Recent experience to pandemic A(H1N1)2009 in Japan and collaboration with Asia

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Surveillance system for influenza in Japan

- Pre-existing system
  - Sentinel surveillance system for ILI:
    - January 1987-
    - year-round, weekly report
    - clinically diagnosed / lab-confirmed
    - sentinel sites: 5,000 (including 3,000 pediatric clinic/hospital)
  - Sentinel influenza virus surveillance
    - 1973-
    - year-round, daily report
    - monitor the virological feature for vaccine
Surveillance system for influenza in Japan, Pre-existing system-cont’d

- School absentee reporting system for ILI
  - 1973-
  - Late Oct – Mid July (about 40 – 30 epi wk)
  - day-care center, Kindergarten, elementary and middle high school
  - school should report the number of absentees and closed classes
  - local health care center should take samples from the cluster(s) of absentee in a flu-season for laboratory test
Surveillance system for A(H1N1)2009 in Japan

- Case-based surveillance
  - 28 April - 23 July
  - Lab-confirmed cases
  - Daily report by fax
  - Case definition:
    - **suspected case** of influenza A(H1N1)v virus infection is defined as a person with high fever (>38°C) OR at least two acute respiratory symptoms (nasal obstruction/rhinorrhea, sore throat, cough, fever/feverishness) AND who meets at least one of the following criteria:
      a) within the last seven days returned from a country or region with an epidemic of influenza A(H1N1)v;
      b) was in close contact (within two meters) with a confirmed case within the past seven days;
      c) handled samples suspected of containing influenza A(H1N1)v virus in a laboratory or other setting within the past seven days;

- **confirmed case** of influenza A(H1N1)v virus infection is defined as a person with high fever (>38°C) OR at least two acute respiratory symptoms (nasal obstruction/rhinorrhea, sore throat, cough, fever/feverishness) AND influenza A(H1N1)v virus infection that has been laboratory confirmed by real-time PCR and/or viral isolation.
Timeline of situation of A(H1N1)2009 in Japan

WHO declared the emergence of the novel flu
- Japanese gov’t: launched case-based surveillance for novel flu and strengthened quarantine to travelers from affected areas

2009
25 Apr

Notification about Swine flu

28

29
(5 May)

9 May

1st cases: travelers returned from Canada

1st domestic case

13 June

Outbreaks among several schools

16 May

Ceased strengthened quarantine

16 July

Shifted to cluster surveillance and hospitalized-case surveillance

27 July

Expanded School absentee reporting system

15 Aug

1st fatal case

Extensive school closure:
over 4,200 schools w/ 650,000 children/students

13

27

All 47 prefectures reported cases

15

Prime for RT-PCR became available
Reported cases w/ A(H1N1)2009, 28 Apr-23 July
(n=4,496*)
(By case-based surveillance; *Cases the data of onset available)
Effectiveness of school closures in Osaka and Kobe
ILI cases from sentinel sites:
Sentinel surveillance from 5,000 sites
Number of ILI cases/sentinel/week in Japan (from 2000 to 2010)

Lower peak, and highest number of ILR patients, in 2009

2000~2010, week 13 (upto April 4, 2010)
Geographical spread of A(H1N1)2009 during Aug. to Nov.
### Reported and estimated No. of patients

<table>
<thead>
<tr>
<th>Year</th>
<th>Reported ILI</th>
<th>Total estimated ILI</th>
</tr>
</thead>
<tbody>
<tr>
<td>2003-04</td>
<td>0.77 million</td>
<td>9.23 m</td>
</tr>
<tr>
<td>2004-05</td>
<td>1.5 m</td>
<td>17.70 m</td>
</tr>
</tbody>
</table>

**2009.29w～2010.13w (by H1N1pdm)**

- Estimated ILI cases: 20.7m
- (infection rate per population: 15.1%)

**at 30 March**

- Confirmed Admitted patients No.: 17,646
- with underlying diseases: 6,599
- in ICU: 1,022
- pregnant women: 74
- Influenza encephalopathy: 543
- Fatal case No.: 171

