Pandemic Influenza: Global and Philippine Situation

Beatriz Puzon-Quiambao, MD, FPPS, FPIDSP
Research Institute for Tropical Medicine

17th Annual PIDSP Convention, February 3-4, 2010
Chronology of Events

March-April, 2009

Outbreaks of ILI in Mexico

Same virus as the one isolated from children in California

April, 2009

Spread of virus all over Mexico and the US

Spread of virus to other countries
### Phases of WHO pandemic alert

<table>
<thead>
<tr>
<th>Phase</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase 1</td>
<td>No animal influenza virus circulating among animals have been reported to cause infections in humans</td>
</tr>
<tr>
<td>Phase 2</td>
<td>An animal influenza virus circulating in domesticated or wild animals is known to have caused infection in humans and is therefore considered a specific potential pandemic threat</td>
</tr>
<tr>
<td>Phase 3</td>
<td>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</td>
</tr>
<tr>
<td>Phase 4</td>
<td>Human-to-human of an animal or human-animal influenza reassortant virus able to sustain community level outbreaks has been verified</td>
</tr>
<tr>
<td>Phase 5</td>
<td>The same identified virus has caused sustained community level outbreaks in two or more countries in one WHO region</td>
</tr>
<tr>
<td>Phase 6</td>
<td>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</td>
</tr>
</tbody>
</table>

- **Nov, 2005**
- **April 27, 2009**
- **April 29, 2009**
- **June 11, 2009**
The pandemic has not ended
World Health Organization

Status as of: week 01, 2010 (28 December 2009–03 January 2010)

Timeline
Trend of respiratory disease activity
Compared to previous week

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* Trend refers to the change in the level of respiratory disease activity compared to the previous week.
Full genomic sequence
A/California/04/2009 A(H1N1)

Symptoms of Influenza:
- Central: Headache
- Systemic: Fever (usually high)
- Muscular: (Extreme) tiredness
- Joints: Aches
- Nasopharynx: Runny or stuffy nose
- Sore throat
- Aches
- Respiratory: Coughing
- Gastric: Vomiting

Transmitted by coughing, sneezing.
World Health Organization

Timeline (22 July 2009 onwards)
Pandemic (H1N1) 2009 laboratory confirmed cases
And number of deaths as reported to WHO

Status as of: 10 January 2010

Chinese Taipei has reported thirty-six deaths associated with pandemic (H1N1) 2009.
## Global situation
WHO update 85, 24 Jan 2010

<table>
<thead>
<tr>
<th>Region</th>
<th>Cumulative # of Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>South East Asia</td>
<td>1426</td>
</tr>
<tr>
<td>Western Pacific</td>
<td>1555</td>
</tr>
<tr>
<td>Eastern Mediterranean</td>
<td>1002</td>
</tr>
<tr>
<td>Africa</td>
<td>131</td>
</tr>
<tr>
<td>Americas</td>
<td>7166</td>
</tr>
<tr>
<td>Europe</td>
<td>3429</td>
</tr>
<tr>
<td>Global</td>
<td>14711 *</td>
</tr>
</tbody>
</table>

* The reported number of fatal cases is an under representation of the actual numbers as many deaths are never tested or recognized as influenza related.
Estimates

- US (April–July 2009) - Actual number of cases may have been up to 140× greater than the reported number of laboratory confirmed cases.
- Median multiplier of reported to estimated cases was 79: that is, every reported case of pandemic (H1N1) 2009 may represent 79 (range 47-148) total cases.
- Every hospitalized case of PI may represent a median of 2.7 total hospitalized persons (range 1.9–4.3).

Reed et al. EID Dec 2009
2009 H1N1 influenza virus is the predominant virus in circulation worldwide.

Influenza B 48.8%
**PHILIPPINES**

Specimens Tested for Pandemic H1N1
May 1, 2009 to January 15, 2010

<table>
<thead>
<tr>
<th>Result</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative</td>
<td>5224 (45.0)</td>
</tr>
<tr>
<td>Seasonal Influenza</td>
<td>521 (4.5)</td>
</tr>
<tr>
<td>Pandemic H1N1</td>
<td>5864 (50.5)</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td>11,618</td>
</tr>
</tbody>
</table>

92 % of all influenza isolates

Molecular Biology Laboratory (MBL), RITM
Sources:
Influenza Surveillance (data up to week 25)
RITM Molecular Biology Results for Pandemic H1N1 Tests
(data up to week 29)

