A/H1N1 2009 influenza in Israel: Preparedness and response

Prof. Itamar Grotto MD, MPH, PhD
Director, Public Health Services
Israel Ministry of Health

Science → Policy

1. Agenda Setting
   - Public attention focuses on a public problem or issue.
   - Officials’ words and actions help focus attention.

2. Policy Formulation
   - Policy makers in the legislature and the bureaucracy take up the issue.
   - They create legislative, regulatory, or programmatic strategies to address the problem.

3. Policy Adoption
   - Policy makers formally adopt a policy solution, usually in the form of legislation or rules.

4. Policy Implementation
   - Government agencies begin the job of making the policy work by establishing procedures, writing guidance documents, or issuing grants-in-aid to other governments.

5. Policy Evaluation
   - Policy analysts inside and outside government determine whether the policy is addressing the problem and whether implementation is proceeding well.
   - They may recommend REVISIONS in the agenda, in the formulation of policy, or in its implementation.
Preparedness
Previous influenza pandemics

1918
"Spanish flu"
50-100 Million deaths (H1N1)

1957
"Asian flu"
1-4 Million deaths (H2N2)

1968
"Hong Kong flu"
1-4 Million deaths (H3N3)

2009
“Mexican flu”
??? deaths (H1N1)
“Spanish flu” - 1918
Human cases of H5N1 influenza (reported to WHO)

Total: 512 cases, 304 deaths (59%)
Local experience/lessons learned from avian influenza in Israel

Multifocal Avian Influenza (H5N1) Outbreak

Ran D. Balicer,† Shmuel Reznikovich,† Byakum Berman,‡ Michael Pirak,‡ Amnon Inbar‡ Shimon Pokamunski,‡ and Itamar Grotto†

During March 2006, an outbreak of highly pathogenic avian influenza (H5N1) occurred in multiple poultry farms in Israel. The epidemiologic investigation and review of outbreak mitigation efforts uncovered gaps in planning for and containing the outbreak, thus affording valuable lessons applicable to other countries in similar settings.

in Indonesia (3); they belonged to a single strain and were closely related to other HPAI (H5N1) strains isolated during this period in European, Asian, and African countries.

Turkey farms, accounting for 10% of Israeli poultry farms, were unproportionally involved in this outbreak (6/9 outbreak foci). The relative prevalence of turkey farms in the southern district near the Gaza Strip (50% of farms); the close interactions between personnel at farms of the same poultry type; and the higher susceptibility of turkeys to avian influenza virus (4) may be plausible explanations.

Several epidemiologic links between outbreak foci were identified (Table 1). These links and the near-simultaneous detection of several outbreak foci specifically on turkey farms, increase the likelihood that the virus disseminated through use of shared vehicles or by personnel. Alternatively, the involvement of 2 heavy breeder farms (farms F, H) characterized by strict biosafety procedures to prevent such transmission, and the fact that all 9 farms...
Mathematical modeling: Israeli reference scenarios

- **Level 5**: (1918-like)  
  - Case fatality: >2%  
  - Hospital cases: 240,000  
  - Deaths: 45,000

- **Level 4**:  
  - Case fatality: <2%  
  - Hospital cases: 150,000  
  - Deaths: 30,000

- **Level 3**:  
  - Case fatality: <1%  
  - Hospital cases: 90,000  
  - Deaths: 15,000

- **Level 2**: (1957-like)  
  - Case fatality: <0.5%  
  - Hospital cases: 26,000  
  - Deaths: 6,000
“Waves” of mortality..

