Country perspectives: experiences on pandemic H1N1 vaccine and seasonal influenza vaccine usage in China

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Outline

• Pandemic H1N1 influenza vaccination
  – Vaccine clinical trials
  – Vaccination program
  – AEFI surveillance
  – Vaccine effectiveness

• Influenza vaccine production capacity

• GAPs and Plans
## Timeline of H1N1pdm response in China

<table>
<thead>
<tr>
<th>Date</th>
<th>Responding actions</th>
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<tr>
<td>April 27, 2009</td>
<td>The response planning committee was set up</td>
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<td>April 30, 2009</td>
<td>H1N1 was categorized as a notifiable and quarantinable disease</td>
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<td>May 2, 2009</td>
<td>Developed real-time PCR diagnostic kits for the H1N1 virus</td>
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<td>May 11, 2009</td>
<td>First imported case confirmed</td>
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<td>June 18, 2009</td>
<td>First school outbreak reported</td>
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<td>July 8, 2009</td>
<td>Adjustment of control strategy, from containment to mitigation</td>
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<td>July 10, 2009</td>
<td>H1N1 was removed from the list of quarantinable diseases</td>
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<td>July 22, 2009</td>
<td>Initiated the multi-center clinical trials for H1N1 vaccine</td>
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<td>August 21-22, 2009</td>
<td>Organized the International Scientific Symposium on Influenza Pandemic Response and</td>
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<td>Preparedness associated with WHO</td>
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<td>August 23, 2009</td>
<td>SFDA approved the H1N1 vaccine</td>
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<td>September 21, 2009</td>
<td>The first public H1N1 vaccination occurred</td>
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<tr>
<td>January 11-17, 2010</td>
<td>H1N1 began to be overtaken by influenza B as the dominant virus</td>
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Epicurve of H1N1pdm cases in China

- May 11, First imported case
- June 18, School outbreak
- July 8, Adjustment of the measures for prevention and control
- July 10 - Aug. 31, Summer holidays
- Sep. 1 Term began
- Sep 30, 2nd version of surveillance protocol released
- Oct 1st - 8th, National Day vacation
- H1N1 was overtaken by type B influenza as the dominant circulating seasonal influenza virus in China
Timeline of H1N1pdm vaccine development

- **June 3**: Vaccine developed by manufactures
- **July 22**: Clinical trials conducted
- **Aug 23**: SFDA approval
- **Sep 21**: Vaccination

Day 0  Day 49  Day 81  Day 110
Vaccine Clinical Trials

Organized by China CDC
Clinical trials for persons aged >3 years

- Multicentre, double-blinded, randomized, placebo-controlled
  - Targeting those aged > 3 years
  - 10 manufacturers, 12,691 volunteers
- Safety in all vaccine formulations
  - Well tolerated without immediate serious adverse events
- Effective among both 15µg and 30µg groups using split vaccine without adjuvant.
  - Seroconversion and protective rates were >85%
- One dose of 15µg recommended

Long-term Observation of H1N1pdm Vaccines

- Shanghai institute of biological products
- Participants: 480 adults aged 18-60 years old
- Procedure: One dose, 15 μg, 30 μg or 45 μg H1N1pdm vaccine or placebo
- Safety monitoring:
  - 30mins, 6h, 24h, 48h, 72h after receipt
  - Long-term observation till 6
- Immunogenicity assessment
  - Blood collection on day 0, 28, 90, 180
Summary of long-term observation of H1N1pdm Vaccines

- One dose of split-virion vaccine containing 15 μg, 30 μg or 45 μg HI induced strong immune response respectively.

- Antibody levels peaked at Day 28, declined at Day 90.

The titer of antibodies remains a high levels status till Day 180.
Clinical trials for children aged 6-35 months

• Double-blinded, randomized, controlled trial, Dec 2009
• 300 children aged 6-35 months per sites, three sites
• 2 doses (Day 0, Day 21)
• Group
  • 7.5 μg H1N1 non-adjuvant vaccine (120 participants per sites)
  • 15 μg H1N1 non-adjuvant vaccine (120 participants per sites)
• Placebo: Seasonal Influenza (60 participants per sites)
• Blood samples collected at Day 0, 21, 42
• Safety monitoring
• Active surveillance at 30 min, 6h, 24h, 48h, 72h after every dose, all adverse events reported within 4-21 days
Findings- clinical trial for 6-35 moths children

- Seroconversion rate was >40% among both 7.5µg and 15µg group after 2 doses, and protective rate was >70%
- Neither 7.5µg nor 15µg after 1 dose among 6-35 months aged children could induce seroprotection rate >70%
- The AEs occurrence rate of H1N1pdm vaccine was similar with seasonal influenza vaccine
Vaccination Program
China’s Immunization Strategy

- Informed consent; voluntary; free of charge
- Government provided vaccine and operational costs

☆ 15 Sept 2009 High priority populations aged ≥3 years:
  1. Public service staffs in key positions (e.g., health staff)
  2. Students and teachers
  3. Chronic disease patients

☆ 11 Dec 2009 Pregnant women

☆ 7 Jan 2010 6~35 months children (2 doses, 7.5ug/dose)
Pandemic Influenza Vaccines