Number of Specimen Positive for Influenza and Other Viruses,
January - July 2009

- Pandemic A(H1N1)
- Influenza A (Seasonal)
- Influenza A (Unsubtypeable)
- Influenza A (Not Subtyped)
- Influenza B
- Other Viruses
Number of Specimen Positive for Seasonal Influenza and Pandemic A(H1N1), RITM-MBL from May 1, 2009 to January 10, 2010

Note: RITM-NIC Lab did not perform Influenza A screening in weeks 25-26
Oseltamivir resistance

- WHO network of laboratories - viruses from all outbreaks remain virtually identical
  - no signs that the virus has mutated to a more virulent or lethal form
- Only a handful of pandemic viruses resistant to oseltamivir have been detected worldwide, despite the administration of many millions of treatment courses of antiviral drugs
  - No instances of onward transmission of drug-resistant virus have been documented to date
  - Intense monitoring continues through the WHO network of laboratories
Clinical Characteristics

- Clinical picture - consistent across all countries
  - Majority of patients continue to experience mild illness
  - Although the virus can cause very severe and fatal illness, also in young and healthy people, the number of such cases remains small

WPRO update, 11 Jan 2010

- “moderate” severity - majority of patients recovering, even without medical treatment, within a week of the onset of Sx

PAHO regional update, 11 Jan 2010
Clinical Characteristics

• Teenagers & young adults = majority of cases
  • Nearly 80% of all cases are < 30 years of age
  • hospitalization rates highest in very young children
• hospitalization – 1 to 10 %
  • 10% to 25% require ICU admission
  • 2% to 9% have a fatal outcome
• 7% to 10% pregnant women in 2\textsuperscript{nd} or 3\textsuperscript{rd} trimester
  • Pregnant women are 10x more likely to need ICU care compared with the general population
Clinical Characteristics

• As much as 41% did not fulfil the case definition for probable case
  • 19% did not have fever > 38°C or Hx of fever
• ICU care – 7-19%
  • 13% required mechanical ventilation
• Death – 5% due to refractory hypoxemia
• Pre-existing conditions – 32-40%
• Bacterial co infection – 10-16%
• Viral co infection – 19%
  • Those with concomitant viral infection were younger

Hackett et al, Lancet, Aug 09
Libster et al, NEJM, Jan 2010
## Comparison with seasonal flu

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Seasonal Flu</th>
<th>Pandemic Flu</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seasonality</td>
<td>winter</td>
<td>Summer and winter</td>
</tr>
<tr>
<td>Mean age</td>
<td>53 yrs (1-75 yrs)</td>
<td>21 yrs (2-63 yrs)</td>
</tr>
<tr>
<td>Severe cases</td>
<td>90 % in adults &gt; 65 yrs</td>
<td>Children &lt; 5 yrs, adults &lt; 50 yrs</td>
</tr>
<tr>
<td>Risk factors</td>
<td>Pregnancy, underlying diseases, extremes of age</td>
<td>Pregnancy, underlying diseases, Obesity</td>
</tr>
<tr>
<td>GI symptoms</td>
<td>5 %</td>
<td>25 % diarrhea, 33 % nausea/ vomiting</td>
</tr>
<tr>
<td>Bacterial co-infection</td>
<td>24 %</td>
<td>4 %</td>
</tr>
</tbody>
</table>

California Pandemic (H1N1) working group, JAMA Kelly H, Grant K. Euro Surveill, Aug 2009
## Comparison with seasonal flu

<table>
<thead>
<tr>
<th>Characteristics in CHILDREN</th>
<th>Seasonal Flu (US)</th>
<th>Pandemic Influenza (B. Aires)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospitalization rate</td>
<td>10.3/100,000</td>
<td>20.9/100,000</td>
</tr>
<tr>
<td>Death rate</td>
<td>0.2/100,000</td>
<td>7.6/100,000</td>
</tr>
<tr>
<td>Co infection with RSV</td>
<td>11 %</td>
<td>19 %</td>
</tr>
<tr>
<td>ICU admission</td>
<td>5 %</td>
<td>19 %</td>
</tr>
<tr>
<td>Oxygen supplementation</td>
<td>22%</td>
<td>82 %</td>
</tr>
<tr>
<td>Mechanical ventilation</td>
<td>0</td>
<td>17 %</td>
</tr>
</tbody>
</table>

Libster et al, NEJM 362 (1): 45-55, Jan 2010
Risk factors

• The groups experiencing severe disease and requiring hospitalization the most are:
  • young children (younger two years of age)
  • people with chronic underlying medical conditions, e.g. asthma or other chronic respiratory disease (33% vs 13%)
  • massive obesity (BMI > 35) - 29% vs 5%
  • pregnant women (9% vs 1%),

