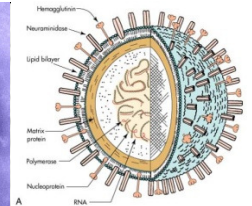
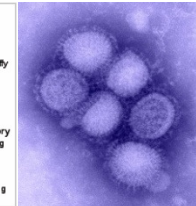
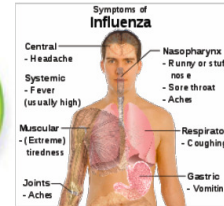


# Pandemic Influenza: Global and Philippine Situation

**Beatriz Puzon-Quiambao, MD, FPPS, FPIDSP**  
**Research Institute for Tropical Medicine**

**17<sup>th</sup> Annual PIDSP Convention, February 3-4, 2010**

# Chronology of Events



**March-  
April, 2009**

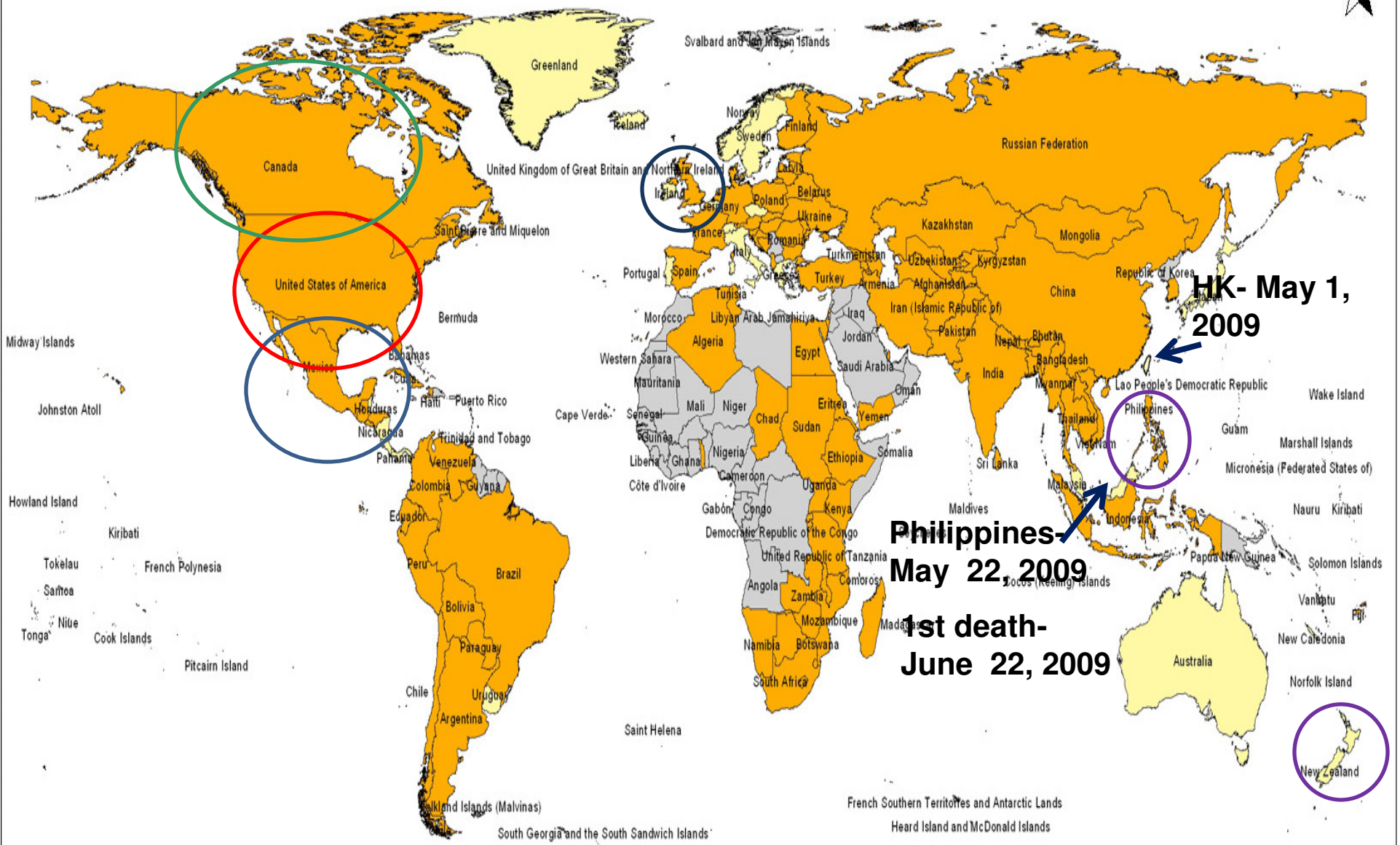
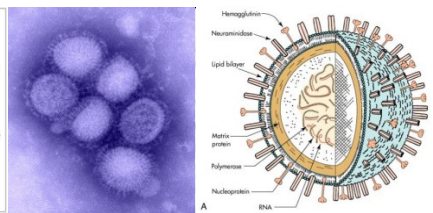
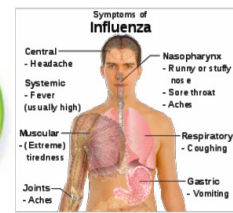
**Outbreaks of ILI  
in Mexico**

**Same virus as the  
one isolated from  
children in  
California**

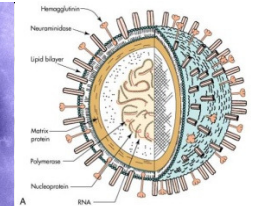
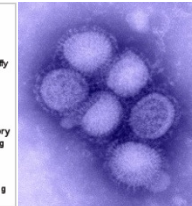
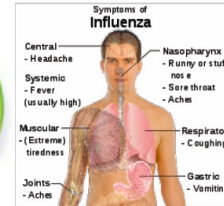
**April, 2009**

**Spread of virus all  
over Mexico and  
the US**

**Spread of virus  
to other countries**

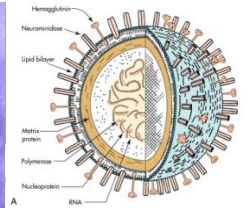
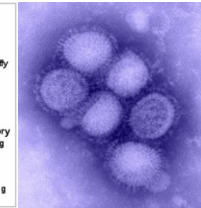
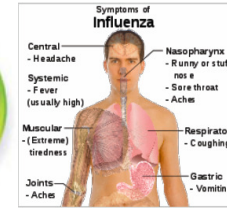


