Epidemiology and Illness Severity of Pandemic (H1N1) 09 Virus

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Outline

1. Timeline and geographical spread of the pandemic
2. Viral characteristics and pathogenesis
3. Impact
    1. Speed and effectiveness of transmission
    2. Severity of the disease
    3. Burden on the health care system
    4. Groups at risk for complications
4. Pandemic and seasonal influenza

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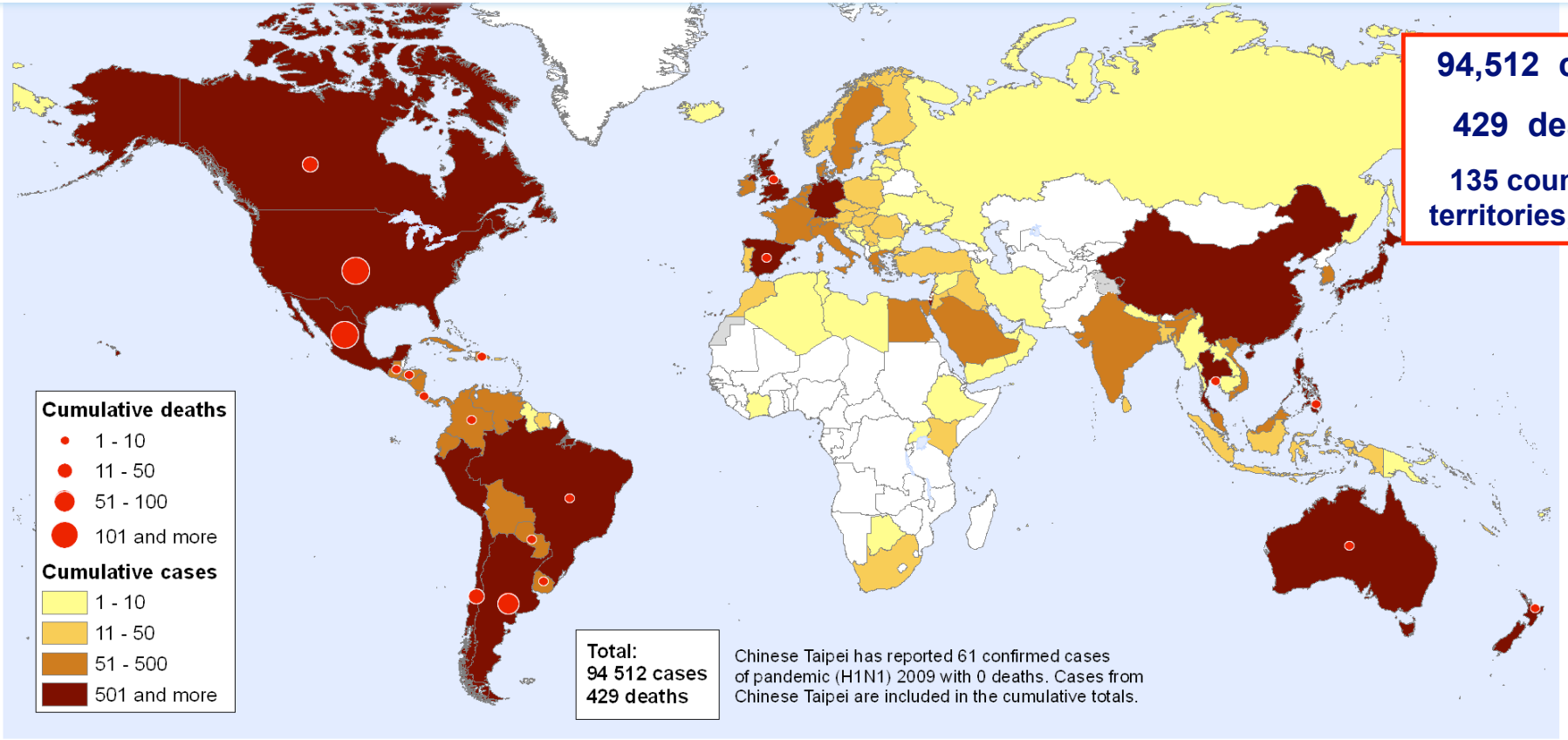
Timeline of events