Napolitano et al, MMWR, July 2009
Risk factors

Age and gender distribution of deaths

14 % of all pandemic H1N1 related deaths in the US occurred among children < 18 yrs

Vaillant et al, Eurosurveillance Aug 2009

CDC, Jan 22, 2010 update
Risk factors

• Underlying illnesses
  • Of 241 deaths, 90% had underlying disease
  • 27% of children and 20% of young adults had no underlying disease

Vaillant et al, Eurosurveillance Aug 2009
Risk factors

• Obesity (BMI > 30)
  • Most frequently identified underlying condition
  • 9/10 severely ill patients with H1N1 infection needing ventilatory support were obese
    • 7 were severely obese
    • 9 had multi-organ dysfunction
    • 5 had pulmonary emboli
  • 2/3 deaths were obese
  • Obese are more likely to have underlying medical conditions

Napolitano et al, MMWR, July 2009
Risk factors

- Pregnancy
  - 4x more likely to need admission
  - Shortness of breath 2.3x more common
  - Of 45 deaths in the 1st 2 months of the outbreak in the US, 6 (13%) were pregnant
    - All developed viral pneumonia and ARDS
    - None received anti-virals within 48 hrs of Sx onset

Jamieson et al. Lancet 2009
Risk factors

- Minority populations
  - Hospitalization rates for the pandemic (H1N1) 2009 virus in Wisconsin
    - non-Hispanic whites – 11 per 100,000 population
    - Blacks - almost 38 per 100,000 population
    - Hispanics - > 320 per 100,000 population
  - Reasons - higher rates for some of the underlying medical conditions (DM, CV disease, obesity), poorer access to health care

Milwaukee Wisconsin Journal sentinel, Jan 2010
Influenza-like Illness surveillance

- H1N1 integrated in national ILI surveillance
- 73,341 ILI cases from Jan 1 to Nov 9, 2009
  - peak of activity on wks 25-28, decreased activity noted by wk 29
  - Median age 11 yrs (1-109 yrs)
    - 19 % in 1-4 yr old age group
    - 51 % males
  - 161 deaths (CFR 0.2 %)
- 7.5 % due to H1N1
  - Increase by wk 22, peak on wk 25 and decline by wk 26
  - 32 deaths (CFR 0.6 %)

44th Disease Surveillance Report, NEC, Nov 2009
11,645 have been tested for A(H1N1)  
5784 PCR positive (50%)  

Number of Specimen Positive for Pandemic A(H1N1), RITM-MBL,  
May 1, 2009 to January 9, 2010
Number of Specimen Positive for Pandemic A(H1N1)
According to Island Group,
RITM-MBL, May 1, 2009 to January 10, 2010

MINDANAO

VISAYAS

LUZON

NCR

<table>
<thead>
<tr>
<th>Month</th>
<th>MINDANAO</th>
<th>VISAYAS</th>
<th>LUZON</th>
<th>NCR</th>
</tr>
</thead>
<tbody>
<tr>
<td>May</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>June</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>July</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>August</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Sep</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Oct</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Nov</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Dec</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

(Continue table with data for each month from May to January 2010)
Age and Sex Distribution of Patients Positive for Pan A(H1N1), RITM-MBL, May 1, 2009 to January 10, 2010

60.7% below 18 yrs

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1 yrs</td>
<td>0.32</td>
<td>0.41</td>
</tr>
<tr>
<td>1-5 yrs</td>
<td>3.61</td>
<td>5.06</td>
</tr>
<tr>
<td>6-14 yrs</td>
<td>29.19</td>
<td>32.70</td>
</tr>
<tr>
<td>15-19 yrs</td>
<td>25.23</td>
<td>25.96</td>
</tr>
<tr>
<td>20-29 yrs</td>
<td>19.96</td>
<td>17.04</td>
</tr>
<tr>
<td>30-39 yrs</td>
<td>6.86</td>
<td>6.92</td>
</tr>
<tr>
<td>40-49 yrs</td>
<td>4.56</td>
<td>3.55</td>
</tr>
<tr>
<td>50-59 yrs</td>
<td>4.39</td>
<td>2.41</td>
</tr>
<tr>
<td>60-69 yrs</td>
<td>0.64</td>
<td>0.55</td>
</tr>
<tr>
<td>70-79 yrs</td>
<td>0.35</td>
<td>0.31</td>
</tr>
<tr>
<td>&gt;80 yrs</td>
<td>0.07</td>
<td>0.10</td>
</tr>
<tr>
<td>Missing</td>
<td>4.81</td>
<td>4.99</td>
</tr>
</tbody>
</table>
### Clinical Manifestations