# Phases of WHO pandemic alert

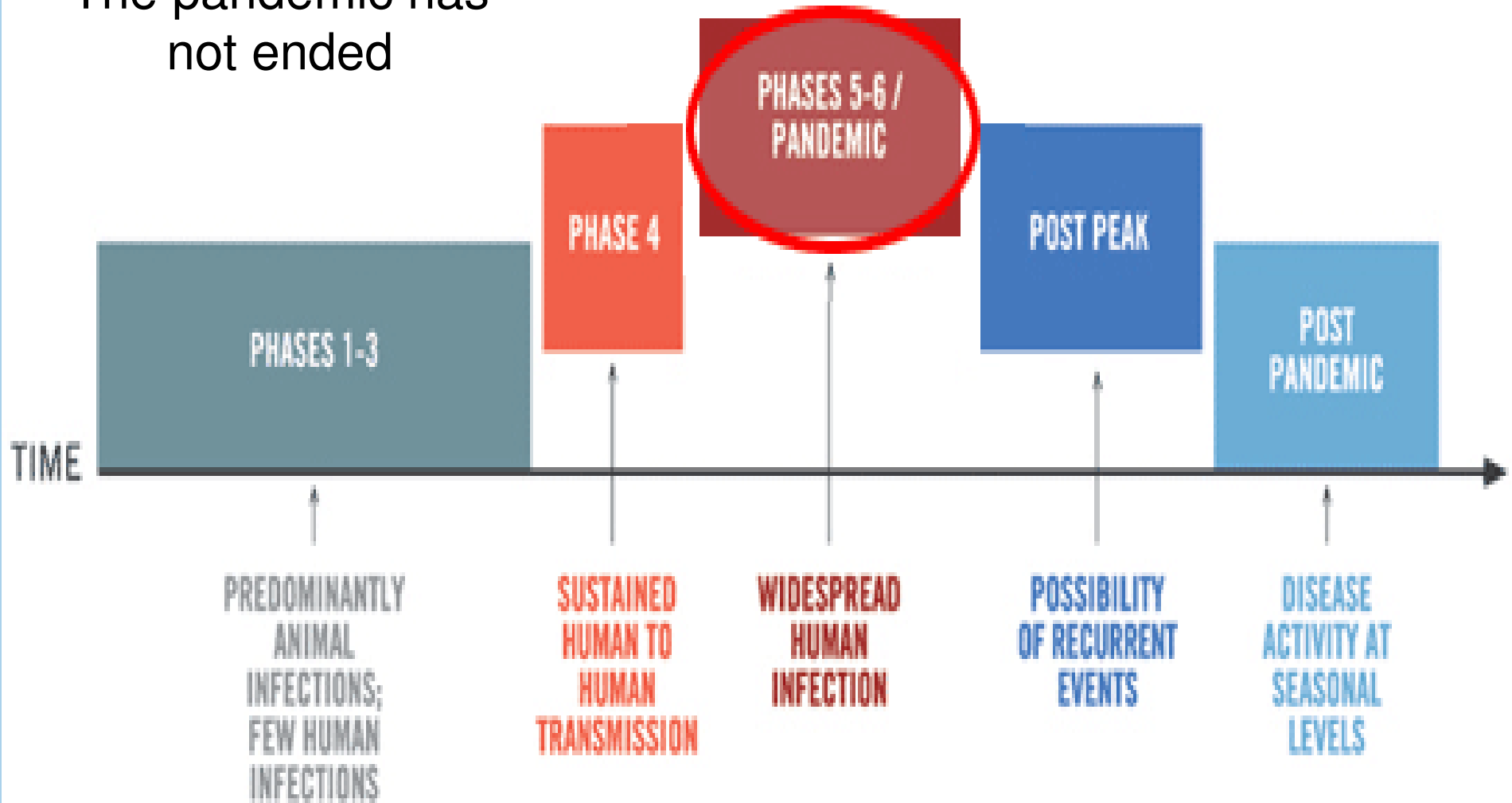


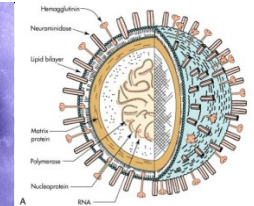
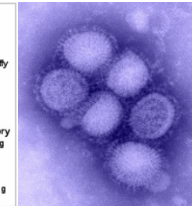
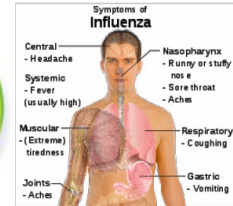
Phase 1	No animal influenza virus circulating among animals have been reported to cause infections in humans
Phase 2	An animal influenza virus circulating in domesticated or wild animals is known to have caused infection in humans and is therefore considered a specific potential pandemic threat
Phase 3	An animal or human-animal influenza reassortant virus has caused sporadic cases or small clusters of disease in people, but has not resulted in human-to-human transmission sufficient to sustain community level outbreaks
Nov, 2005	
Phase 4	Human-to-human of an animal or human-animal influenza reassortant virus able to sustain community level outbreaks has been verified
April 27, 2009	
Phase 5	The same identified virus has caused sustained community level outbreaks in two or more countries in one WHO region
April 29, 2009	
Phase 6	In addition to the criteria defined in Phase 5, the same virus has caused sustained community level outbreaks in at least one other country in another WHO region
June 11, 2009	

# PANDEMIC INFLUENZA PHASES



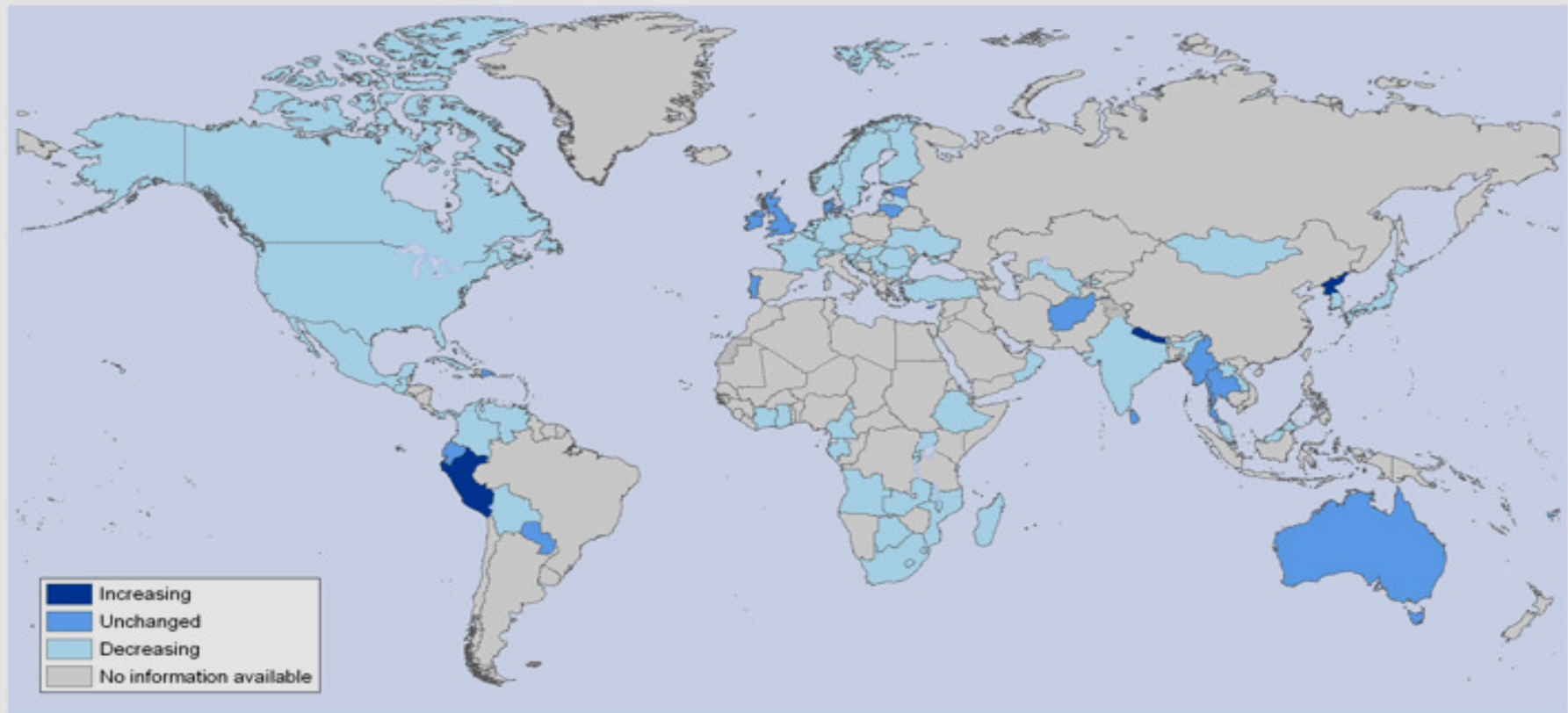
The pandemic has not ended





## Timeline Trend\* of respiratory disease activity Compared to previous week

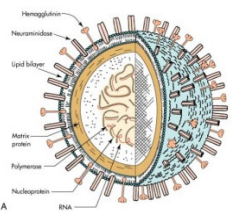
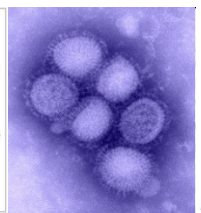
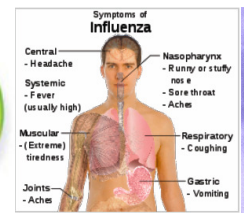
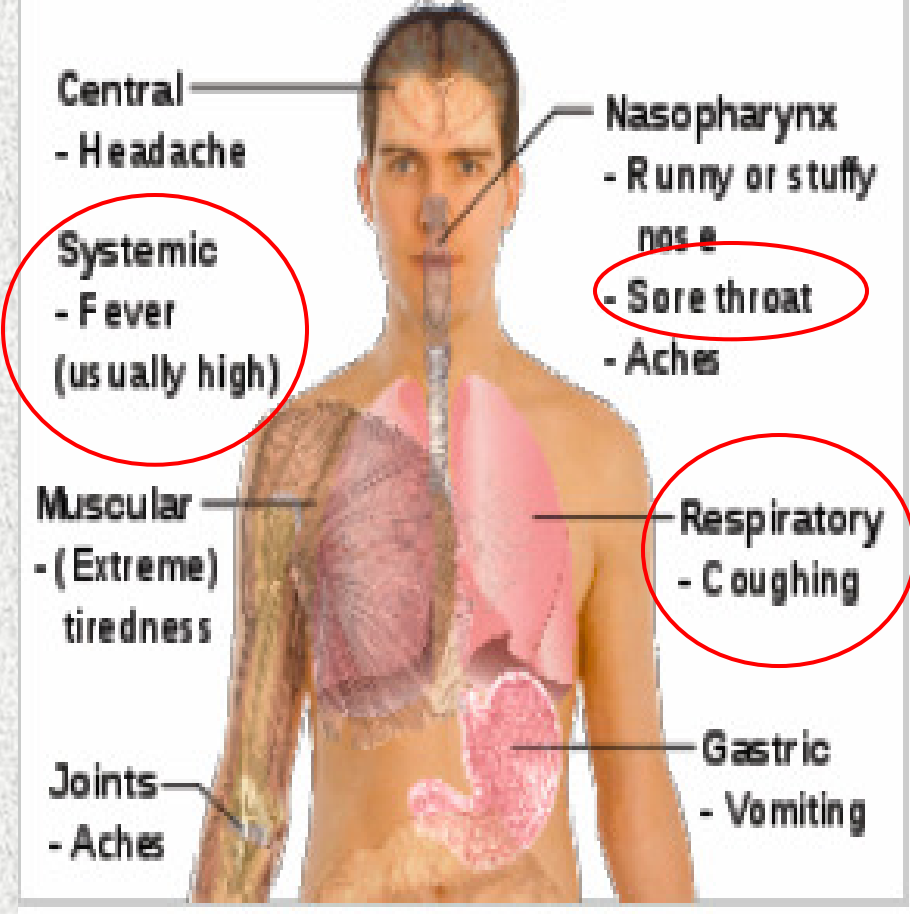
Status as of: week 01, 2010 (28 December 2009–03 January 2010)



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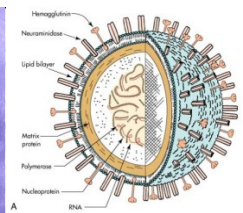
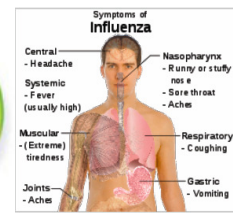
\* Trend refers to the change in the level of respiratory disease activity compared to the previous week.