- April 12: an **outbreak of influenza-like illness** in Veracruz, Mexico, reported to WHO
- April 15-17: two cases of a **new A(H1N1) virus infection** identified in two southern **California** counties in U.S.A.
- April 23: **new influenza A (H1N1) virus infection** confirmed in several patients in **Mexico**
- April 24: WHO declares a public health event of international concern (**PHEIC**).
- April 27: WHO declares pandemic **phase 4** - sustained community transmission in Mexico
- April 29: WHO declares pandemic **phase 5** (2 countries affected)
- June 11: WHO declares pandemic **phase 6** (spread to 2 WHO regions)
- **In 9 weeks**, **all WHO regions** reporting cases of **pandemic (H1N1) 2009**

Pandemic (H1N1) 2009
Epidemiological situation, 6July 2009



Data Source: World Health Organization
Map Production: Public Health Information and Geographic Information Systems (GIS)
World Health Organization

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Map produced: 06 July 2009 09:00 GMT

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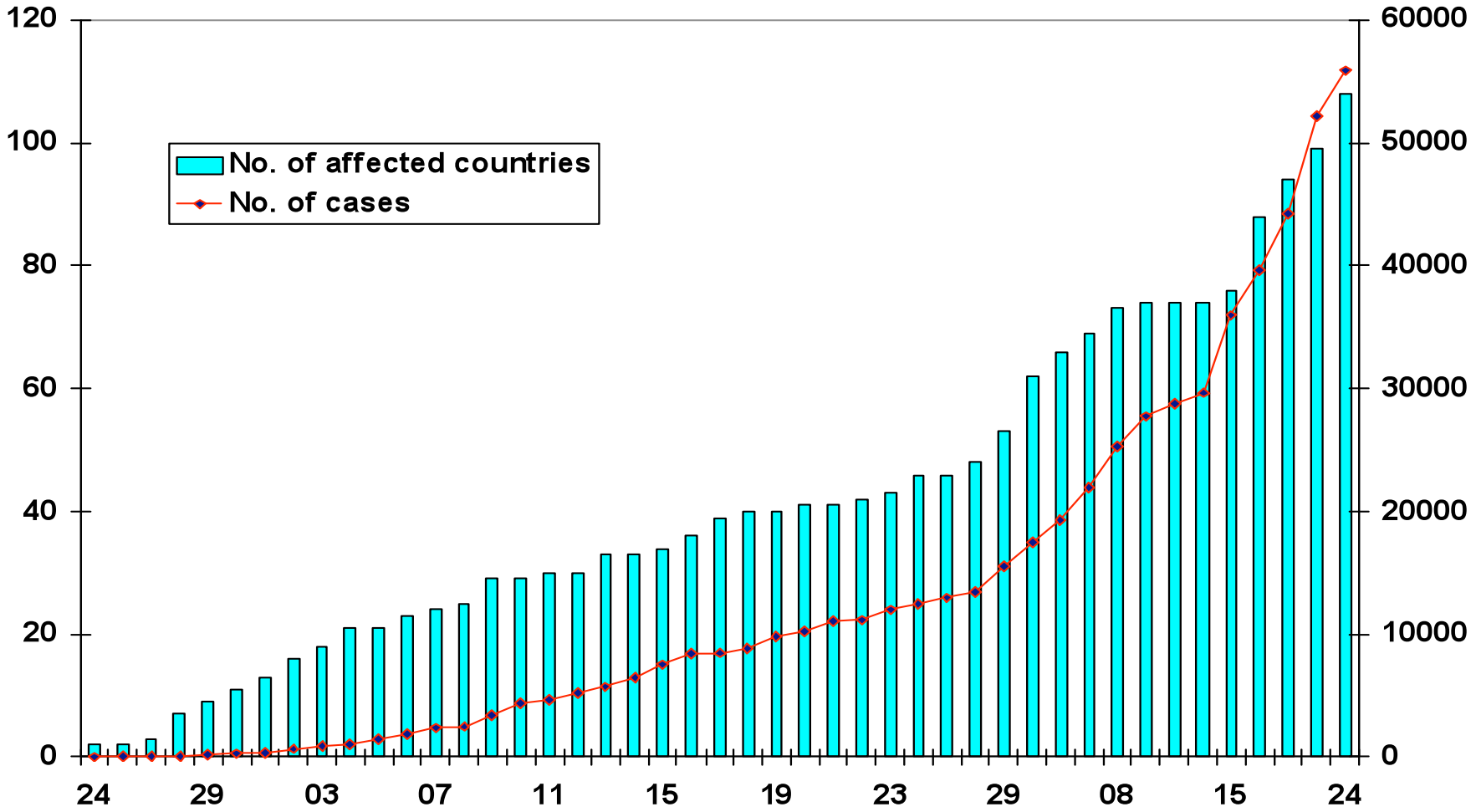
Pandemic (H1N1) 09 virus characteristics