*Japanese population 130 m*
Age distribution of ILI（2009.28w～2010.10w）

Estimated total ILI = 20.7m

インフルエンザ推計受診患者数年齢群別推移（2009年第28週～2010年第10週）単位：万人

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>0～4 years</td>
<td>229</td>
<td></td>
</tr>
<tr>
<td>5～9 years</td>
<td>520</td>
<td></td>
</tr>
<tr>
<td>10～14 years</td>
<td>476</td>
<td></td>
</tr>
<tr>
<td>15～19 years</td>
<td>280</td>
<td></td>
</tr>
<tr>
<td>20～29 years</td>
<td>219</td>
<td></td>
</tr>
<tr>
<td>30～39 years</td>
<td>155</td>
<td></td>
</tr>
<tr>
<td>40～49 years</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>50～59 years</td>
<td>47</td>
<td></td>
</tr>
<tr>
<td>60～69 years</td>
<td>17</td>
<td></td>
</tr>
<tr>
<td>70 years and over</td>
<td>15</td>
<td></td>
</tr>
</tbody>
</table>

男, 1066, 51.6%
女, 1000, 48.4%
Age distribution of admitted patients

新型インフルエンザ入院例年齢群別グラフ（2009年11月3日まで）

2009年11月3日現在
Age distribution for fatal cases of PI

![Age distribution for fatal cases of PI](image)

With underling diseases

2010年3月16日現在
Mortality rate of PI among 100,000 population in several counties

<table>
<thead>
<tr>
<th>Date collected date</th>
<th>US</th>
<th>Canada</th>
<th>Mexico</th>
<th>Australia</th>
<th>UK</th>
<th>France</th>
<th>NZ</th>
<th>Japan</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death case No.</td>
<td>Estimate 12,000</td>
<td>429</td>
<td>1,111</td>
<td>191</td>
<td>457</td>
<td>309</td>
<td>20</td>
<td>198</td>
</tr>
<tr>
<td>Mortality rate</td>
<td>(3.96)</td>
<td>1.32</td>
<td>1.05</td>
<td>0.93</td>
<td>0.76</td>
<td>0.50</td>
<td>0.48</td>
<td>0.15</td>
</tr>
</tbody>
</table>

Infection rate: 15~17% in all countries

※尚、各国の死亡数に関してはそれぞれ定義が異なり、一義的に比較対象とならないことに留意が必要。
Influenza-associated encephalopathy in Japan, week 1-45, 2009

Number of reported cases of influenza per sentinel sites

*including both lab-confirmed and clinically diagnosed cases
Age distribution of influenza-associated encephalopathy in Japan, week 28-45, 2009
Concluding Observations

• This pandemic's overall impact is mild, fortunately.
• Patient number is estimated as 15% of population, however mortality rate is very low (0.15/100,000 population), in Japan.

• The global and domestic context is becoming increasingly complex & unforgiving and handling future pandemics & global public health events will become more challenging
  – Where are the main gaps?
  – How do we become better prepared & more flexible?
  – How do we respond more effectively?

• Influenza (not only pandemic) surveillance and control measure should be strengthen more
Influenza virus surveillance
Role and International Cooperation between NIID and Neighboring Asian Countries

Influenza Virus Research Center at NIID & WHO CC on Influenza (Tokyo Center)
- Surveillance kit (Ref viruses, antisera)
- Tech Supports (Manuals, Reagents)
- Sending staff for training of lab staff
- Host for Tech WS

National Influenza Centers (NICs)
(Korea, China, Taiwan, Myanmar, Laos, Mongolia, Singapore, Vietnam)
- Outbreak information
- Virus isolates and specimens
- Sending staff to attend T-WS

WHO CCs
- WHO HQ

Analyzed Data
- NIID-WG for Vaccine strain selection

MOH, Japan
- Local Governments
- Vaccine Manufacturers
- Public

Vaccine strain selection for Northern & Southern Hems
Preparation of Guidelines
Vaccine Manufacturers
Public (Global)
## Development of H1pdm detection system