# Symptoms of Influenza



Transmitted by coughing, sneezing

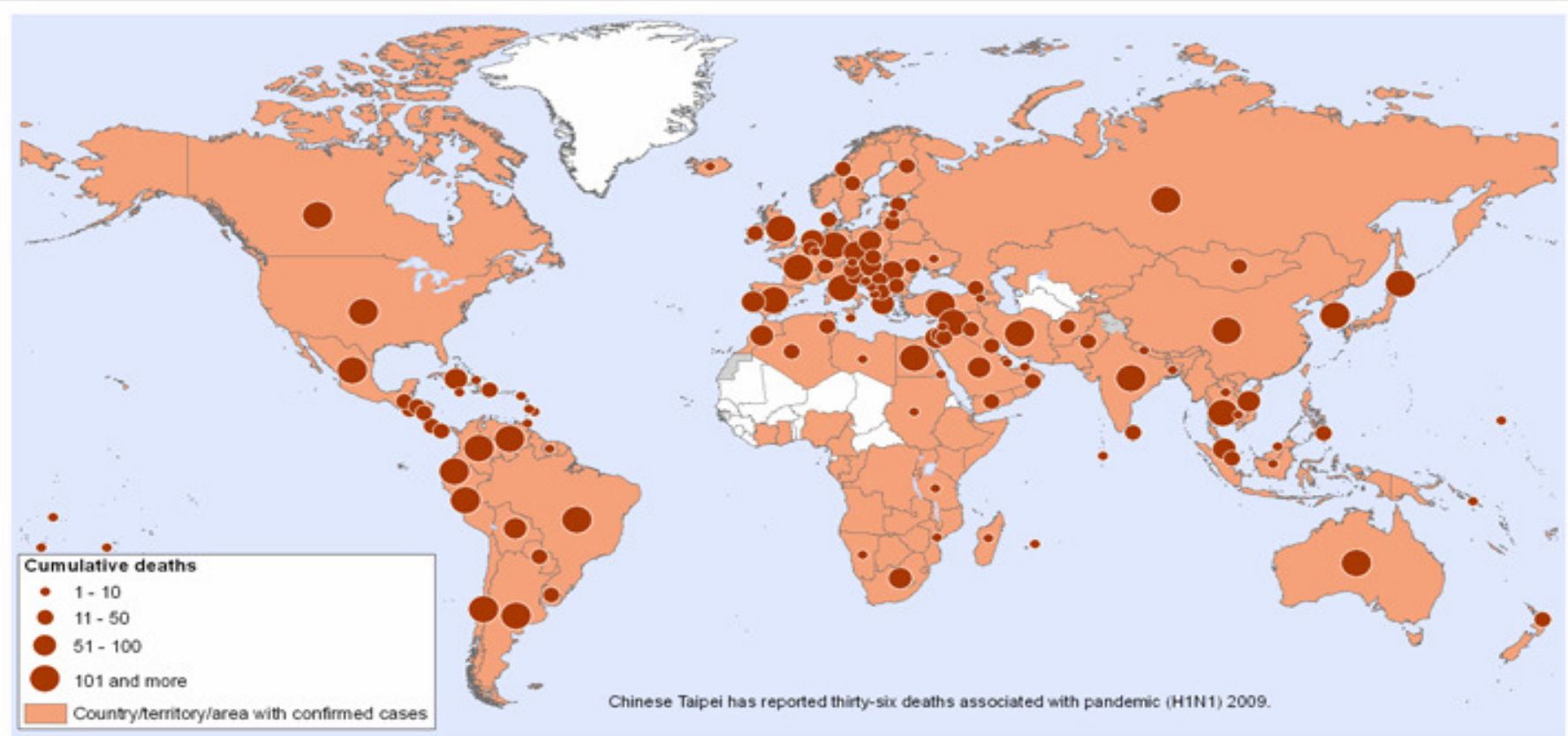
Full genomic sequence  
**A/California/04/2009 A(H1N1)**



**Timeline (22 July 2009 onwards)  
Pandemic (H1N1) 2009 laboratory confirmed cases  
And number of deaths as reported to WHO**

**Status as of: 10 January 2010**

Previous

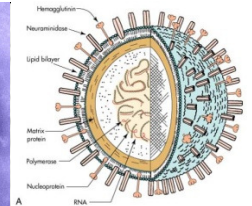
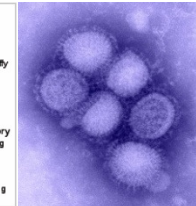
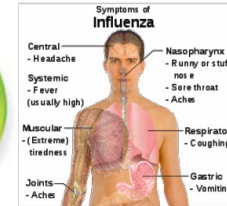


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# Global situation

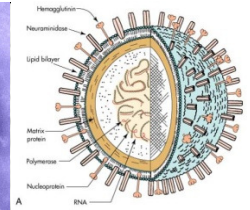
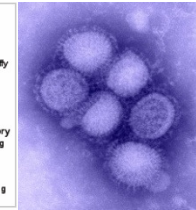
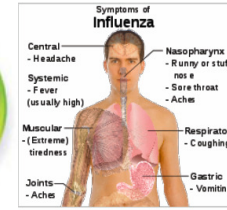
## WHO update 85, 24 Jan 2010



Region	Cumulative # of Deaths
South East Asia	1426
Western Pacific	1555
Eastern Mediterranean	1002
Africa	131
Americas	7166
Europe	3429
Global	14711 *

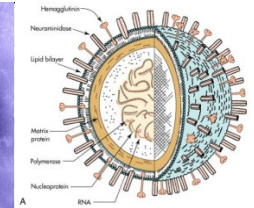
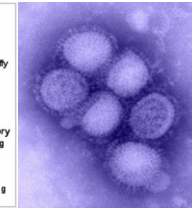
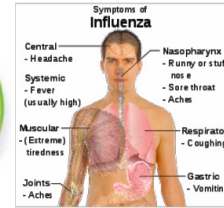
\* The reported number of fatal cases is an under representation of the actual numbers as many deaths are never tested or recognized as influenza related.

# Estimates



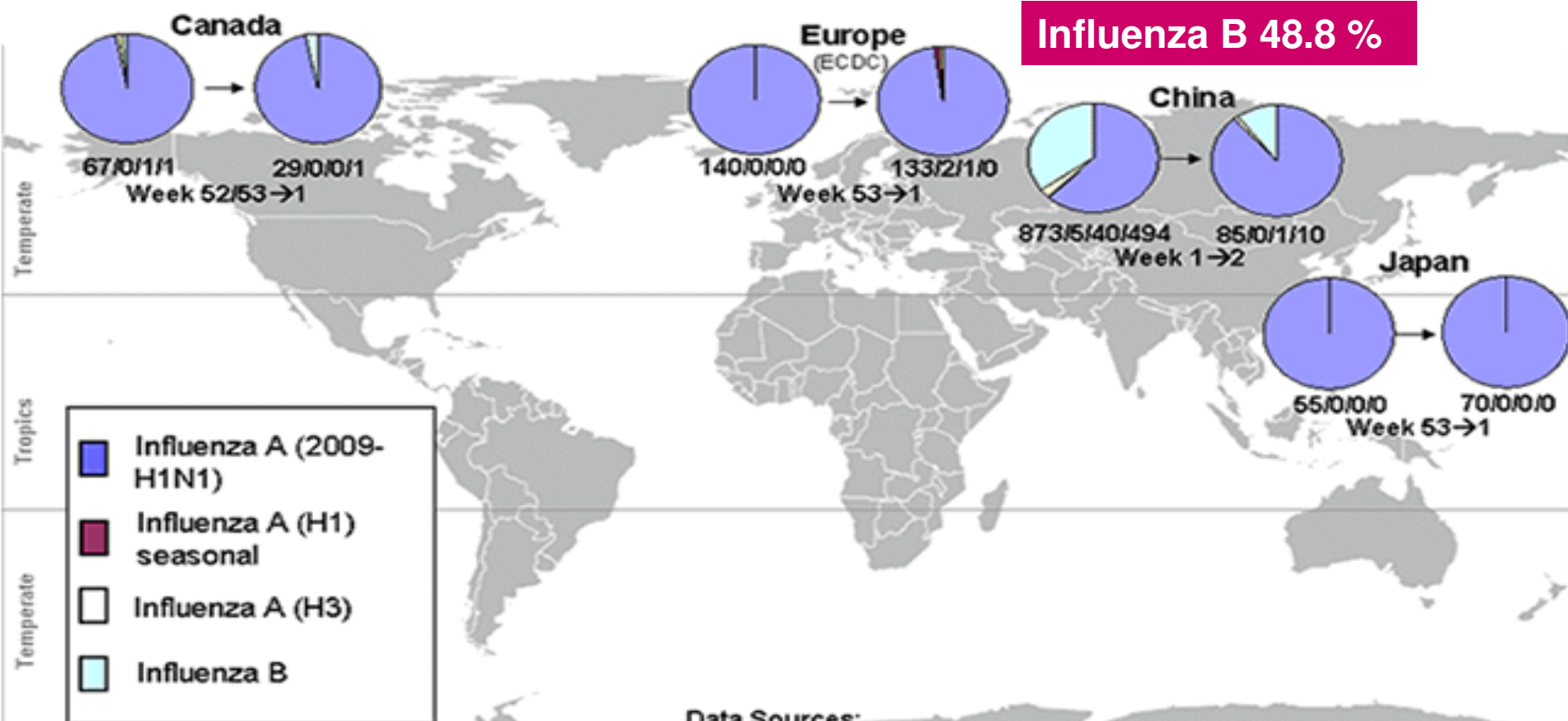
- US (April–July 2009) - Actual number of cases may have been **up to 140×** greater than the reported number of laboratory confirmed cases
- Median multiplier of reported to estimated cases was 79: **that is, every reported case of pandemic (H1N1) 2009 may represent 79 (range 47-148) total cases**
- Every hospitalized case of PI may represent a median of 2.7 total hospitalized persons (range 1.9–4.3)

