SPECTRUM OF DISEASE
INFLUENZA A H1N1

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Use of health services

Proportion of the population affected

ARDS

PNEUMONIA

ILI (fever)

Respiratory infections (mild)

ASYMPTOMATIC INFECTIONS

DEATHS

Self-care

No care needed

Proportion of the population affected

Use of health services
Hospital cases

Primary care

Hidden to health system or hospitals
FIGURE 5. Summary curves of viral shedding and total symptoms scores in experimental influenza virus infection. Thirteen curves were used for viral shedding (refer to figure 2 legend), and 17 curves were used for total symptoms scores (refer to figure 3 legend).
Gathering the “true” spectrum of H1N1

- **Community based seroprevalence study**
- Surveillance system including primary care
- Contacts of clinical cases
  - Health workers
  - Family contacts
- Hospital patients
Importance

- True risk of disease: proportion of severe cases,
- How risk varies with age and other factors.
- Transmission dynamics: schools, health personnel.
- Vaccine targeting
Severe cases
A H5N1 virus–infected mouse lung 6d postinoculation

B control

Family cluster of H1N1

Mother, 50, smoker 1 pack/day, 35 p-y, asthmatic 
arrived to emergency w disease of 15 days, with respiratory failure. 
28 days in mechanical ventilation, 
39 days in hospital, had renal dysfunction, shock, cardiac arrest, myopaty

discharged well.

Daugther, 19, asthmatic, 2 days in emergency room, chest x ray almost normal, febrile disease 
SaO2 86% BF 28, PO2 55 
arrived with 7 days of symptoms.

Son 18, mild respiratory symptoms, no consults, no chest X ray
Characteristic of severe cases

- ILI
- Multiple bilateral cottonny opacities
- ARDS → multiorganic failure → high mortality
- High LDH, CK, aminotransferases
- Normal total WBC, low lymphocytes
### Severe Cases of H1N1

<table>
<thead>
<tr>
<th></th>
<th>H5N1 (26) Yu et al.</th>
<th>MEX H1N1 Hospital (18)</th>
<th>California H1N1 (30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (median)</td>
<td>29</td>
<td>38</td>
<td>28</td>
</tr>
<tr>
<td>Fever</td>
<td>92</td>
<td>100</td>
<td>97</td>
</tr>
<tr>
<td>Cough</td>
<td>58</td>
<td>100</td>
<td>77</td>
</tr>
<tr>
<td>ARDS</td>
<td>81</td>
<td>55%</td>
<td>4-20</td>
</tr>
<tr>
<td>Aminotransferases</td>
<td>43</td>
<td>61%</td>
<td></td>
</tr>
<tr>
<td>Renal Dysfunction</td>
<td>17%</td>
<td>22%</td>
<td></td>
</tr>
<tr>
<td>Diarrhea</td>
<td>8</td>
<td>22</td>
<td>10</td>
</tr>
<tr>
<td>LDH</td>
<td>95</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>LDH (IU/L)</td>
<td>1141</td>
<td>1226</td>
<td></td>
</tr>
<tr>
<td>WBC</td>
<td>4.3</td>
<td>6.0</td>
<td></td>
</tr>
<tr>
<td>Lymphocytes</td>
<td>0.7</td>
<td>0.85</td>
<td></td>
</tr>
<tr>
<td>CPK (IU/L)</td>
<td>801</td>
<td>366</td>
<td></td>
</tr>
<tr>
<td>Mortality</td>
<td>65%</td>
<td>40%</td>
<td></td>
</tr>
</tbody>
</table>

“Mild” influenza in an hospitalized patient

24 years, previously healthy ILI with fever and dyspnea.

Typical chest X ray abnormalities
EMERGENCY CONSULTS FOR PNEUMONIA AND INFLUENZA

NOT ALL POSITIVE FOR H1N1

Severe pneumonia, INER
June 30, 2009

<table>
<thead>
<tr>
<th>Total</th>
<th>swine+</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cummulative</td>
<td>205</td>
</tr>
<tr>
<td>Deaths</td>
<td>52</td>
</tr>
<tr>
<td>Admitted</td>
<td>6*</td>
</tr>
<tr>
<td>Intubated</td>
<td>1</td>
</tr>
</tbody>
</table>

We had 45 patients admitted in the epidemic peak.
Contacts of hospital cases
Spectrum in contacts

<table>
<thead>
<tr>
<th>VARIABLE</th>
<th>Index cases (395)</th>
<th>2ary cases with consult (313)</th>
<th>2ary Cases with no consult (504)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic disease</td>
<td>24</td>
<td>14</td>
<td>11</td>
</tr>
<tr>
<td>Fever &gt;38</td>
<td>93</td>
<td>32</td>
<td>16</td>
</tr>
<tr>
<td>Cough</td>
<td>90</td>
<td>78</td>
<td>56</td>
</tr>
<tr>
<td>Time to improvement</td>
<td>8</td>
<td>7</td>
<td>4</td>
</tr>
<tr>
<td>Lost workdays</td>
<td>4</td>
<td>2.9</td>
<td>0.3</td>
</tr>
<tr>
<td>Did not stop working</td>
<td>9</td>
<td>6</td>
<td>56</td>
</tr>
</tbody>
</table>

H3N2 influenza in 1997-1998 in France
No difference in age, gender, smoking habits. Carrat F, ArchIntMed 2002; 162:1842
Health workers (elder et al)

