic (H1N1) 2009 virus, especially at the beginning of a new community outbreak or for unusual cases, has important

implications for case management, such as infection control procedures, consideration of antiviral treatment options and avoiding the inappropriate use of antibiotics. Currently, the diagnostic tests can be done by specialized laboratories in many countries. Reverse transcriptase polymerase chain reaction (RT-PCR) will provide the most timely and sensitive detection of the infection.<sup>13</sup> Bangladesh is well capable of diagnosis of Influenza A H1N1 (swine influenza) at the laboratories of Institute of Epidemiology, Disease Control and Research (IEDCR) and ICDDRDB with RT-PCR to provide preliminary lab results within 24 hours.<sup>12</sup>

Clinical specimens to be collected for laboratory diagnosis are respiratory samples. Samples from the upper respiratory tract, including a combination of nasal or nasopharyngeal samples, and a throat swab are advised. Recent evidence supports viral replication and recovery of pandemic (H1N1) 2009 virus from lower respiratory tract samples (tracheal and bronchial aspirates) in patients presenting lower respiratory tract symptoms and in these patients, such samples have higher diagnostic yields than samples from the upper respiratory tract.

When influenza viruses are known to be circulating in a community, patients presenting with features of *uncomplicated influenza* can be diagnosed on clinical and epidemiological grounds. All patients should be instructed to return for follow-up, should they develop *any signs or symptoms of progressive disease or fail to improve within 72 hours of the onset of symptoms*.

Diagnostic testing, when available, should be prioritized for patients in whom confirmation of influenza virus infection may affect clinical management, including patients considered at-risk and/or those with complicated, severe, or progressive respiratory illness. In addition, results of diagnostic testing may also be valuable in guiding infection control practices and management of a patient's close contacts. However, laboratory test is not required to start antiviral treatment where indicated. *Under no circumstances should influenza diagnostic testing delay initiation of infection control practices or antiviral treatment, if pandemic (H1N1) 2009 disease is suspected clinically and epidemiologically*. Furthermore, the results of all diagnostic tests for influenza are dependent upon several factors, including specimen type, quality of specimen collection, and timing of collection, storage, and transport conditions. Deficiencies along this chain

can result in false negative results. When clinical suspicion is high, clinicians should consider repeat/serial testing.<sup>13</sup>

### Treatment

The majority of people with pandemic influenza experience mild illness without any need for medical care and recover fully without treatment<sup>13,15</sup>. To date, most people with pandemic (H1N1) 2009 virus infection have had self-limiting uncomplicated illness. Supportive care can be provided as needed, such as antipyretics (e.g. paracetamol or acetaminophen) for fever or pain and fluid rehydration. Salicylates (such as aspirin and aspirin-containing products) should NOT be used in children and young adults (aged <18 years) because of the risk of Reye's syndrome.<sup>13</sup>

Some patients need antiviral drug therapy and other supportive measures. Prompt empiric treatment is recommended for persons with suspected or confirmed influenza and illness requiring hospitalization, progressive, severe, or complicated illness, regardless of previous health status, and/or patients at risk for severe disease.<sup>16</sup>

Antiviral drugs: There are two approved antiviral drugs for treatment of pandemic influenza. These are the neuraminidase inhibitors oseltamivir and zanamivir.<sup>14, 16-18</sup>

There are different approaches for different category of patients for treatment. For patients with symptoms of severe illness, oseltamivir should be started immediately, no matter when the illness started and without waiting for laboratory results to confirm infection. For patients at higher risk for serious disease from pandemic influenza, treatment should be started with either oseltamivir or zanamivir as soon as possible after the onset of symptoms. People who are not from a higher risk group but who have persistent or rapidly worsening symptoms should be treated with antivirals. These symptoms include difficulty breathing or a high fever that lasts beyond three days.

In all cases, where oseltamivir is unavailable or cannot be used for any reason, zanamivir may be given. Antivirals should only be used when prescribed by a qualified health care provider, as they will be able to assess each situation and make the appropriate decisions on care.

For oseltamivir, the standard adult treatment course is one 75 mg capsule twice a day for five days. For

severe or prolonged illness, physicians may decide to use a higher dose or continue the treatment for longer. Consideration may be given to the use of higher doses up to 150 mg bid, and longer duration of treatment depending on clinical response (up to 10 days). This recommendation applies to all patient groups, including pregnant women, and young children <5 years, including neonates.

