2009 Pandemic Public Health Measures: Vaccine

Comprehensive Family Immunization Project
Family and Community Health

2 July 2009

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Immunization Unit
5 Years of Partnership

- Followed the 3 pillars of Pandemic Preparedness Strategies
  - Preparedness and Communication
  - Surveillance and Detection
  - Response and Containment
- Presented opportunity to test new strategies (e.g. new generic protocol for influenza surveillance in the Caribbean)
Creating Vaccine Demand and Managing Supply
ProVac Policy Framework

Technical criteria
Programmatic criteria
Financial criteria

www.paho.org/immunization

Influenza Vaccination among Risk Groups in Costa Rica: An Evidence-based Decision

Influenza is a highly infectious viral disease characterized by seasonal outbreaks. Attack rates are usually high, resulting in an increase in doctor visits and hospitalizations that can be quite concerning, especially in the event of a pandemic. Influenza mortality refers not only to the disease caused by the virus, but also to complications that can cause among people suffering from chronic diseases and among demographic groups at risk.

Following an analysis of the epidemiology of influenza and its complications, the health authorities of Costa Rica officially introduced a plan of action aimed at strengthening surveillance for influenza virus through the development of a nation-wide surveillance system. The three components of the plan of action were:

1. Strengthening surveillance for influenza and other respiratory viruses;
2. Vaccinating high-risk groups against influenza; and

The implementation of this plan has helped to define more accurately the burden of influenza in the country, allowing for the identification of seasonal trends and supported international virus surveillance for development of an effective influenza vaccine. In addition, the management protocols for respiratory infections have been updated, and influenza vaccination of high-risk groups has been added to Costa Rica's official immunization schedule.

Strengthening of laboratory surveillance

From 1998, the National Hospital of Children (HNH: Hospital Nacional de Niños) started diagnosing respiratory viral infections and collecting samples from hospitalized children. The HNH clinical samples with positive results were sent to the virology laboratory of the School of Microbiology of the University of Costa Rica (UCR), where, in collaboration with the Centre for Vaccine Development (CVD) at the University of Cambridge, the strains were isolated and studied. The results showed that the A/Sydney/05/97(H3N2) influenza strain circulated from 1998 through 2000, the A/Nea Caledonia/20/99(H1N1) strain circulated in September 2000, and the A/Panama/20079/99 (H3N2) strain circulated in July 2001. In 1999 and 2001, several influenza B strains were also isolated.

In 2002, the sentinel surveillance network for influenza and other respiratory viruses was implemented (Figure 2). Protocols were established for the proper management and study of samples from two sentinel sites: the HNH and the National Hospital of Guanacaste. These centers systematically send the National Reference Laboratory (INCENSA) viral samples from suspected influenza cases reported by inpatients and outpatients, including emergency services. Results are published weekly for users of the network and accessible online.
Urged Member States to:

Expand legal and fiscal space and identify new revenue sources to sustainably finance the introduction of new vaccines against rotavirus, pneumococcus, influenza, and human papillomavirus;

Support the mortality reduction targets, consistent with GIVS and the MDGs, for HPV, RV, influenza, and pneumo associated disease;

Utilize the PAHO Revolving Fund for Vaccine procurement to purchase new and underutilized vaccines
• All children aged 6-23 months and pregnant women
• Health care workers
• Persons with chronic illness
• All elderly persons
Number of Countries with Seasonal Influenza Vaccination Programs in the Americas, 1975-2008

- 35 Countries
PAHO’s Revolving Fund

PAHO’s EPI Revolving Fund promotes:
- Maintenance of adequate vaccine supply
- Affordable prices
- Quality, e.g. managing the exceptional case of Southern Cone countries in May 2005 with Sanofi-Pasteur supply

Lessons learned indicate that increasing vaccine use will help:
- Decrease the morbidity and mortality caused by influenza virus
- Expand the manufacturing capacity with more reliable forecasting
- May increase likelihood that more vaccine is available in case of pandemic
Pandemic Response
Pandemic Response

• Activation of the EOC

• Mobilization of rapid response teams

• Coordination with countries and partner organizations

16 April 2009

26 June 2009
PAHO’s Response to the Influenza A(H1N1) Pandemic

- Alert and response
- IHR
- Surveillance
- Clinical management
- Risk communication
- Vet Public Health
Future Response to the Influenza A(H1N1) Pandemic