- All viruses to date are **homogeneous antigenically** and react well with antisera raised against California/4/2009 and California/7/2009
- To date, **no recognized genetic markers associated with virulence**
  - Viruses isolated from severe cases do not show sequence differences
- Virus **replicates more** in lungs and causes **more severe pneumonia** in animals (ferrets, mice, primates) than **seasonal H1N1** (*unpublished)*
- **Sensitive to neuraminidase inhibitors** (oseltamivir, zanamivir)
  - Resistant to amantadine and rimantadine
  - Sporadic resistant virus to oseltamivir reported from Denmark, Japan and HK (3 July 2009)
- Virus evolution (genetically and antigenically) is **unpredictable**

Global spread: Affected countries and laboratory-confirmed cases (24 April-24 June 2009)



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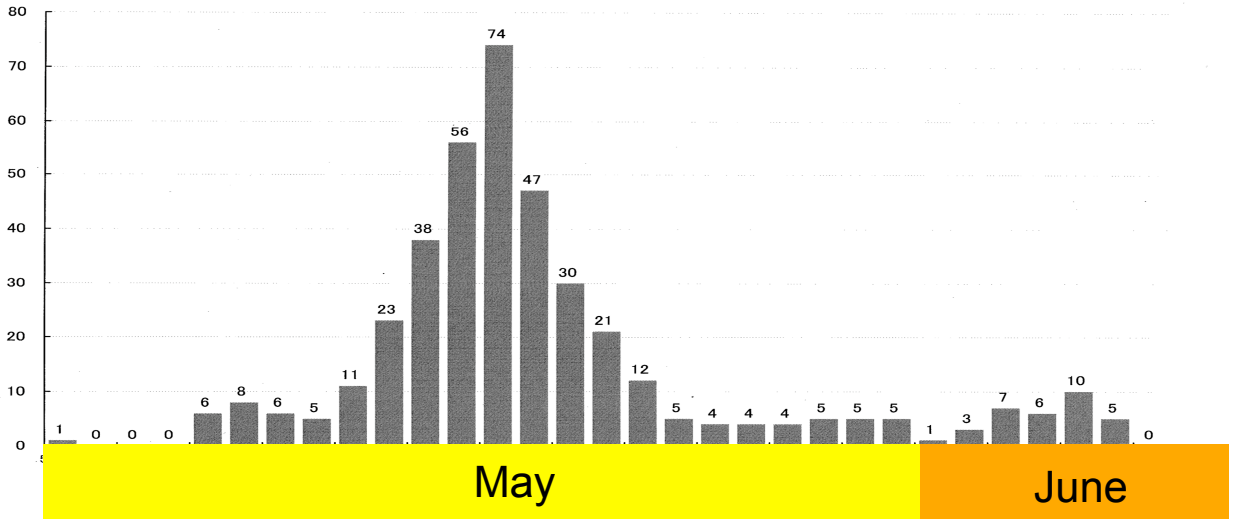
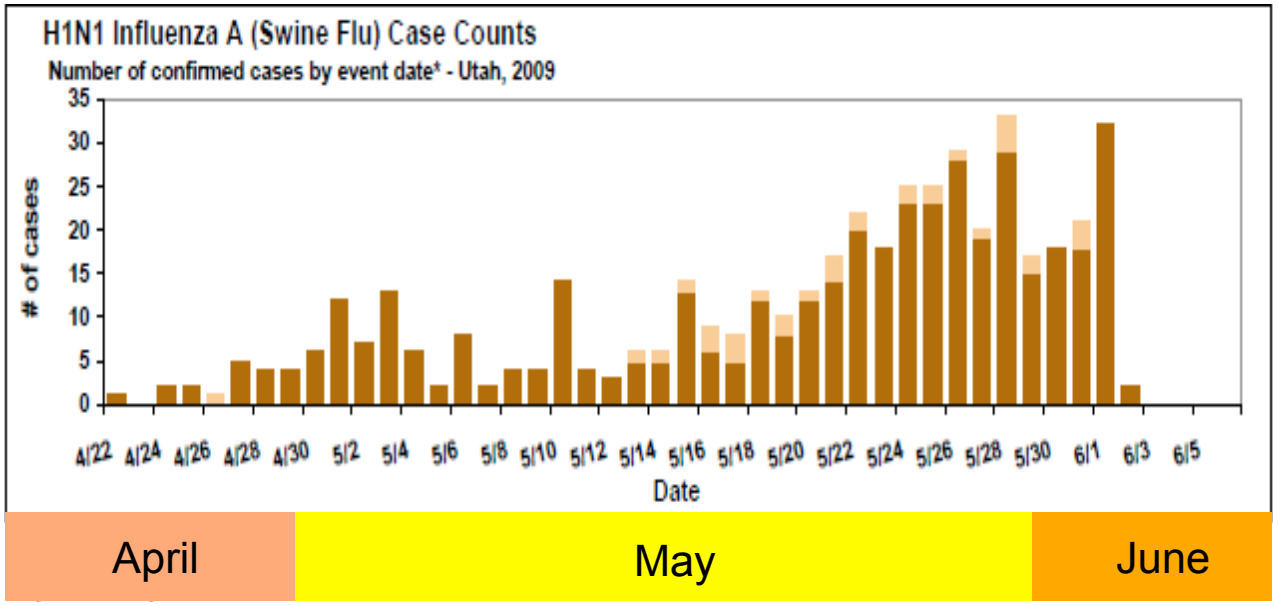
Different patterns in different settings