Zanamivir is taken as a powder by inhalation. The recommended dose for treatment of adults and children from the age of 5 years is two inhalations (2 x 5mg) twice daily for five days.

Reduction of dose of oseltamivir is recommended for person with creatinine clearance below 30ml/min. Immunoglobulin or other unapproved therapies, steroids should not be given. The dose and dosage of oseltamivir should be completed preferably supervised. Oseltamivir is a well tolerated medicine.

**Table III**

*Recommended dosage of Oseltamivir for treatment of H1N1 influenza*

Age group	Dose
<3 months	12 mg twice daily
3 to 5 months	20 mg twice daily
6 to 11 months	25 mg twice daily
1-12 years weight adjusted dose	30 mg twice daily for < 15 kg 45 mg twice daily for > 15 - 23kg 60 mg twice daily for >23-40 kg 75 mg twice daily for > 40 kg
Adult	75 mg twice daily

Source: WHO<sup>18</sup>, MOH&FW<sup>14</sup>

Occasional adverse effects include nausea, vomiting, abdominal pain, dyspepsia, diarrhoea, head ache, fatigue, insomnia, dizziness, conjunctivitis, epistaxis, rash etc. Rarely hypersensitivity reaction and very rarely acute hepatitis and Steven Johnson syndrome may occur.<sup>14</sup>

A third neuraminidase inhibitor peramivir formulated for intravenous (IV) administration is an investigational product currently being evaluated in clinical trials. Efficacy and safety have not been evaluated in hospitalized patients. Peramivir IV is available through the CDC upon request of a licensed

**Table IV**  
*H1N1 patient management protocol*

Category A	Category B	Category C
Home self isolation and social distancing till symptoms resolve (about 7 days)	Home self isolation and social distancing till symptoms resolve (about 7 days)	Patient should be managed at hospital
Supportive care (rest, adequate nutrition and oral fluid)	Supportive care (rest, adequate nutrition and oral fluid)	Antiviral (oseltamivir) drug
Paracetamol if needed (do not use Aspirin/NSAID)	Paracetamol if needed (do not use Aspirin/NSAID)	Other Supportive management including appropriate antibiotic
Antihistamine if needed	Antihistamine if needed	Some patients may require critical care; patient requiring ICU/HDU care should be transferred to a tertiary care hospital
Follow the instructions given by health care provider	Follow the instructions (Watch for danger sign)	
Respiratory etiquette	Respiratory etiquette	
No antiviral (oseltamivir) is recommended	Antiviral (oseltamivir) is recommended	

Source: MOH&FW<sup>14</sup>

physician.<sup>16</sup> In Bangladesh oseltamivir is the only antiviral recommended for five days treatment of H1N1 influenza.<sup>14</sup>

Patients may have co-infection with bacterial pathogens or other respiratory viruses; therefore, investigations and/or empiric therapy for other pathogens should also be considered. A decision to treat an influenza patient with antiviral medication should not preclude consideration of other infections and their treatment, especially those endemic febrile diseases with similar presentations (e.g. dengue, malaria).<sup>13</sup>

Hospitalized patients should be discharged if afebrile for > 24 hours, feel well, vital signs are stable, no respiratory distress for > 24 hours and chest findings are improved.<sup>14</sup>

#### ***Prevention and Control***

Resistance to oseltamivir has been increased worldwide.<sup>19-22</sup> So, prevention and control of this infection is important. To minimize exposure to infection is the key to control. For this, individuals and communities should take measures like social distancing, respiratory etiquette, hand hygiene, and household ventilation. These are the most feasible measures available to reduce or delay disease.<sup>23</sup>

At individual level it is advised to cover nose and mouth with a tissue/cloths during cough or sneeze and throw the tissue in the trash after use, washing hands often with soap and water, especially after coughing or sneezing (if soap and water are not available, use an alcohol-based hand rub and avoid touching eyes, nose or mouth, stay home if get sick and contact health care providers if there is fever with breathing difficulty.<sup>14, 24</sup>