# 2009 H1N1 influenza virus is the predominant virus in circulation worldwide



Week 53: December 28- January 3

**Influenza B 48.8 %**

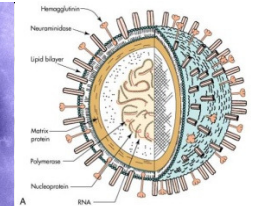
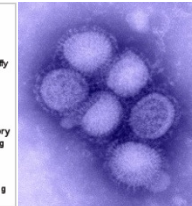
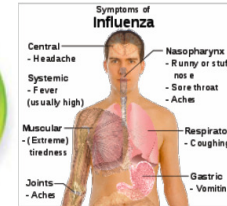


Data Sources:

Canada: FluWatch (<http://www.phac-aspc.gc.ca/fluwatch/index-eng.php>)  
 China and Japan: FluNet (<http://gamapservet.who.int/GlobalAtlas/home.asp>)  
 Europe: ECDC (<http://www.ecdc.europa.eu/en/Pages/home.aspx>)  
 United States: CDC

www.who.int

# PHILIPPINES



## Specimens Tested for Pandemic H1N1

May 1, 2009 to January 15, 2010

Result	Number (%)
Negative	5224 (45.0)
Seasonal Influenza	521 (4.5)
<b>Pandemic H1N1</b>	<b>5864 (50.5)</b>
TOTAL	11,618

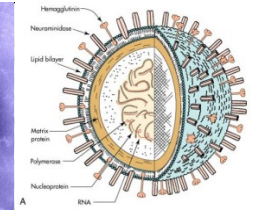
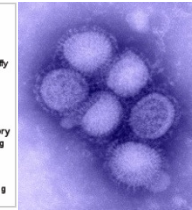
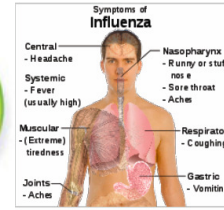


**92 % of all influenza isolates**

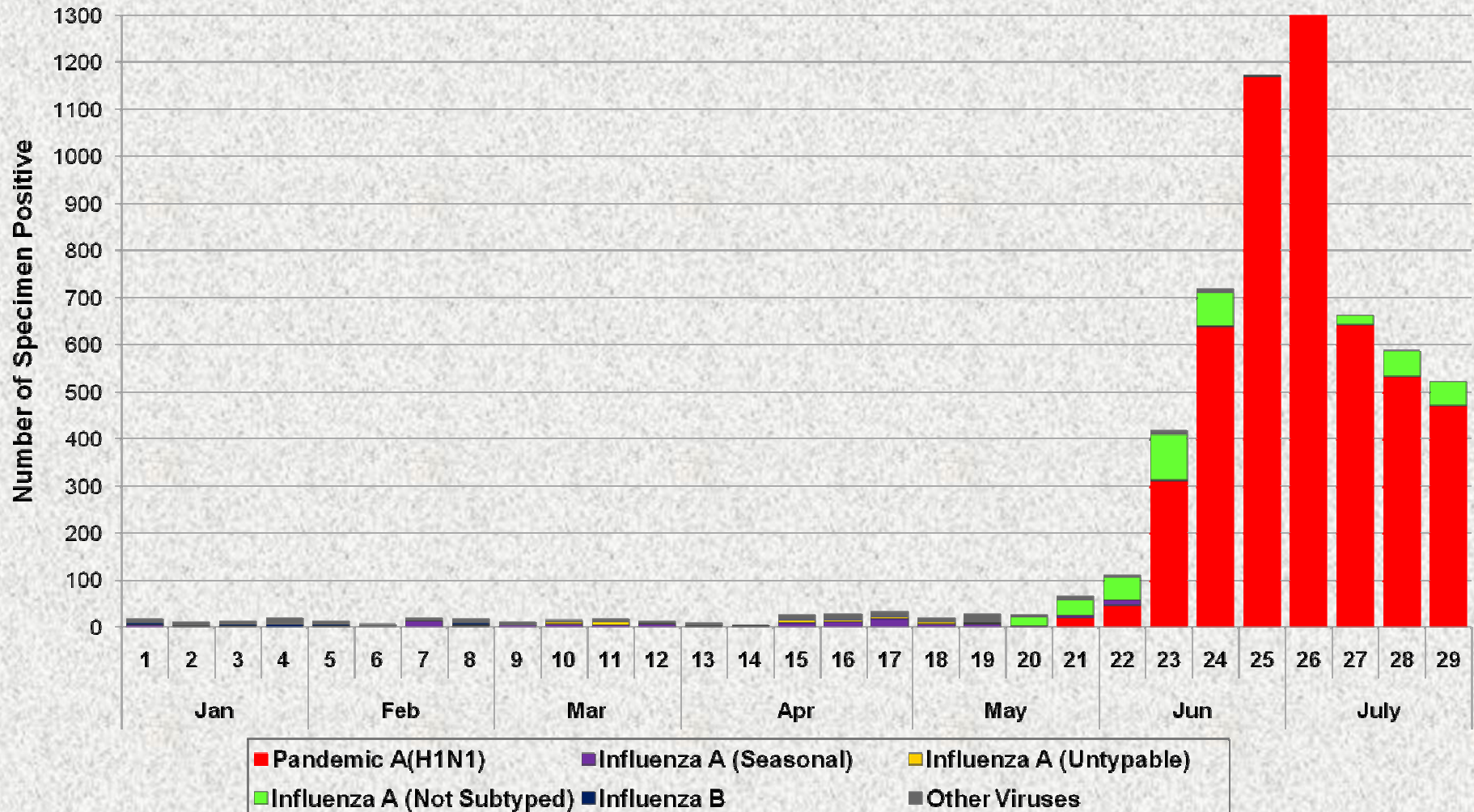
**Sources:**

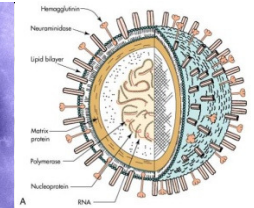
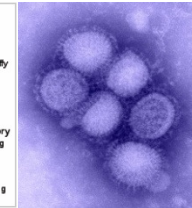
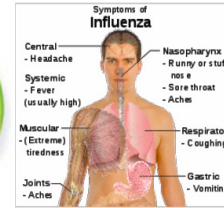
**Influenza Surveillance (data up to week 25)**