- Continue to prepare health services
- Influenza A(H1N1) vaccine and immunization
- Antivirals and case management
- Surveillance
- Risk communication
Mapping of all potential influenza A(H1N1) Vaccine Manufacturers
Pandemic vaccine baseline capacity was estimated at 94.5M doses per week

Assumptions / Methodology

- Survey sent to 36 potential influenza vaccine manufacturers
  - 100% response rate
  - All 21 current influenza vaccine producers responded
  - 26 manufacturers intend to produce pandemic vaccines
  - Includes LAIV and one recombinant vaccine capacity

- Survey assumes
  - 1:1 H1N1 to seasonal yields
  - Most dose-sparing formulation for each manufacturer
  - Use of full production capacity

Estimated H1N1 Vaccine Capacity
At 1:1 yields, most dose-sparing formulation, full capacity

Source: WHO survey
Countries are drawing against this capacity in different ways

<table>
<thead>
<tr>
<th>Segments</th>
<th>Access Strategy</th>
<th>Population</th>
<th>% of H1N1 Capacity¹</th>
</tr>
</thead>
</table>
| High-income (e.g., U.S., Canada, Europe, Japan, Australia) | Mostly open system: Countries negotiate contracts for vaccine with major, industrialized country manufacturers  
  – Facilities serve home countries and export to other markets | 893 M      | 90%                 |
| Low / Middle Income with local supply (e.g., China, Russia) | Mostly closed system: Will procure vaccine mainly from within country  
  – Limited or no plans by manufacturers to export | 3,114 M    | 10%                 |
| Low / Middle Income without local supply           | No current access to H1N1 vaccine                                              | 2,662 M    | N/A                |

¹Refers to portion of capacity located within these countries.

Source: UNPD population dataset, WHO survey

Pan American Health Organization

World Health Organization
Several strategies to be considered for ensuring developing country access to H1N1 vaccines

### Allocate vaccine on real-time basis as it gets produced
- Discussion with manufacturers to reserve vaccine for developing countries on a rolling basis, through donations or agreements
  - Reserve a proportion of capacity
- Discussion with high-income country governments to access some portion of their already purchased vaccine doses

### Shorten contracting window
- Broaden use of adjuvants (ongoing consultations on adjuvanted-vaccine safety)
- Purchasing capacity between current contracts and planned extensions
- Consideration of reduced seasonal production
- Selection of high yield strain (ongoing)

### Increase developing country capacity to produce vaccine
- Enhanced support to new manufacturers already engaged into development of capacity to produce influenza vaccines
  - Financial and technical assistance
- Acceleration of new technologies (e.g., live; ongoing in Thailand, India, China)
- Provision of access to new adjuvants for local suppliers on preferential terms
Key questions for vaccination

Given limited supply, who are the most vulnerable population groups to prioritize for Influenza A(H1N1) vaccination?

What will be the recommendations for seasonal influenza vaccination?

- July SAGE review of the situation with recommendations
- August PAHO/TAG review with recommendations

Source: Country reports.
Yellow Fever Deaths, Laurelty, Paraguay, 2008

Fuente: SENEPA
Summary

• In the last 5 years, substantial progress has been made with accelerated seasonal vaccine introduction (35 countries now routinely using vaccine).
• Never in history has the world been so prepared.
• PAHO’s Revolving Fund plays a critical role.
• Influenza vaccine supply remains an essential issue. Efforts must ensure equity and access to vaccine and antiviral agents.
Several factors will determine how developing countries will have access to pandemic vaccine

**Uncertainties**
- Yields achieved
- Regulatory requirements
- Antigen per dose
- Number of doses/immunized person (1 or 2?)

**Key Factors**
- How will production capacity be used to produce H1N1 vaccines?
  - Utilization of current downtime
  - Utilization of seasonal SH and/or 2010/11 NH production window
- What H1N1 vaccine orders have been negotiated?
  - Number of doses
  - Timing of vaccine delivery
- What other countries intend to purchase H1N1 vaccine?
- What are the most vulnerable population groups who should priority have access to H1N1 vaccine?
Current contract commitments are for 850 - 900M doses, with potential to extend to 1.8B