Japan - Kinki area
390 confirmed cases
No severe case
(as of 4 June 2009)

Source: Japanese Ministry of Health, Labour and Welfare



USA - Utah
489 confirmed cases
35 hospitalisations
2 deaths
(as of 4 June 2009)

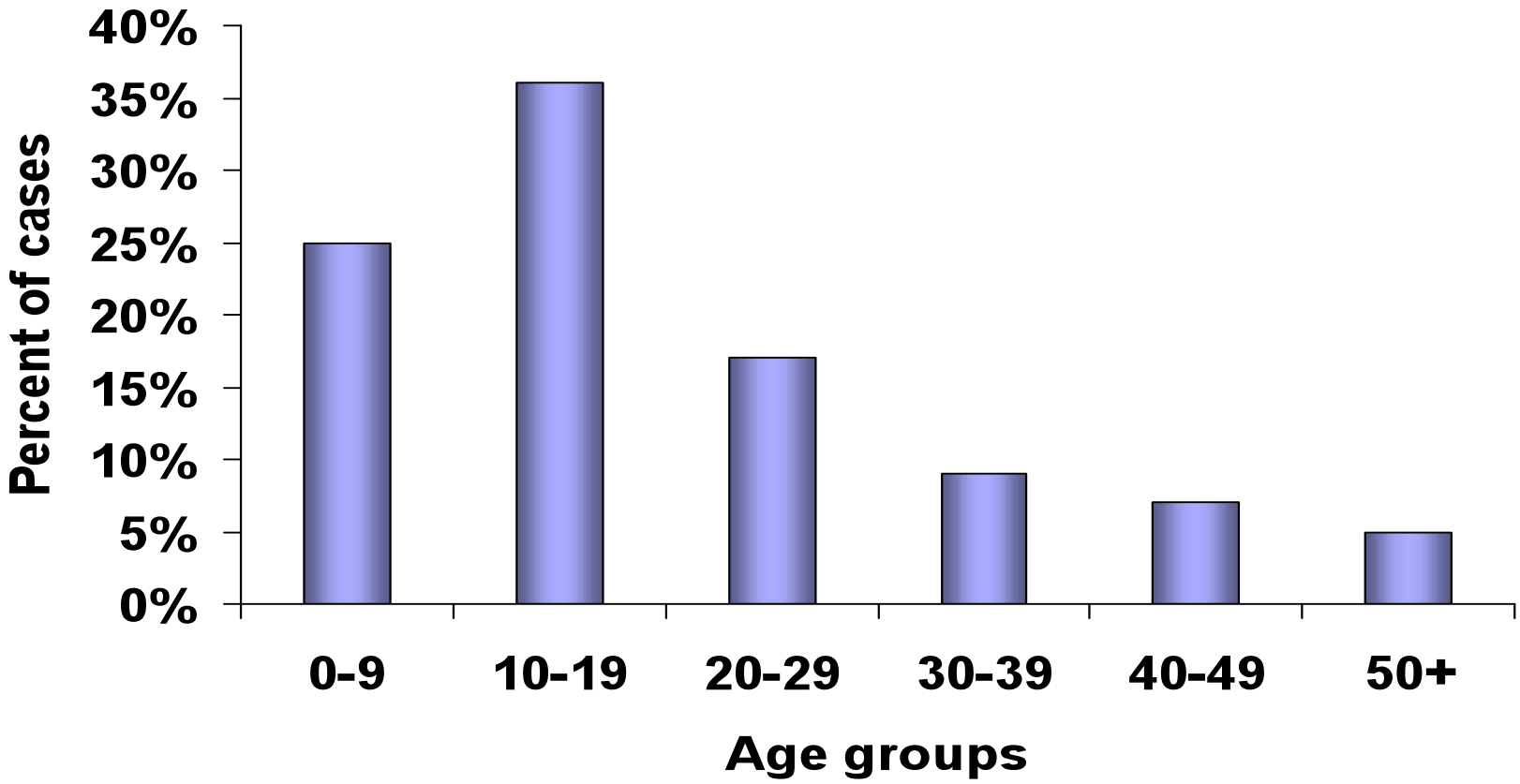
Source: Utah Department of Health

Transmissibility

- Secondary attack rate estimates
  - School outbreaks: 22-33% (USA)
  - Households: 19% (USA) to 43% (Chile)
- Community transmission in multiple countries
  - NYC community-based telephone survey: 6.9% of the population developed an influenza-like illness between May 1 and May 20, 2009
- Explosive outbreaks / amplification in schools
- Ro estimates
  - Pandemic (H1N1) 2009: 1.4 - 3.5
  - Seasonal influenza: 1.2 - 1.4

Distribution of cases by age group

Laboratory-confirmed cases (Chile, EU and EFTA, Japan, Panama, Mexico)



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Clinical spectrum of infection

- Majority of cases have uncomplicated influenza illness that resolves without antiviral treatment
  - More GI complaints (emesis, diarrhea…) than for seasonal influenza
  - Non-febrile, mild, and asymptomatic (viral RNA+) cases
- Hospitalization: up to 10% of confirmed cases
  - 1-10% in US, 2-6% in Canada, 3.5% in Chile
- CFR: < 1% of confirmed cases
  - **Higher risk in adults** (> 20 yrs old) and **those with co-morbidities**
  - US < 0.4%; Mexico < 1.5%; Chile- 0.1%; Argentina < 1.5%

Severe outcomes

- Majority of **deaths** caused by **severe viral pneumonia**→ ARDS