**RITM Molecular Biology Results for Pandemic H1N1 Tests  
(data up to week 29)**

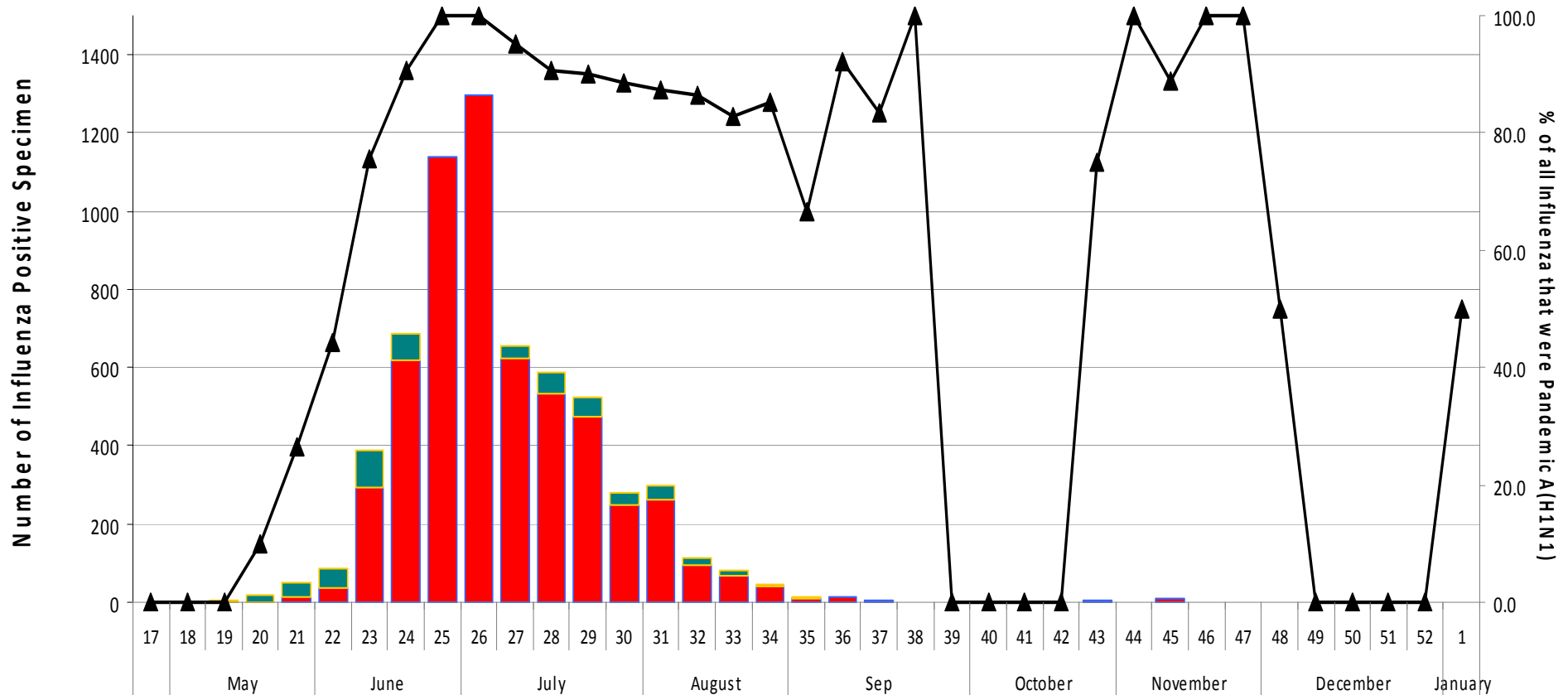


## Number of Specimen Positive for Influenza and Other Viruses, January - July 2009





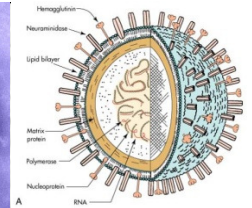
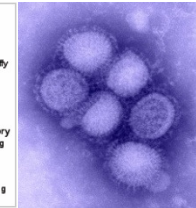
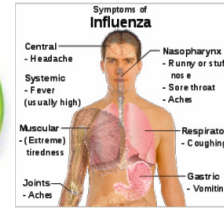
**Number of Specimen Positive for Seasonal Influenza and Pandemic A(H1N1), RITM-MBL  
from May 1, 2009 to January 10, 2010**



Note: RITM-NIC Lab did not perform  
Influenza A screening in weeks 25-26

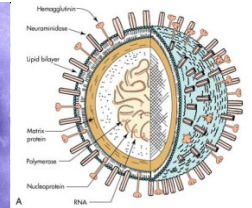
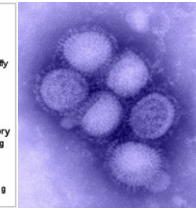
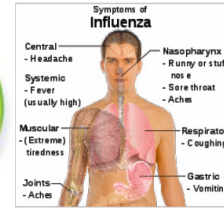


# Oseltamivir resistance



- WHO network of laboratories - viruses from all outbreaks remain virtually identical
  - no signs that the virus has mutated to a more virulent or lethal form
- Only a handful of pandemic viruses resistant to oseltamivir have been detected worldwide, despite the administration of many millions of treatment courses of antiviral drugs
  - No instances of onward transmission of drug-resistant virus have been documented to date
  - Intense monitoring continues through the WHO network of laboratories

# Clinical Characteristics



- Clinical picture - consistent across all countries
  - Majority of patients continue to experience mild illness
  - Although the virus can cause very severe and fatal illness, also in young and healthy people, the number of such cases remains small

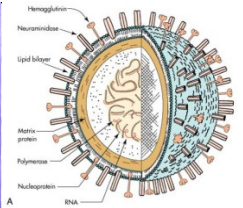
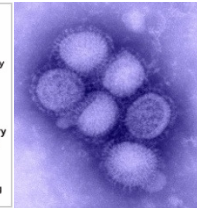
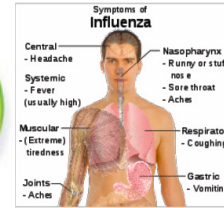
WPRO update, 11 Jan 2010

- “moderate” severity - majority of patients recovering, even without medical treatment, within a week of the onset of Sx

PAHO regional update, 11 Jan 2010

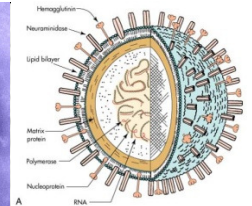
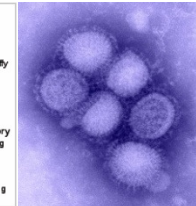
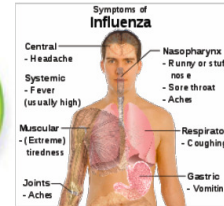


# Clinical Characteristics



- Teenagers & young adults = majority of cases
  - Nearly 80% of all cases are < 30 years of age
  - hospitalization rates highest in very young children
- hospitalization – 1 to 10 %
  - 10% to 25% require ICU admission
  - 2% to 9% have a fatal outcome
  - 7% to 10% pregnant women in 2<sup>nd</sup> or 3<sup>rd</sup> trimester
- Pregnant women are 10x more likely to need ICU care compared with the general population

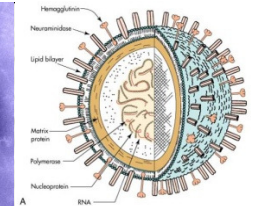
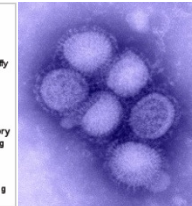
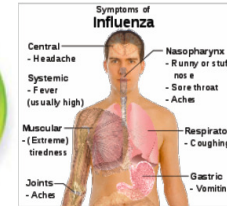
# Clinical Characteristics



- As much as 41 % did not fulfil the case definition for probable case
  - 19 % did not have fever  $> 38^{\circ}\text{C}$  or Hx of fever
- ICU care – 7-19 %
  - 13 % required mechanical ventilation
- Death – 5 % due to refractory hypoxemia
- Pre-existing conditions – 32-40 %
- Bacterial co infection – 10-16 %
- Viral co infection – 19 %
  - Those with concomitant viral infection were younger

Hackett et al, Lancet, Aug 09  
Libster et al , NEJM, Jan 2010

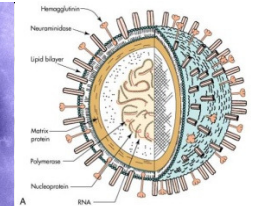
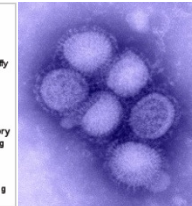
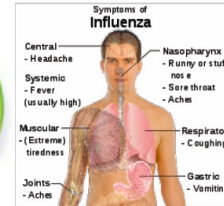
# Comparison with seasonal flu



Characteristics	Seasonal Flu	Pandemic Flu
Seasonality	winter	Summer and winter
Mean age	53 yrs (1-75 yrs)	21 yrs (2-63 yrs)
Severe cases	90 % in adults > 65 yrs	Children < 5 yrs, adults < 50 yrs
Risk factors	Pregnancy, underlying diseases, extremes of age	Pregnancy, underlying diseases, Obesity
GI symptoms	5 %	25 % diarrhea, 33 % nausea/ vomiting
Bacterial co-infection	24 %	4 %

California Pandemic (H1N1) working group, JAMA  
 Kelly H, Grant K. Euro Surveill, Aug 2009

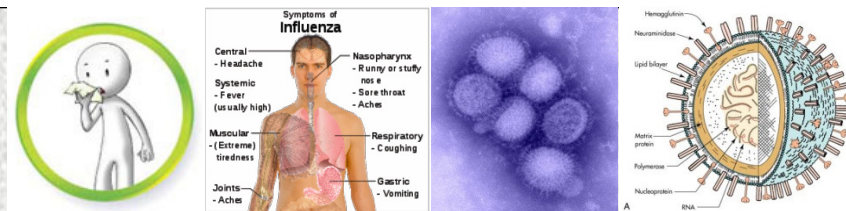
# Comparison with seasonal flu



Characteristics in <u>CHILDREN</u>	Seasonal Flu (US)	Pandemic Influenza (B. Aires)
Hospitalization rate	10.3/100,000	20.9/100,000
Death rate	0.2/100,000	7.6/100,000
Co infection with RSV	11 %	19 %
ICU admission	5 %	19 %
Oxygen supplementation	22%	82 %
Mechanical ventilation	0	17 %

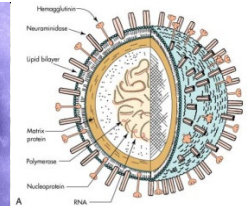
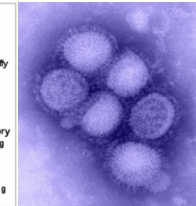
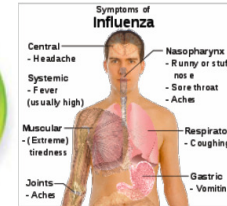
Libster et al, NEJM 362 (1): 45-55, Jan 2010