- Governments have contracted in two ways – for specific amounts of production capacity or number of doses
- On average, governments have committed to 1.0 doses per person in their populations, resulting in contracts for 850-900 million doses
- In addition, most countries have options, or are considering additional contracts, to cover their entire populations with 2 doses
  - Would result in 1.8 billion doses
- Dosage levels, yields, and production schedule choices will impact time required to fill contracts
Local Capacity-Building

- Drills
- Health Serv. Resp.
- RR teams
- Surveillance/Lab
- Communication & Soc. Mobilization
- Pandemic Preparedness
- Impact of a Pandemic
- Basics of Influenza & Pandemic
- MOPECE

Influenza surveillance as part of a wider technical cooperation plan at PAHO
Pregnancy and Influenza Vaccine

- Risk of hospitalization 4 times higher than nonpregnant women

- Risk of complications comparable to nonpregnant women with high risk medical conditions

- Vaccination recommended if \( \geq 14 \) weeks gestation during influenza season
Number of childhood vaccines routinely used in industrialized countries and in Latin America and the Caribbean, 1975-2010

- Measles, DPT, Poliomyelitis, BCG
- Haemophilus Influenzae b
- Rubella
- Mumps
- Hepatitis B**
- Measles, DPT, Poliomyelitis, BCG
- Measles, DPT, Poliomyelitis, BCG
- Measles, DPT, Poliomyelitis, BCG
- HPV
- Varicella
- Hepatitis A
- Meningococcal
- Seasonal flu - 2006
- Rotavirus - 2006
- Pneumococcal - 2006

Current GAP
Pro-Vac
Tools, Workshops, Long-term Support

- **Tools for Economic Analysis**
  - Vaccine Intro Costs Tool
  - Burden of Disease Tools

- **Regional Workshops**
  - Answer questions with economic analyses
  - Economics for Decision Making
  - Work with Partners
  - Gather data, perform analyses

- **5-year plan for ongoing support to Countries**

Pan American Health Organization
Country Experiences - Brazil

Since 2004, Brazil has administered yearly ~13 million doses of influenza vaccine to persons > 60 years, reaching a coverage of 85%. Brazil launches these yearly campaigns during Vaccination Week in the Americas.

Note: Brazil prioritizes the strengthening of surveillance for viral circulation in tropical areas. Lessons learned should help other tropical countries.
Global seasonal trivalent vaccine production capacity

<table>
<thead>
<tr>
<th>Companies</th>
<th>Total annual capacity (10^6 doses)</th>
<th>2008 Northern hemisphere production (10^6 doses)</th>
<th>2009 Southern hemisphere production (10^6 doses)</th>
<th>2009 planned Northern hemisphere production (10^6 doses)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Companies A</td>
<td>560.1 (64%)</td>
<td>299.6</td>
<td>103.0</td>
<td>322.8</td>
</tr>
<tr>
<td>Companies B</td>
<td>316.4 (36%)</td>
<td>170.4</td>
<td>9.5</td>
<td>170.0</td>
</tr>
<tr>
<td>All companies</td>
<td>876.4</td>
<td>470.0</td>
<td>112.5</td>
<td>492.8</td>
</tr>
</tbody>
</table>

*Companies A (n=7): with capacity to produce at least 2.10^6 doses of new H1N1 vaccine / week
Companies B (n=18): other smaller companies

Source: WHO survey
Fergenson et al:

\[ R_0 = 1.2 \text{ to } 1.6 \]

\[ CFR = 0.4\% (0.3\%-1.5\%) \]

<table>
<thead>
<tr>
<th>Disease</th>
<th>Transmission</th>
<th>( R_0 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measles</td>
<td>Airborne</td>
<td>12-18</td>
</tr>
<tr>
<td>Pertussis</td>
<td>Airborne droplet</td>
<td>12-17</td>
</tr>
<tr>
<td>Diphtheria</td>
<td>Saliva</td>
<td>6-7</td>
</tr>
<tr>
<td>Smallpox</td>
<td>Social contact</td>
<td>5-7</td>
</tr>
<tr>
<td>Polio</td>
<td>Fecal-oral route</td>
<td>5-7</td>
</tr>
<tr>
<td>Rubella</td>
<td>Airborne droplet</td>
<td>5-7</td>
</tr>
<tr>
<td>Mumps</td>
<td>Airborne droplet</td>
<td>4-7</td>
</tr>
<tr>
<td>HIV/AIDS</td>
<td>Sexual contact</td>
<td>2-5[2]</td>
</tr>
<tr>
<td>SARS</td>
<td>Airborne droplet</td>
<td>2-5[3]</td>
</tr>
<tr>
<td>Influenza (1918 pandemic strain)</td>
<td>Airborne droplet</td>
<td>2-3[4]</td>
</tr>
</tbody>
</table>