  - Renal failure / multiple organ failure, hypotension and shock
  - Bacterial co-infection in minority at presentation and nosocomial
  - Other: myocardial infarction, paediatric encephalopathy
- **50-80% of severe cases have underlying conditions**
  - Pregnancy, asthma or other lung disorders, cardiovascular, diabetes, immunosuppression, neurologic disorders
  - Obesity appears to be newly recognized risk factor
- **Severe cases and deaths** have occurred in **young and previously healthy adults** and less often children

Age distribution for outpatients and hospitalised patients

- Age distribution: older for severe / fatal cases than for all cases
- **Laboratory-confirmed** cases:
  - Median 12-17 yrs (UK, USA, Japan, Chile, Canada)
- **Hospitalized** cases:
  - USA (n= 567): 46% < 18 yrs (median 26 yrs)
  - California, USA (n=30) (median 27.5 yrs)
- **Fatal** cases:
  - USA (n=87): 61% aged 30-64 yrs (median 37 yrs)
  - Mexico (n=74): 68% aged 20-49 yrs

Underlying conditions in hospitalized patients

- **New York City**: **80%** of hospitalized patients had ≥ one risk factor (including < 2 yrs, >65 yrs)
  - Asthma 30%, diabetes 12%, chronic respiratory failure 11%, pregnancy 6%
- **Chile**: **~50%** of hospitalized patients had underlying conditions (obesity, diabetes, hypertension)
- Fatal cases
  - Mexico (N=45): 54% had no recognized co-morbidity
  - USA (N= 99): morbid obesity 11%, asthma 11%, other respiratory 24%, diabetes 13%, cardio-vascular 14%, neurologic 33%, pregnancy 8%, other 13%; no recognized 12%