<table>
<thead>
<tr>
<th>SYMPTOM</th>
<th>NEGATIVE N(%), where N=5389</th>
<th>POSITIVE N(%), where N=5451</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>4494</td>
<td>4847*</td>
</tr>
<tr>
<td>Cough</td>
<td>4130</td>
<td>4615*</td>
</tr>
<tr>
<td>Sore throat</td>
<td>2557</td>
<td>2727*</td>
</tr>
<tr>
<td>Runny nose</td>
<td>2374</td>
<td>2626*</td>
</tr>
<tr>
<td>Muscle pain</td>
<td>1251</td>
<td>1488*</td>
</tr>
<tr>
<td>Headache</td>
<td>971</td>
<td>1043</td>
</tr>
<tr>
<td>Body pain</td>
<td>634</td>
<td>702</td>
</tr>
<tr>
<td>Difficulty of Breathing</td>
<td>190</td>
<td>212</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>239</td>
<td>230</td>
</tr>
<tr>
<td>No symptom at all</td>
<td>109*</td>
<td>80</td>
</tr>
</tbody>
</table>

* Significantly higher (p<0.05, Binomial test)
Mortalities

- As of Nov 2009, 32 deaths
- Analysis of 1st 29 deaths:
  - Age range – 10 days to 77 yrs
    - 17% below 5 years old, 10% elderly
    - 59% between 20 to 59 yrs
  - 66% females
  - 52% had co-morbid conditions; 2 were pregnant
  - 1 with Hx of travel, 2 with contact to a known case
  - 2 had seasonal flu vaccine

National Epidemiology Center, DOH
Pediatric Mortalities

- 9/29 (31%) were children < 18 yrs
  - Age range – 10 days to 17 yrs
  - 3 M (33%), 6 F (67%)
- Symptoms
  - Fever 89%; Cough 78%; Colds 33%; Vomiting 33%; Sore throat 22%; Difficulty of breathing 22%
- Duration of illness – ave 14 days (range 4 days to 5wks)
- Duration of illness upon consult – ave 4.7 days (range 0 to 14 days)
- Underlying illnesses – seizure disorder, asthma, toxic goiter
- Cause of death – sepsis, pneumonia

National Epidemiology Center, DOH
**Molecular epidemiology**

- Preliminary results show that Philippine Pdm H1N1 isolates belong to Clade 7, with other isolates possible belonging to new clades

**Oseltamivir resistance**

- Mutations associated with resistance have not been detected
- D225G change noted in Norway was not detected in Philippine isolates

Mercado et al, RITM-Tohoku flu project
DOH response

• PANDEMIC declared - Can no longer prevent the spread of infection
• June 24, 2009: Shifted from Rapid containment (case finding and contact tracing) ↦ mitigation (care of sick individuals)
  • Selective admission, laboratory confirmation and anti-viral treatment
  • Home quarantine for all uncomplicated cases
Preparing for the 2nd wave

- Health facility development
  - Referral hospitals - RITM, SLH, LCP, VSMC, DMC
- Laboratory upgrade
  - RITM – national reference laboratory
  - SLH, LCP, Med City, Baguio GH, Vicente Sotto MC, Davao MC
- Expansion of ILI surveillance
  - 2005 - 17 sentinel sites in 4 regions (5 hosp, 12 HC)
  - 2007 – 29 sites in 9 regions
  - 2009 - 53 sites in 2009 in 9 regions (20 hosp, 33 HC)
Preparing for the 2nd wave

- Development of Interim guidelines 1-22
  - IG 22: Clinical management of suspected and confirmed Human Pandemic (H1N1) 2009 infection
- IG 2: Infection control
- Vaccination with H1N1 vaccine
Thank you

PANDEMIC

Thank you
History of the Outbreak

• March - early April 2009
  • outbreaks of respiratory illness and increased reports of patients with ILI in several areas of Mexico
  • April 12 - outbreak of ILI in a small community in the state of Veracruz reported to PAHO in accordance with International Health Regulations
  • April 17 - a case of atypical pneumonia in Oaxaca State prompted enhanced surveillance throughout Mexico
  • 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
  • Sequence analysis revealed that the patients were infected with the same S-OIV strain detected in two children residing in California
History of the Outbreak

• USA
  • April 24, 2009 - CDC reported 8 confirmed cases of S-OIV infection in Texas and California
  • The strain identified in U.S. patients was genetically similar to viruses subsequently isolated from patients in Mexico
  • April 28 - approximately half of all U.S. cases of S-OIV infection had been confirmed among students and staff members at a New York City (NYC) high school