1. ^ Unless noted \( R_0 \) values are from: *History and Epidemiology of Global Smallpox Eradication*. From the training course titled "Smallpox: Disease, Prevention, and Intervention". The CDC and the World Health Organization. Slide 16-17.
Influenza Virus

• Single-stranded RNA virus

• Family Orthomyxoviridae

• 3 types: A, B, C

• Subtypes of type A determined by hemagglutinin and neuraminidase
Influenza Virus Strains

- **Type A** - moderate to severe illness
  - animals and humans
  - all age groups

- **Type B** - milder epidemics
  - humans only
  - primarily affects children

- **Type C** - no epidemics
  - rarely reported in humans
Influenza Virus

Type of nuclear material

Neuraminidase

Hemagglutinin

A/Beijing/32/92 (H3N2)

<table>
<thead>
<tr>
<th>Virus type</th>
<th>Geographic origin</th>
<th>Strain number</th>
<th>Year of isolation</th>
<th>Virus subtype</th>
</tr>
</thead>
</table>

CDC logo
Influenza Antigenic Changes

- Structure of hemagglutinin (H) and neuraminidase (N) periodically change

- **Shift**  Major change, new subtype
  Associated with pandemics

- **Drift**  Minor changes, same subtype
  Associated with epidemics
Examples of Influenza Antigenic Changes

• Antigenic shift:
  - H2N2 circulated in 1957-1967
  - H3N2 appeared in 1968 and completely replaced H2N2

• Antigenic drift
  - In 1997, A/Wuhan/359/95 (H3N2) virus was dominant
  - A/Sydney/5/97 (H3N2) appeared in late 1997 and became the dominant virus in 1998
### Influenza Type A Antigenic Shifts

<table>
<thead>
<tr>
<th>Year</th>
<th>Subtype</th>
<th>Severity of Pandemic</th>
</tr>
</thead>
<tbody>
<tr>
<td>1889</td>
<td>H3N2</td>
<td>Moderate</td>
</tr>
<tr>
<td>1918</td>
<td>H1N1</td>
<td>Severe</td>
</tr>
<tr>
<td>1957</td>
<td>H2N2</td>
<td>Severe</td>
</tr>
<tr>
<td>1968</td>
<td>H3N2</td>
<td>Moderate</td>
</tr>
<tr>
<td>1977</td>
<td>H1N1</td>
<td>Mild</td>
</tr>
</tbody>
</table>
Influenza Pathogenesis

- Respiratory transmission of virus
- Replication in respiratory epithelium with subsequent destruction of cells
- Viremia usually not demonstrable
- Viral shedding in respiratory secretions for 5-10 days
# Influenza Epidemiology

- **Reservoir**: Human, animals (type A only)
- **Transmission**: Respiratory
  - Probably airborne
- **Temporal pattern**: Peak December - March in temperate areas
  - May occur earlier or later
- **Communicability**: Maximum 1-2 days before to 4-5 days after onset
Influenza
Clinical Features

- Incubation period 1-5 days

- Abrupt onset of fever, myalgia, sore throat, nonproductive cough, headache

- Severity of illness depends on prior experience with related variants

- Case-fatality ~0.5-1 per 1000 cases
Influenza Complications

- Pneumonia
  - primary influenza
  - secondary bacterial

- Reye syndrome

- Myocarditis

- Death
Impact of Influenza

• >20,000 excess deaths in each of 5 epidemics between 1972 and 1995

• >40,000 excess deaths in each of 6 epidemics

• >90% of deaths among persons 65 years of age or older
Influenza Vaccine Recommendations

- All persons 50 years of age or older
- Persons >6 months of age with chronic illness
- Residents of long-term care facilities
- Pregnant women
- Persons 6 months to 18 years receiving chronic aspirin therapy
Influenza Vaccine Recommendations

• Persons with the following chronic illnesses should be considered for influenza vaccine:
  - pulmonary (e.g., asthma, COPD)
  - cardiovascular (e.g., CHF)
  - metabolic (e.g., diabetes)
  - renal dysfunction
  - hemoglobinopathies
  - immunosuppression, including HIV infection