Pregnancy and Influenza: Outcomes in Pregnant Women

- Seasonal influenza associated with ↑ cardiopulmonary hospitalizations
  - Risk ↑ with duration of pregnancy; highest in 3rd trimester
    - ~ 3 - 5 fold ↑ rates than non-pregnant during season
  - Risk ↑ further if co-morbidities
    - ~ 2 - 5 fold ↑ rates than healthy pregnant and ~ 3 - 8 fold ↑ rates than non-pregnant with co-morbidities
- Prior pandemics (USA)
  - 1918: 27 to 45% mortality; 52% pregnancy loss
  - 1957: up to 1/2 of deaths in women of reproductive years
- Pandemic (H1N1) 2009 (USA)
  - Among 20 pregnant women, 3 hospitalizations and 1 death
  - Reports of spontaneous abortion, premature labor

Neuzil et al. Amer J Epidmiol 148:1094, 1998; Dodds et al. Can Med Assoc J 176:463, 2007; Rasmussen et al. Emerg Infect Dis 14:95, 2008; CDC. MMWR 12 May 2009

Burden on the health care system

- New York City: > 2500 patient visits at peak (50 hospitals)
  - 30-50 hospitalization daily
- Utah: 4% of total ED visits compared to < 2% at the peak of past winter season
- Intensive care unit: about 15-30% of hospitalized cases were admitted to ICU (USA, Canada)
- Mechanical ventilation: about 10% of hospitalized cases had mechanical ventilation (USA, Canada)

Pandemic (H1N1) 2009 and Health care workers

- Difficulty to dissociate community from workplace exposure
- Not over-represented in cases of pandemic (H1N1) 09 (to date)
- USA experience to 13 May 2009
  - 48 Health care workers (HCW) reported with pandemic (H1N1) 09 illness (2 hospitalized, no deaths)
  - On 26 documented reports, 50% acquired in healthcare setting, 46% in community, 4% without known exposure
  - Transmission in 12 "patient → HCW" and 1 "HCW → HCW"

MMWR 19 June 2009

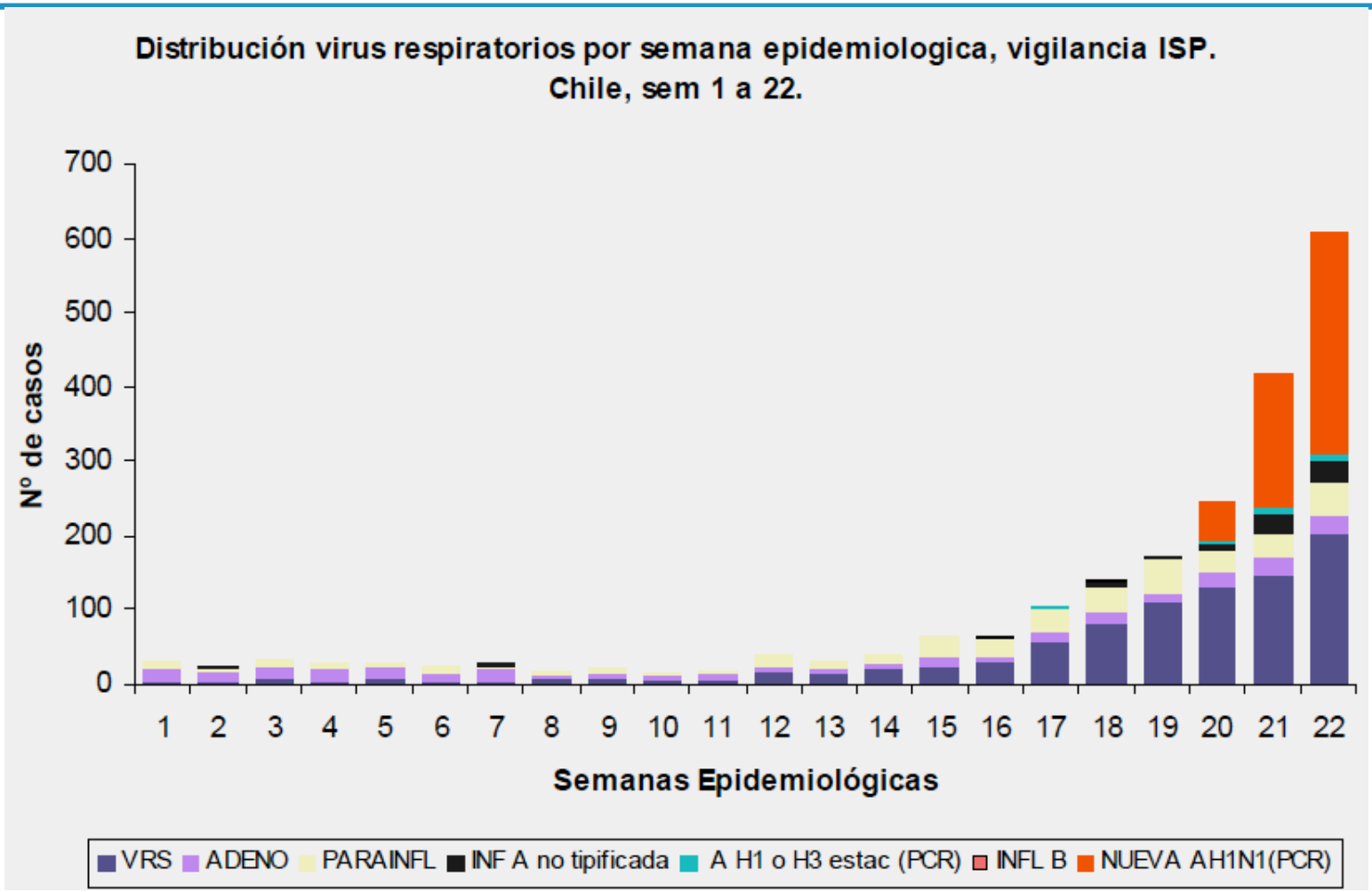
Pandemic (H1N1) 2009 and seasonal influenza viruses co-circulation