- 518 health workers Scotland
- Serologic tests in 1993 after influenza epidemic
- 120 (23%) increased titre (107 type A)
  - 28% no respiratory symptoms
  - 59% no Influenza Like Illness
Oaxaca case contacts

HOSPITAL (105)
- Emergency room contacts
- 45% respiratory infection (“common cold”)
- No fever
- No hospital

COMMUNITY (106)
- 24 cases (23%)
- Fever 83%
- Cough 75%
- Headache 87%
- No complications

Missing: asymptomatic infections, shedding asymptomatic individuals-
28% no respiratory symptoms, 59% no ILI in a seroprevalence survey of
518 health workers in Scotland (Elder et al)
### SYMPTOMATIC CONTACTS (INER)

<table>
<thead>
<tr>
<th></th>
<th>FAMILY</th>
<th>HOSPITAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>120</td>
<td>190 (emergency room, ICU)</td>
</tr>
<tr>
<td>Symptomatic (ILI)</td>
<td>21</td>
<td>22 (3, S-OIV+)</td>
</tr>
<tr>
<td>Hospitalized</td>
<td>4 (2 deaths with Down)</td>
<td>0</td>
</tr>
</tbody>
</table>

*ILI*: Influenza Like Illness
La Gloria, Veracruz, MEXICO

• 2155 inhabitants
• 616 respiratory disease (29%)
• Age group attack rate from 16%-61% higher in younger
• No hospitalization, no deaths
• One patient identified H1N1
• 82% cough
• 68% fever
La Gloria, attack rate
Ministry of health, Veracruz

At the end, one H1N1 identified
No deaths, no hospitalization
Lessons from experimental influenza infection
Experimental infection with influenza virus

Carrat et al, AJEpi, 167(7): 775-785 2008
## Reported symptoms H1N1

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Spain, UK, France</th>
<th>Japan (217)</th>
<th>Mexico, SINAVE (6376)</th>
<th>Mexico, INER, triage (190)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>62-96</td>
<td>91</td>
<td>43</td>
<td>55</td>
</tr>
<tr>
<td>Cough</td>
<td>75-100</td>
<td>59</td>
<td>40</td>
<td>72</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>13-41</td>
<td>6</td>
<td>7.4</td>
<td>20</td>
</tr>
<tr>
<td>Vomiting</td>
<td>6-36</td>
<td>2</td>
<td>7.4</td>
<td>17</td>
</tr>
<tr>
<td>Headache</td>
<td>20-78</td>
<td>13</td>
<td>40</td>
<td>78</td>
</tr>
<tr>
<td>Coryza</td>
<td>33-65</td>
<td>33</td>
<td>33</td>
<td>55</td>
</tr>
<tr>
<td>Sore throat</td>
<td>57-80</td>
<td>39</td>
<td>22</td>
<td>76</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>6-26</td>
<td>-</td>
<td>7.4</td>
<td>48</td>
</tr>
</tbody>
</table>

Data to May 2009, Spain (91), UK (175), France (16), Japan (217), from Eurosurveillance 2009
# CASE-FATALITY OF H1N1

<table>
<thead>
<tr>
<th></th>
<th>H5N1 ALL</th>
<th>EGYPT H5N1</th>
<th>WORLD H1N1</th>
<th>USA</th>
<th>MEX</th>
<th>CAN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>433</td>
<td>78</td>
<td>77,201</td>
<td>27,717</td>
<td>8,680</td>
<td>7,983</td>
</tr>
<tr>
<td>Fatalities</td>
<td>262</td>
<td>27</td>
<td>332</td>
<td>127</td>
<td>116</td>
<td>25</td>
</tr>
<tr>
<td>% Fatality</td>
<td>61%</td>
<td>35%</td>
<td>0.4%</td>
<td>0.45%</td>
<td>1.3%</td>
<td>0.3%</td>
</tr>
</tbody>
</table>

Data from June 3 (H5N1, WHO) July 1 (H1N1, Who)
“Anomalous” distribution of cases
influenza H1N1, morbidity and mortality

- cases/100,000
- case-fatality (%)
- DEATHS/million

Edad (age)
Figure 3. Influenza plus pneumonia (P&I) (combined) age-specific incidence rates per 1,000 persons per age group (panel A), death rates per 1,000 persons, ill and well combined (panel B), and case-fatality rates (panel C, solid line), US Public Health Service house-to-house surveys, 8 states, 1918 (36). A more typical curve of age-specific influenza case-fatality (panel C, dotted line) is taken from US Public Health Service surveys during 1928–1929 (37).
Severe cases

- 6 days delay to seek care (3-15)
- Most cases: no previous disease
- Half between 17-50 years of age
- On arrival: higher LDH, CPK, Xray abnormalities, less lymphocytes, higher APACHE, SOFA scores
- Milder disease in those with negative test (same syndrome)
Risk factors reported

- Pregnancy
- Obesity-DM
- Comorbidities typical risk factors of influenza
  - Asthma, COPD, cardiovascular disease
  - Neuromuscular diseases
- No treatment, no diagnosis
Indicators of severity higher in S-OIV positive
Conclusions

- Missing seroprevalence study. (milder extreme of disease).
- Need more sources of real time info (schools? Health care centers?)
- Ongoing viral survey: all types
- Pattern may change with time, observe:
  - Disease severity, age distribution, disease in contacts, primary care
  - Response to treatment, test positivity etc.