<table>
<thead>
<tr>
<th>Date</th>
<th>Events</th>
</tr>
</thead>
<tbody>
<tr>
<td>24. Apr</td>
<td>The sequence of H1N1 pdm virus was disclosed by CDC USA</td>
</tr>
<tr>
<td>25. Apr</td>
<td>Primers and probes for conv. and real-time RT-PCR were designed by NIID</td>
</tr>
<tr>
<td>27. Apr</td>
<td>Primers and probes were obtained</td>
</tr>
<tr>
<td>28. Apr</td>
<td>Primers and probes were obtained</td>
</tr>
<tr>
<td>29. Apr</td>
<td>Usefulness of our detection system using swine Flu (H1N2) virus was verified</td>
</tr>
<tr>
<td>30. Apr</td>
<td>Regents, positive control RNA(swine H1N2), primers and probes were provided to 76 Local Institutes of Health and 15 Quarantines in Japan</td>
</tr>
<tr>
<td>2. May</td>
<td>A/California/4/2009 (H1N1) pdm virus was sent from CDC</td>
</tr>
<tr>
<td>3. May</td>
<td>Our detection system using H1N1 pdm virus was validated</td>
</tr>
<tr>
<td>~ 5. May</td>
<td>H1N1 pdm diagnosis system was established in all Local Institutes of Health and Quarantines</td>
</tr>
<tr>
<td>6. May</td>
<td>The information of our detection system was reported to the WHO (Published on 21. May)</td>
</tr>
<tr>
<td>8. May</td>
<td>The first case traveled in Canada was detected in Narita Airport Quarantine</td>
</tr>
<tr>
<td>13. May</td>
<td>The information of our detection system was reported to the ASEAN</td>
</tr>
<tr>
<td>16. May</td>
<td>The first case with no travel history was detected in Kobe city</td>
</tr>
</tbody>
</table>
Local Institutes of Health and Quarantine Laboratory in Japan

- Local Institutes of Health: 76 places
- Quarantine Laboratory: 15 places

NIID
Influenza virus detected in Local Pub Health Lab (2008 36w~2010 15w), in Japan
Influenza virus isolation, wk28, 2008～wk47, 2009
OTV resistant- H1N1pdm viruses
(as of April 2010)
67 Resistant / 5422 tested (1.2%)
All were sensitive to zanamivir

<table>
<thead>
<tr>
<th>Country</th>
<th>H3N2 Resistant (Outlier)</th>
<th>B Resistant (Outlier)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=</td>
<td>Zana</td>
</tr>
<tr>
<td>Japan</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>China</td>
<td>12</td>
<td>1</td>
</tr>
<tr>
<td>Taiwan</td>
<td>30</td>
<td>1</td>
</tr>
<tr>
<td>Korea</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Laos</td>
<td>9</td>
<td>0</td>
</tr>
<tr>
<td>Mongolia</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Myanmar</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>57</td>
<td>2</td>
</tr>
</tbody>
</table>
Training on Laboratory Diagnosis of Influenza including H1N1 Pandemic virus
Tokyo, Japan
1-2 September 2009

Information Note

This information note aims to provide logistical and administrative guidance to the participants of the training. Please take note of the following information to ensure a worry-free and prompt arrival at the training venue.

Training Venue and Contact Details
The Training on Laboratory Diagnosis of Influenza including H1N1 Pandemic Virus will be held at the Murayama branch of National Institute of Infectious Diseases of Japan in Tokyo. The training will be for a period of 2 days, 1-2 September 2009.
Training on laboratory diagnosis

Participants; Brunei, Cambodia, Indonesia, Lao PDR, Malaysia, Philippines, Singapore, Thailand, Vietnam

Training and lecture;
PT-PCR, Real time PCR, Sequencing(lecture)

Reagents provided;
● RNase Inhibitor (Appliedbiosystems)
● QuantiTect Probe RT-PCR Kit (QIAGEN)
● TaqMan MGB Probe and primers for real-time RT-PCR
  Type A detection, H1 pdm detection
● Primers for conventional RT-PCR
  Type A detection, H1 pdm detection, H1(seasonal) detection
  H3(seasonal) detection
● Control RNA (A/Narita/1/2009(H1N1pdm)
Time of virus introduced in Japan, which was analyzed from the genome evolution


Sapporo | Iwate | Akita | Fukushima | Niigata | Utsunomiya | Tochigi | Saitama | Narita | Chiba | Yokohama | Kanagawa | Shizuoka | Nagano | Aichi | Mie | Gifu | Shiga | Wakayama | Osaka | Sakai | Amagasaki | Kobe | Hyogo | Himeji | Tokushima | Hiroshima | Yamaguchi | Fukuoka | Kagoshima | Okinawa

Extensive school closure
Conclusion

1) Rapid development of new virus detection methods is required especially in the WHO CC on influenza

2) Technical transfer and sharing of information among countries are very important to control the spreading of diseases

3) Characterization of virus genomes will tell us the evolitional steps of virus and may explain the effectiveness of countermeasures to the influenza isolation
Rapid detection of pathogens emerging in Asia and prevention of their spreading

Target pathogens;
Bacteria (Enteric bacteria)
Virus (Dengue fever virus, JE)
Parasites (Malaria etc.)

1) Standardization of protocol for the detection of pathogens and genotyping
2) Quality control, validation of the protocol
3) Construction of database
4) Exchange of information and researchers