People with exposure to an infected person and a higher risk of developing severe or complicated illness, should have to closely monitor for symptoms, followed by prompt early antiviral treatment if required<sup>25,26</sup>. In case of mild illness, patients should be provided with supportive care at home by a designated caregiver and only referred to health care facilities if they deteriorate or develop danger signs. Separation of sick from well individuals, with rigorous respiratory etiquette and hygiene measures should be practiced.<sup>23</sup> People with influenza-like illness should remain at home until at least 24 hours after they are free of fever (temperature of 100° F [37.8°C] or more), or signs of a fever without the use of fever-reducing medications<sup>24</sup>. In health-care settings, a system of triage, patient separation, prioritization of use of antiviral medicines and personal protective equipment (PPE) according to risk of exposure, and patient management should be in

place to focus efforts on the most effective interventions to reduce mortality and any further morbidity.<sup>23</sup>

### Chemoprophylaxis

Use of antiviral drugs for prevention of pandemic influenza is not recommended.<sup>14,25</sup> For individuals at very high risk like organ transplant recipients, AIDS and patients with immuno-suppression oseltamivir might be used as post exposure chemoprophylaxis.<sup>14</sup>

### Vaccination

CDC recommends influenza vaccination as the first and most important step in protecting against the flu.<sup>24</sup>

Health workers are given first priority for early vaccination to protect themselves and their patients. Other groups at higher risk for severe illness should also be considered as priorities. A single dose of vaccine is recommended in adults and adolescents from 10 years of age and above. Where national authorities have made children a priority for early vaccination, experts are advising one dose of vaccine to as many children as possible over the age of 6 months as and younger than 10 years of age. Recommendations on numbers of dosages may need to be adapted rapidly as new data emerges. National authorities will develop and implement vaccination plans based on circumstances within the country.<sup>27</sup>

CDC is encouraging anyone who wants to protect themselves against 2009 H1N1 to get vaccinated. The U.S. Food and Drug Administration (FDA) has approved the use of one dose of vaccine against 2009 H1N1 influenza virus for persons 10 years of age and older. For children who are 6 months through 9 years of age, two doses of the vaccine are recommended. These two doses should be separated by 4 weeks. Infants younger than 6 months of age are too young to get any influenza vaccine.<sup>24</sup>

There is shortage of vaccine supply worldwide. There is need for more effective newer vaccines. Fu-Shi Quan and et al generated influenza virus-like particles (VLPs) containing proteins derived from the A/California/04/2009 virus, and tested their efficacy as a vaccine in mice. A single intramuscular vaccination with VLPs provided complete protection against lethal

challenge. This study demonstrates that VLP vaccination provides highly effective protection against the 2009 pandemic influenza virus. The results indicate that VLPs can be developed into an effective vaccine, which can be rapidly produced and avoid the need to isolate high growth reassortants for egg-based production.<sup>28</sup>

**Table V**

*Country levels during pandemic*

Country Level	
Level 0	No lab Confirmed cases in Bangladesh
Level 1	When a single novel influenza lab confirmed case or very limited number of cases but no cluster is identified.
Level 2	When single or limited number of lab confirmed cluster are identified.
Level 3	When increased and substantial spread among general population.
Level 4	When pandemic wave is decreasing and/or a new wave of pandemic is arriving or detected.
Post Pandemic/ Recovery	When WHO declared the pandemic is over.

Source: IEDCR<sup>12</sup>

### Surveillance

IEDCR is National Influenza Center (NIC), Bangladesh nominated by WHO. Influenza surveillance is being conducted since 2007 in 12 hospitals covering all the 6 administrative divisions of the country. A community site is also functioning in Kamalapur, Dhaka since 2004. Since September 2009 DMCH and NIDCH has been included in sentinel surveillance This surveillance system is helping us to understand the spread and type of influenza virus circulating in this country.

The National Rapid Response Team (NRRRT) is under 7/24 alert and conducting investigation of reported cases of suspected Influenza A (H1N1).

The Civil Surgeons of all districts are directed by the Director General of Health Services to keep themselves prepared for tackling the situation. They are being updated regularly on Pandemic Influenza H1N1 2009.<sup>12</sup>

### Defining cluster

A cluster of pandemic influenza 2009 is defined as two or more suspect, probable or confirmed cases of pandemic influenza 2009 found at a time in a localized area, having evidence of transmission among them.

### Objective of defining cluster

1. Specimen from one or two persons will be tested
2. If found to be positive, other members of the cluster will be regarded as cases
3. Members of the cluster will be treated with Oseltamivir and other supportive treatment
4. Pharmaceutical and non pharmaceutical interventions will be under taken to limit the spread
5. Small cluster: <25
6. Large cluster: >25

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