A/H1N1 Influenza in Israel

- First (?) case in Mexico – March 17, 2009
- First cases in the US: April 15, 2009
- First case in Israel: April 24, 2009 (“imported” from Mexico)
Pandemic phases

- May-July 2009: “containment” phase
- August-September 2009:
  - “Treatment” phase and...
  - “Modeling” phase
- October 2009-January 2010: “vaccination” phase
- Since February 2010:
  - “Criticism” phase
  - “lessons learned” phase
Epidemiological characteristics
Influenza A (H1N1) 2009, by date of onset (n=9882)
Age distribution of cases Vs. % in Israeli population

- 21% for 10>
- 19% for 10-19
- 21% for 20-30
- 21% for 30-50
- 9% for 50-60
- 8% for 60<
- 3% for 70<
## Severe cases and deaths

<table>
<thead>
<tr>
<th>Age group</th>
<th>In ICU</th>
<th>Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>1 - 18</td>
<td>43</td>
<td>8</td>
</tr>
<tr>
<td>19 - 65</td>
<td>160</td>
<td>68</td>
</tr>
<tr>
<td>66+</td>
<td>24</td>
<td>19</td>
</tr>
<tr>
<td>Total</td>
<td>232</td>
<td>96</td>
</tr>
</tbody>
</table>
Primary (current) lessons

- Dynamic policy
- Changes in public’s level of concern
- Strengthening public health
  - Personnel and infrastructure
  - Public health laboratories
  - Personal hygiene as a permanent measure
- Expansion of decision making circle
- Looking back on major decisions
Decision making (1)

- **Primary containment:**
  - Isolation of patients
  - Voluntary quarantine of contacts
  - Airport clinic

- **Antivirals:**
  - Treatment of patients (all Vs. high risk groups)
  - Treatment to special groups (pregnant women, infants)
  - (no) Post-exposure prophylaxis
Decision making (2)

• Non-Pharmaceutical interventions:
  – Personal hygiene
  – Masks for the general public
  – Protection of healthcare personnel
  – (no) closure of schools

• Vaccines:
  – Vaccine purchase
  – Vaccination campaign
Decision making – vaccine purchase

SAFE

OR

SORRY

www.ezprezzo.com
## Decision making – vaccine purchase

<table>
<thead>
<tr>
<th>Vaccine purchase</th>
<th></th>
<th></th>
<th>Disease severity</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>Yes</td>
<td></td>
<td>Mild</td>
</tr>
<tr>
<td>Successful gamble</td>
<td>Waste of money</td>
<td>Severe</td>
<td>Disease severity</td>
</tr>
<tr>
<td>SORRY</td>
<td>SAFE</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
The disease – uncertainties:

• Severity (and how do we define it?)
• Rate of spread
• Number of waves (1?, 2?, 3?..)
• Changes (mutations) of the virus
The vaccines – uncertainties:

- Will it be available at all?
  - Limited surge capacity
    - 700 Million doses worldwide

- Will it be on time?
  - Time to mass production (6 months?)

- Safety and efficacy

- Target group: high risk? Children? Whole population?

- Complicated vaccination campaign

- Compliance of the population:
  - Willingness to be vaccinated (adults):
    - August 2009: 69%
    - October 2009: 43%

Please remember these numbers
What we knew about disease severity at the time of decision
First data from Mexico

Pneumonia and Respiratory Failure from Swine-Origin Influenza A (H1N1) in Mexico
Fraser C, et al: Pandemic Potential of a Strain of Influenza A (H1N1): Early Findings

Science, 19 June 2009

- Cases ~ 23,000
- Mortality: 0.4%
- Expected AR%
  - Children: 61%
  - Adults: 29%
- $R_0$ ~ 1.5
UK model: August 2009
Reasonable worst case scenario

• 1st wave will peak in August, 2nd peak on autumn or winter
• Expected attack rate: 30-50%
• Of 24 million patients in the UK
  – Pneumonia: 10% (2.4 million)
  – Hospitalizations: 1-2% (360,000)
  – Require assisted ventilation: 0.3-0.6% (108,000)
  – 1 of 1,000 will die (24,000)
• US assumptions: 60,000-90,000 deaths
Disease severity – in retrospect

• > 18,000 confirmed deaths = under-estimation

• Different from seasonal influenza in age distribution

• ~ 25% of deaths – had no medical background

• Animal models – intermediate virulence between seasonal and H5N1 influenza
Age distribution of deaths - UK