# Risk factors

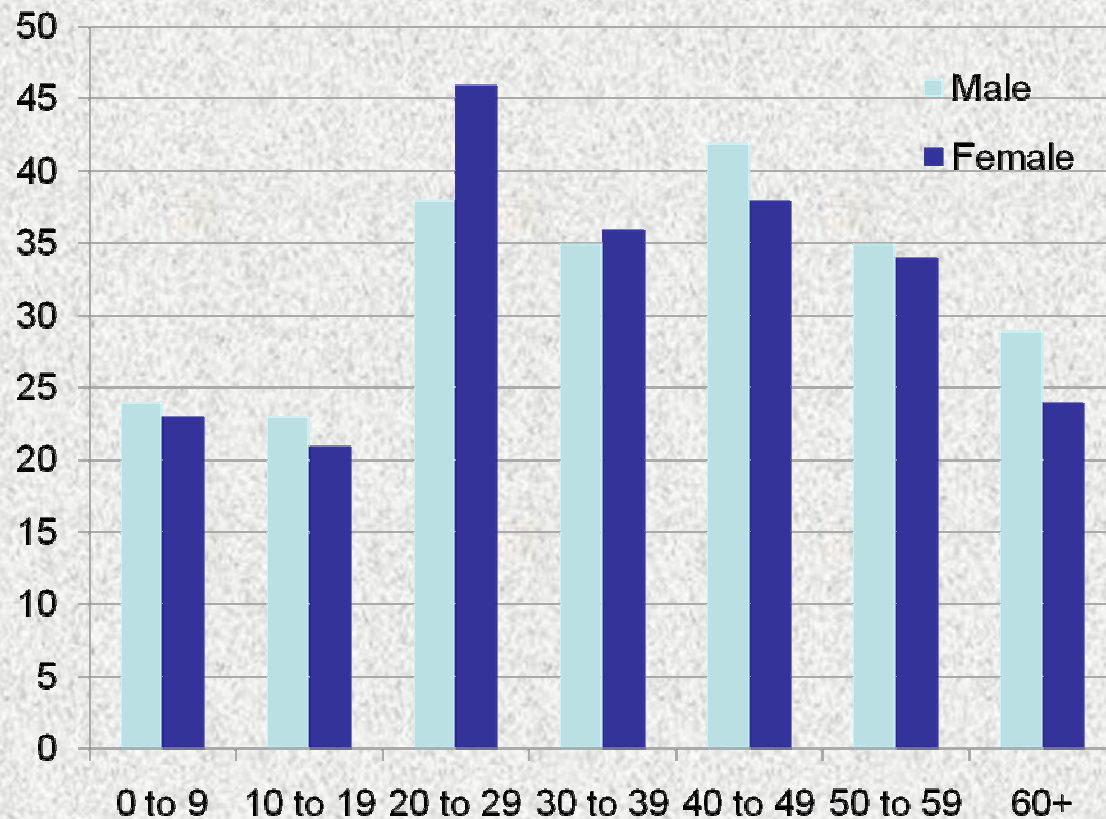


- The groups experiencing severe disease and requiring hospitalization the most are:
  - young children (younger two years of age)
  - people with chronic underlying medical conditions, e.g. asthma or other chronic respiratory disease (33% vs 13%)
  - massive obesity (BMI > 35) - 29% vs 5%
  - pregnant women (9% vs 1%),

# Risk factors



## Age and gender distribution of deaths



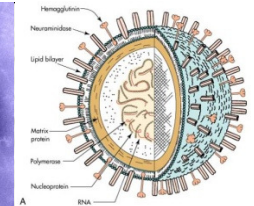
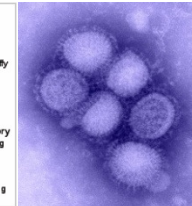
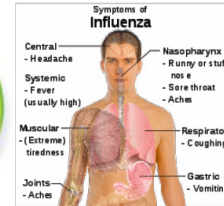
Vaillant et al, Eurosurveillance Aug 2009



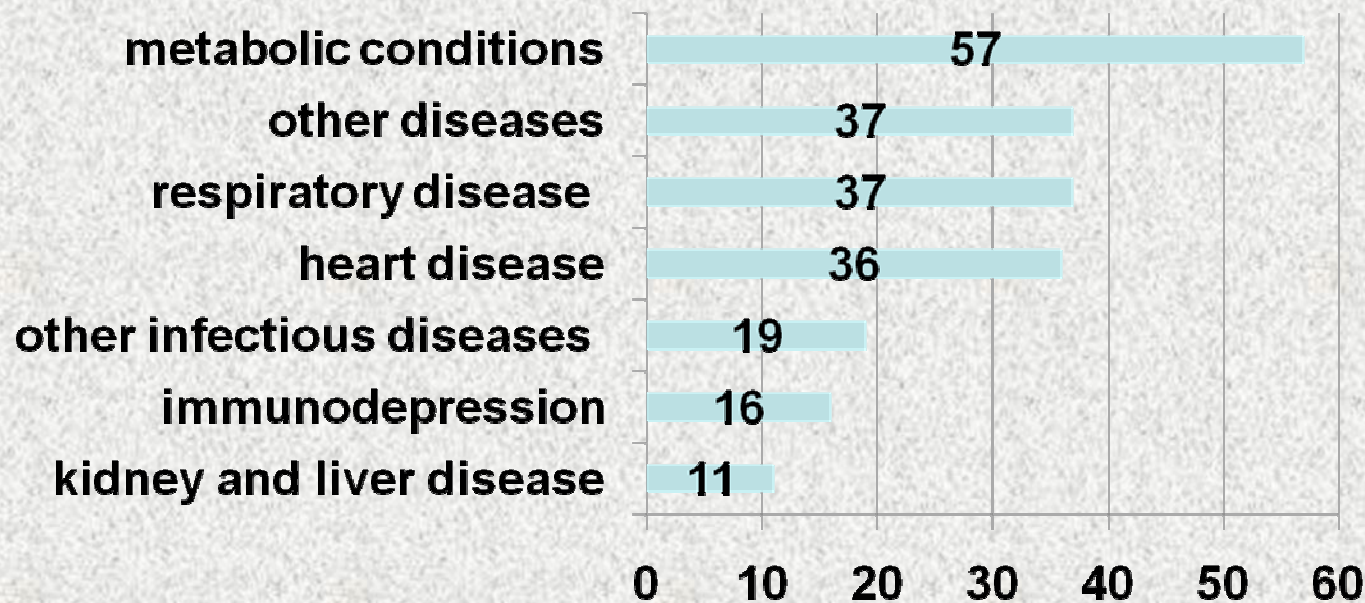
14 % of all pandemic H1N1 related deaths in the US occurred among children < 18 yrs

CDC, Jan 22, 2010 update

# Risk factors

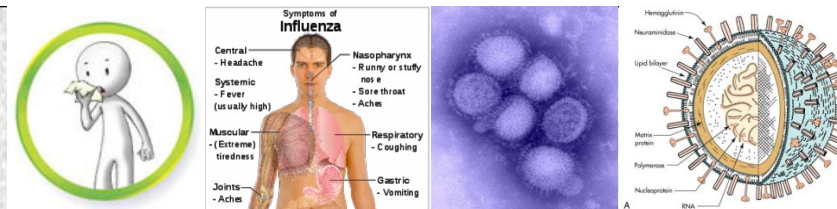


- Underlying illnesses
  - Of 241 deaths, 90 % had underlying disease
  - 27% of children and 20 % of young adults had no underlying disease



Vaillant et al, Eurosurveillance Aug 2009

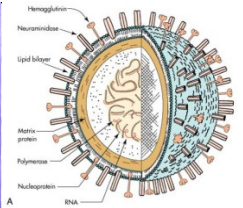
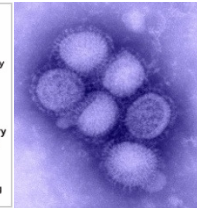
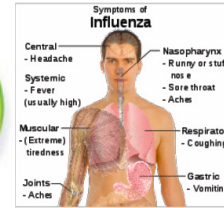
# Risk factors



- Obesity (BMI > 30)
  - Most frequently identified underlying condition
  - 9/10 severely ill patients with H1N1 infection needing ventilatory support were obese
    - 7 were severely obese
    - 9 had multi-organ dysfunction
    - 5 had pulmonary emboli
  - 2/3 deaths were obese
  - Obese are more likely to have underlying medical conditions



# Risk factors

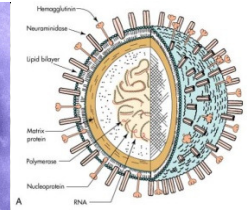
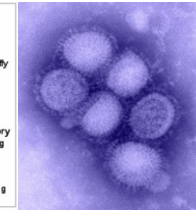
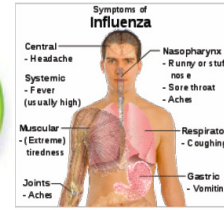


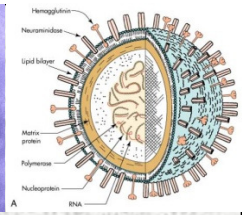
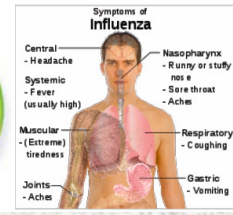
- Pregnancy
  - 4x more likely to need admission
  - Shortness of breath 2.3x more common
  - Of 45 deaths in the 1<sup>st</sup> 2 months of the outbreak in the US, 6 (13%) were pregnant
    - All developed viral pneumonia and ARDS
    - None received anti-virals within 48 hrs of Sx onset

Jamieson et al. Lancet 2009

# Risk factors

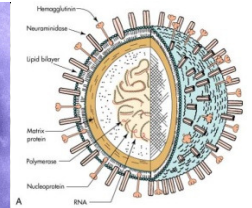
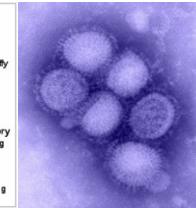
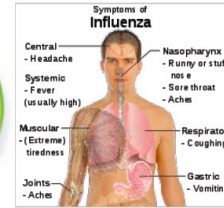
- Minority populations
  - Hospitalization rates for the pandemic (H1N1) 2009 virus in Wisconsin
    - non-Hispanic whites – 11 per 100 000 population
    - Blacks - almost 38 per 100 000 population
    - Hispanics - > 320 per 100 000 population
  - Reasons - higher rates for some of the underlying medical conditions (DM, CV disease, obesity), poorer access to health care