- Pandemic (H1N1) 2009 and seasonal viruses have co-circulated at varying levels over time in multiple countries
  - Potential for reassortments (e.g., oseltamivir resistance in N1)

- Pandemic (H1N1) 2009 (as % of isolates) in:
  - Chile: **~90%**; USA: **> 98%** (since mid-June)
  - Victoria, Australia: **~67%**; South Africa: **< 1%**

- Patterns in upcoming Northern Hemisphere season are uncertain; new drift variant H3N2 is under analysis

Co-circulation of Pandemic (H1N1) 09 and seasonal Influenza in Chile



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Severity of seasonal influenza outbreaks in developing countries

- Madagascar, July-August 2001
  - ARI attack rate: 67% in Ikongo district
  - 27,000 cases + 800 deaths (estimated CFR = 2.5%)
  - 54% of deaths attributed to ARI in children aged < 5years
  - Highest mortality rate in persons aged ≥ 60 years
- Congo, Democratic Republic, Nov-Dec 2002
  - ILI attack rate: 47% in Bosobolo District
  - Estimated CFR: 1.5%
  - CFR higher in: children < 5yrs (3.5%) + adults >65 yrs (3.2%)
- Both outbreaks attributed to **circulating H3N2 virus**

Pandemic (H1N1) 2009
Summary

- **High but variable transmissibility** in countries
  - Explosive outbreaks in semi-closed communities
- **5-45 years old people** most commonly affected
- Hospitalization rates and case-fatality in young adults higher than during seasonal influenza
  - Groups at **risk** for severe illness: **pregnant women**; those with **asthma, obesity, chronic heart or lung disease, cancer, immunosuppression**
- Possible **co-circulation** of seasonal and pandemic viruses
- **Severity** expected to be higher in **developing countries**

Examples of considerations for establishing priorities for use of pandemic vaccine

- As noted by Meltzer et al, "vaccination priorities depend on the objectives".
  - *If the **objective** is maintaining the functioning of a country's critical infrastructure,* then vaccinating the required personnel will be a priority.
    - E.g. Health care staff
  - *If the **objective** is preventing the greatest number of deaths,* then vaccinating groups at high risk of influenza-related mortality would be the first priority.
    - E.g. People with underlying conditions (but severe cases have been reported in healthy young adults)
  - *If the **objective** is to reduce pandemic virus transmission within the community,* then targeting children is a consideration.
    - E.g. School age children depending on local patterns
- We are still at the very early stage of the pandemic – More information is needed on the situation in the southern hemisphere, in developing countries and from specific studies currently ongoing.

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