Seasonal influenza

- 0-14: 0.5%
- 15-44: 5%
- 45-64: 94%

A/H1N1 2009

- 0-14: 21%
- 15-44: 39%
- 45-64: 21%
- +65: 19%
Deaths by risk groups - Israel

- 70.1%: "severe" risk factors
- 16.5%: "Mild" risk factors
- 12.7%: Previously healthy or pregnant women
Start of vaccination campaign in relation to disease spread

Start of campaign
Daniele Ofri, MD, PhD:

*The Emotional Epidemiology of H1N1 Vaccination*

The New England Journal of Medicine, November 25, 2009
Vaccine compliance in Israel

• Total doses purchased: 7.3 - 5 Million doses

• Population vaccinated: ≈ 650,000 (9%)

• Compliance - healthcare personnel: ≈ 30%
Vaccine safety and efficacy

• Were the vaccines effective?
  – Good antibody response
  – Proof of efficacy in animal models
  – Clinical effectiveness?

• Were the vaccines safe?
  – There was no reports on any unexpected adverse events
Despite the excess vaccine, it would be wrong - and dangerous - to fault health authorities for the steps they took to protect their populations. Had the virus been more lethal, the penalty for late delivery and insufficient supplies of vaccine would have been a public health catastrophe. We may not get as lucky next time.
The failure of success..

Steps that reduced morbidity and mortality which resulted in mild pandemic:
- Good surveillance and early detection
- Primary containment measures
- Personal hygiene (public; healthcare personnel)
- Antiviral medications
- Intensive care treatment of severely ill patients
- (Partially) Successful risk communication

Emerging Diseases

Posted January 25, 2010

Face masks, hand hygiene help to reduce the spread of respiratory illness during influenza A (H1N1) pandemic
A look into the future…

- The virus is still active, with a possibility of reassortment, including with H5N1 virus
- Change in virulence in next waves?
- Oseltamivir resistance?
- A/H1N1 as the seasonal virus
- A different pandemic virus

- Are we ready for the next challenge?
Serological findings from Israel: “Before and after”

<table>
<thead>
<tr>
<th>Age Group</th>
<th>April-September 2008</th>
<th>December 2009-March 2010</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-9 years</td>
<td>n=180</td>
<td>n=187</td>
<td>n=7</td>
</tr>
<tr>
<td>10-19</td>
<td>n=224</td>
<td>n=278</td>
<td>n=54</td>
</tr>
<tr>
<td>20-49</td>
<td>n=386</td>
<td>n=512</td>
<td>n=126</td>
</tr>
<tr>
<td>50-79</td>
<td>n=411</td>
<td>n=532</td>
<td>n=221</td>
</tr>
<tr>
<td>80+</td>
<td>n=90</td>
<td>n=76</td>
<td>n=14</td>
</tr>
<tr>
<td>All</td>
<td>n=1376</td>
<td>n=1501</td>
<td>n=325</td>
</tr>
</tbody>
</table>

HI titer at or above 1:40 (%)

- April-September 2008
- December 2009-March 2010
- Difference
The next influenza pandemic?

1918
"Spanish flu"
50-100 Million deaths
(H1N1)

1957
"Asian flu"
1-4 Million deaths
(H2N2)

1968
"Hong Kong flu"
1-4 Million deaths
(H3N3)

2009
“Mexican flu”
??? deaths
(H1N1)
The next influenza pandemic?

20??
“????? flu”
??? deaths
(H?N?)
Influenza vaccine – safe, effective and mistrusted

KM Harris, PhD, J Maurer, PhD and A Kellerman, MD, MPH

The New England Journal of Medicine, December 2, 2010
Accelerating vaccine production is necessary but insufficient. For no matter how quickly a safe and effective vaccine is produced, it will do little good if a large numbers of people refuse to be vaccinated.