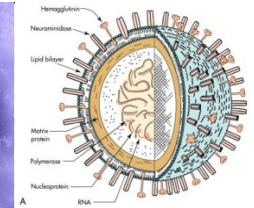
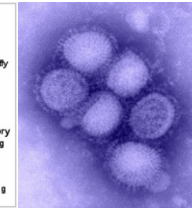
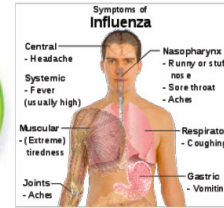


# Local Updates

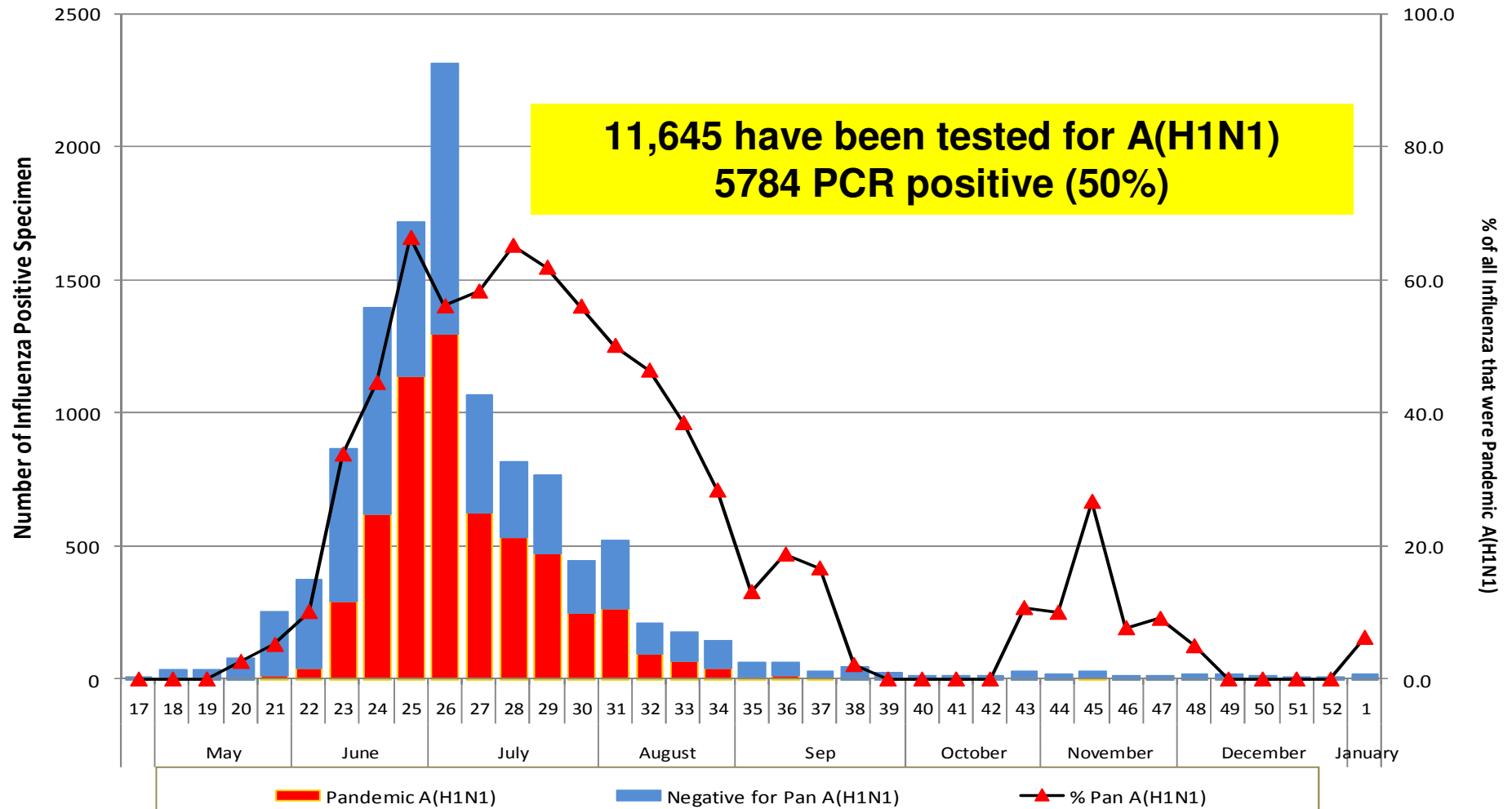
# Influenza-like Illness surveillance



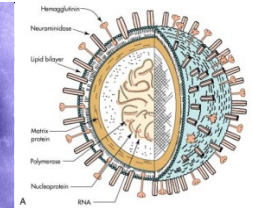
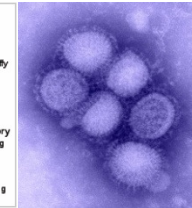
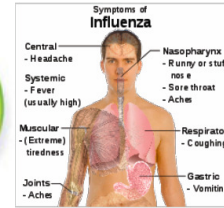
- H1N1 integrated in national ILI surveillance
- 73,341 ILI cases from Jan 1 to Nov 9, 2009
  - peak of activity on wks 25-28, decreased activity noted by wk 29
  - Median age 11 yrs (1-109 yrs)
    - 19 % in 1-4 yr old age group
  - 51 % males
  - 161 deaths (CFR 0.2 %)
- 7.5 % due to H1N1
  - Increase by wk 22, peak on wk 25 and decline by wk 26
  - 32 deaths (CFR 0.6 %)



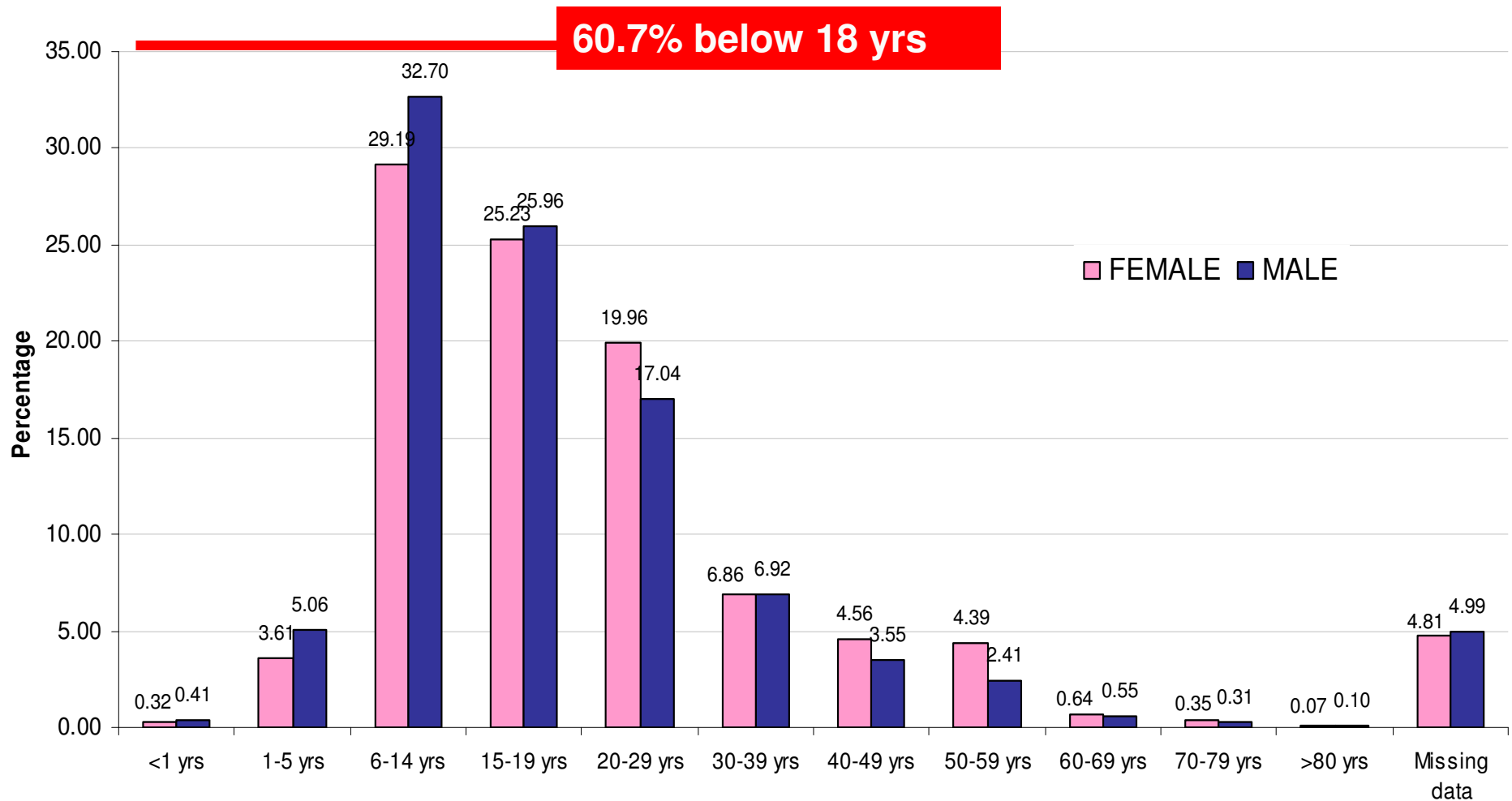
## Number of Specimen Positive for Pandemic A(H1N1), RITM-MBL, May 1, 2009 to January 9, 2010