- 10 domestic manufactures to produce H1N1pdm vaccines: Tiantan, Sinovac, Hualan, Shanghai Ins, Lanzhou Ins, Changchun Ins, Changchun Changsheng, Yalifeng, Tianyuan, Yanshen.
- 151.5 million doses of H1N1pdm vaccines were released by SFDA, as of Apr 13, 2010
H1N1pdm vaccination

- High level official received the vaccine.
  - To dispel public concerns regarding safety
- High level supervision during mass vaccination
  - To ensure vaccination is well carried out at local level
- Risk communication
  - To share information with media
  - Information released through MOH website
- Included in China’s public program
  - Free of charge and carefully monitored
- Cooperation with international community
  - Share information with WHO through regular meeting

Minister Chen Zhu received the first vaccine during clinical trials
Information Management Systems for H1N1pdm

• Vaccine supply and distribution information system
  – 117 million doses received by provinces up to July 2010

• Case-based vaccine immunization information system
  – 102 million (7%) vaccinated up to July 2010
  – 69 million (69%) individual records collected
    • 85% of vaccinees were in priority populations
    • >51,000 pregnant women, >130,000 children < 3 yrs

• Online Case-based AEFI surveillance system
  – Reported by clinics or manufacturers
  – Surveillance managed by local CDCs
  – Investigations and diagnoses by AEFI expert teams at each level
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<th>类别</th>
<th>类别描述</th>
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<tr>
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<td>本软件针对在此之前发布的3.42版本上进行升级，为了减少国家免疫管理平台的压力。对国家客户端软件数据上传机制进行了优化，将原来断点后完整上传，改为断点续传，将上传个案的压缩包扩大了一倍。同时为改善数据录入功能，增加了批量Excel数据导入方式。</td>
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<td>N R A</td>
<td>NRA评估报文文件</td>
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<td>最新4.0.2.0新安装程序、升级包和安装说明书</td>
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Data download
AEFI Surveillance

• Activities planned
  – Report
  – Investigation
  – Data collection
  – Causality assessment
  – Response to AEFIs
  – Analysis and evaluation
  – Risk communication

• Actual activities
  – Reporting within 24 hours after identifying
    • Serious AEFIs within 2 hours
  – Investigating within 48 hours after reporting
  – Timely response to AEFIs by local CDCs
  – Causality assessment by expert panel
  – Feedback by daily (weekly, monthly) bulletin
  – Communication with vaccinees and media
8067 AEFIIs reported as of March 21, 2010 (90.0 per million doses)

- Common reactions: 5469 (68%)
- Rare reactions: 1083 (13%), 12.1 per million doses
  - Anaphylactic reactions: 838 cases of urticaria; 75 HSP, 49 anaphylaxis, 30 anaphylactic laryngeal edema, 11 Arthus reaction, 3 thrombocytolytic purpura, 3 atopic dermatitis, 1 erythema multiforme, 4 others
  - Neurologic disorders: 8 GBS (similar to baseline incidence), 11 febrile convolution, 5 brachial plexus neuritis, 2 ADEM, 1 polyneuritis, 1 encephalopathy, 1 seizure
- Coincidental events: 1064 (13%)
  - 1 GBS, caused by infection
- Psychological reactions: 409 (5%)
- Under investigation: 42 (0.5%)
- No AEFI reported caused by program error
Numbers of Reported AFP and GBS in children under 15 Years of Age in China from Jan 2006 to Mar 2010

Data are from the Chinese Acute Flaccid Paralysis Surveillance System.
Vaccine Effectiveness
Epidemic, Immunization and AEFI surveillance of H1N1pdm in China

- NO. of cases of A(2009 H1N1)
- NO. of doses administered
- NO. of serious cases of A(2009 H1N1)

38 week, before National Day, started Immunization in Beijing

the Spring Festival
Effectiveness of H1N1pdm Vaccine in Beijing

- During Oct 9-Nov 15, 2009, the H1N1 incidence per 100,000 was 35.9 among vaccinated students and 281.4 among unvaccinated students.
- The estimated VE was 87.3% (95% CI, 75.4 to 93.4)

Production Capacity
Seasonal Influenza Vaccine

- 11 domestic and 5 multinational manufactures supplied TIV for the Chinese market.
- The max domestic capacity to produce TIV was 126 million doses in 2009.
- 32.5 million doses of TIV were supplied in 2008-9, while 16.9 million in 2004-5.
- A target population of 570.6 million or 43% of the total population was estimated.
GAPs and Plans for Seasonal Influenza Vaccines

• **GAPs:**
  – Supply and domestic production capacity is currently insufficient to cover target population
  – Coverage rates were rather low

• **Plans:**
  – Improve domestic production
  – Expand successful promotional campaigns
  – Add cost subsidies in high risk groups
GAPs and Plans for pandemic influenza vaccines

- Update national deployment and vaccination plans (NDVPs) for pandemic vaccine
- Develop action plans to address implementation gaps for optimizing vaccine response to future pandemic
- Core areas: Evidences, Vaccine policies, Legal & regulatory, Supply chain & logistics, AEFI surveillance, et al
Thanks