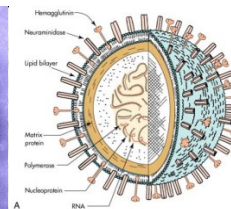
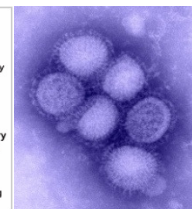
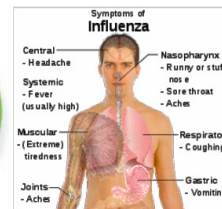




## Age and Sex Distribution of Patients Positive for Pan A(H1N1), RITM-MBL, May 1, 2009 to January 10, 2010



# Clinical Manifestations



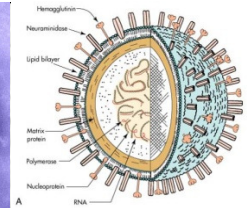
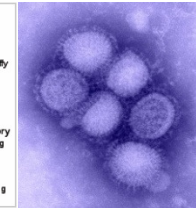
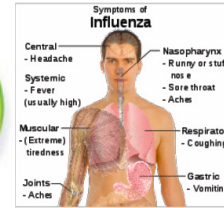
SYMPTOM	NEGATIVE N(%), where N=5389	POSITIVE N(%), where N=5451
Fever	4494	<b>4847*</b>
Cough	4130	<b>4615*</b>
Sore throat	2557	<b>2727*</b>
Runny nose	2374	<b>2626*</b>
Muscle pain	1251	<b>1488*</b>
Headache	971	1043
Body pain	634	702
Difficulty of Breathing	190	212
Diarrhea	239	230
No symptom at all	<b>109*</b>	80

\* Significantly higher ( $p < 0.05$ , Binomial test)

National Influenza Center, 2009



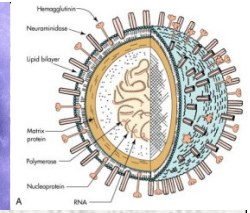
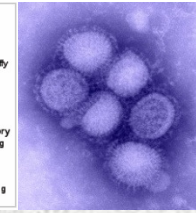
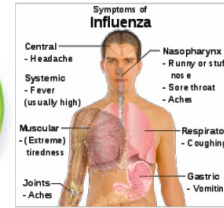
# Mortalities



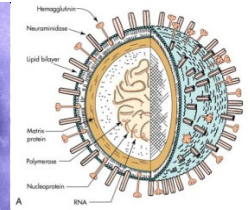
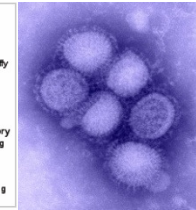
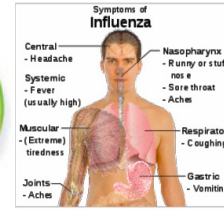
- As of Nov 2009, 32 deaths
- Analysis of 1<sup>st</sup> 29 deaths:
  - Age range – 10 days to 77 yrs
    - 17 % below 5 years old, 10 % elderly
    - 59 % between 20 to 59 yrs
  - 66 % females
  - 52 % had co-morbid conditions; 2 were pregnant
  - 1 with Hx of travel, 2 with contact to a known case
  - 2 had seasonal flu vaccine



# Pediatric Mortalities



- 9/29 (31%) were children < 18 yrs
  - Age range – 10 days to 17 yrs
  - 3 M (33%), 6 F (67%)
  - Symptoms
    - Fever 89%; Cough 78%; Colds 33%; Vomiting 33%; Sore throat 22%; Difficulty of breathing 22%
  - Duration of illness – ave 14 days (range 4 days to 5wks)
  - Duration of illness upon consult – ave 4.7 days (range 0 to 14 days)
  - Underlying illnesses – seizure disorder, asthma, toxic goiter
  - Cause of death – sepsis, pneumonia



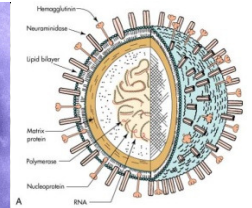
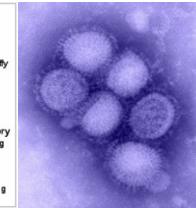
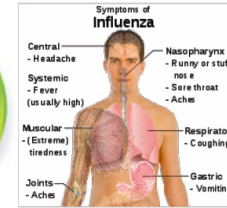
## Oseltamivir resistance

- Mutations associated with resistance have not been detected
- D225G change noted in Norway was not detected in Philippine isolates

## Molecular epidemiology

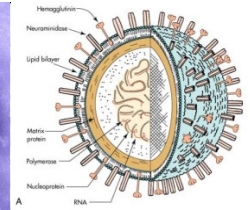
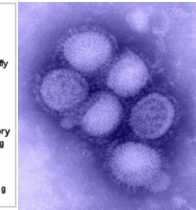
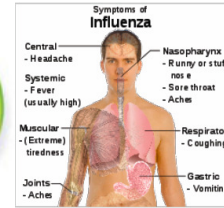
- Preliminary results show that Philippine Pdm H1N1 isolates belong to Clade 7, with other isolates possible belonging to new clades

# DOH response



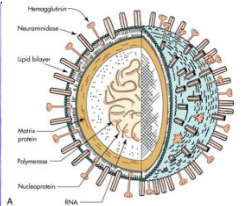
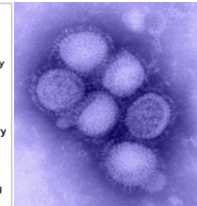
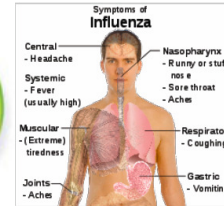
- PANDEMIC declared - Can no longer prevent the spread of infection
- June 24, 2009: Shifted from Rapid containment (case finding and contact tracing) → mitigation (care of sick individuals)
  - Selective admission, laboratory confirmation and anti-viral treatment
  - Home quarantine for all uncomplicated cases

# Preparing for the 2<sup>nd</sup> wave



- Health facility development
  - Referral hospitals - RITM, SLH, LCP, VSMC, DMC
- Laboratory upgrade
  - RITM – national reference laboratory
  - SLH, LCP, Med City, Baguio GH, Vicente Sotto MC, Davao MC
- Expansion of ILI surveillance
  - 2005 - 17 sentinel sites in 4 regions (5 hosp, 12 HC)
  - 2007 – 29 sites in 9 regions
  - 2009 - 53 sites in 2009 in 9 regions (20 hosp, 33 HC)

# Preparing for the 2<sup>nd</sup> wave

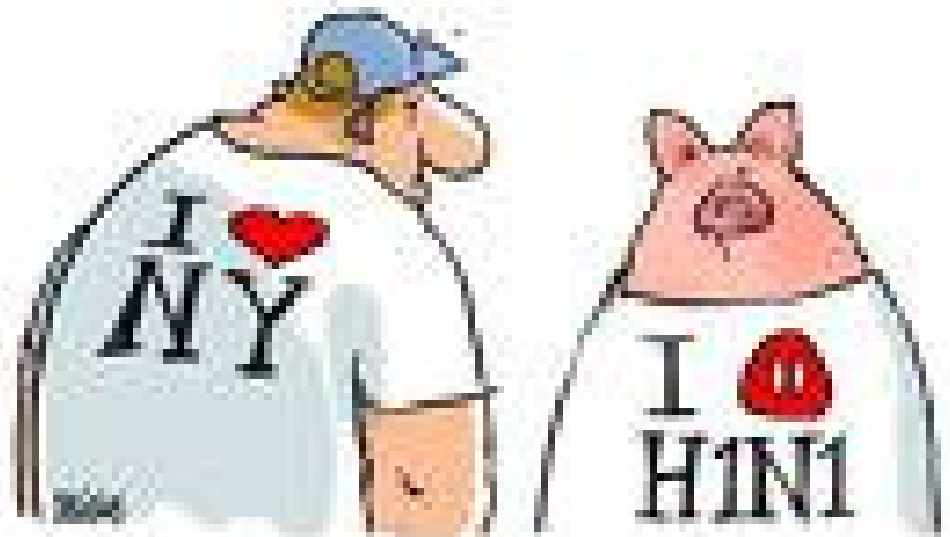


- Development of Interim guidelines 1-22
  - IG 22: Clinical management of suspected and confirmed Human Pandemic (H1N1) 2009 infection
  - IG 2: Infection control
- Vaccination with H1N1 vaccine



PANDEMIC

Thank you



# History of the Outbreak

- **March - early April 2009**
  - outbreaks of respiratory illness and increased reports of patients with ILI in several areas of Mexico
  - April 12 - outbreak of ILI in a small community in the state of Veracruz reported to PAHO in accordance with International Health Regulations
  - April 17 - a case of atypical pneumonia in Oaxaca State prompted enhanced surveillance throughout Mexico
  - April 23 - several cases of severe respiratory illness laboratory confirmed as swine-origin influenza A (H1N1) virus (S-OIV) infection were communicated to the PAHO
  - Sequence analysis revealed that the patients were infected with the same S-OIV strain detected in two children residing in California



# History of the Outbreak

- **USA**
  - April 24, 2009 - CDC reported 8 confirmed cases of S-OIV infection in Texas and California
  - The strain identified in U.S. patients was genetically similar to viruses subsequently isolated from patients in Mexico
  - April 28 - approximately half of all U.S. cases of S-OIV infection had been confirmed among students and staff members at a New York City (NYC) high school