Natural History of Disease and Biological Aspects of Pandemic Influenza A (H1N1)

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Influenza A Viruses

- Influenza A viruses categorized by subtype
  - Classified according to two surface proteins

  - **Hemagglutinin (HA)** – 16 known
    - Site of attachment to host cells
    - Antibody to HA is protective

  - **Neuraminidase (NA)** – 9 known
    - Helps release virions from cells
    - Antibody to NA can help modify disease severity
Influenza A Viruses

- Aquatic birds reservoir for viruses with all HAs and NAs
  - H1 - H16
  - N1 - N9

Aquatic birds

- Poultry
- Humans
- Pigs
- Horses
- Aquatic mammals
- Cats
- Dogs
Influenza A Viruses

- Influenza A viruses are dynamic
  - Continue to evolve in strains – unpredictable
  - Antigenic monitoring needed
  - Genetic monitoring needed
  - Gene reassortment can occur with other influenza A viruses
  - Antiviral susceptibility can change
  - Virulence to cause severe disease can change
Timeline of Emergence of Influenza Viruses in Humans

- B
- H1 “Spanish”
- H2 “Asian”
- H3 “Hong Kong”
- H1 “Russian”
- Avian
  - H9 → H7
  - H5 → H5

Seasonal vaccines

Pandemic vaccines

Seasonal Influenza - Hospitalizations (U.S.)

Average of >200,000 influenza-related hospitalizations/year

- Estimated by modeling studies using retrospective data and influenza surveillance data

Children:

- High rates in young children <2 years
- Children 2-5 years next highest
- High rates for children with chronic high-risk conditions

Adults:

- Highest rates in persons ≥65 years
- High rates in persons with chronic illness

Seasonal Influenza-associated Mortality, U.S.

- Estimated average of
  - ~36,000 influenza-attributable deaths/year (all ages)
- Highest mortality rates:
  - Persons ≥65 years
  - Persons with chronic pulmonary and cardiac disease; other chronic conditions

- Mortality data are limited for children
  - 46 - 153 pediatric influenza-associated deaths reported to CDC/season (2003-09)

Estimated Impact of Influenza Pandemics

1918-19 Spanish Flu (H1N1)
- 20-100 million estimated deaths worldwide
- >600,000 U.S. deaths
- Estimated mortality = 2%

1957-58 Asian Flu (H2N2)
- 70,000 excess U.S. deaths

1968-69 Hong Kong Flu (H3N2)
- 34,000 excess U.S. deaths

2009-10 H1N1 Pandemic???
April 14 First Death Due to Novel H1N1 in Mexico (Identified Later)
Detection of Novel H1N1 Virus

- March 2009
  - 2 cases of febrile respiratory illness in children (un-related, no pig contact)
  - Residents of adjacent counties in southern California, ill in late March

- Novel swine influenza A (H1N1) virus detected on April 15th, 17th

- Both viruses genetically identical
  - Contain a unique combination of gene segments previously not recognized among swine or human influenza viruses in the United States
April 15 First Case of Novel H1N1 Virus Recognized in California
Host and lineage origins for the gene segments of the 2009 A(H1N1) virus (Garten, et al Science 2009)
Phylogenetic Tree of Hemagglutinin H1: Swine vs. Seasonal Influenza Viruses

Novel H1N1 Outbreak
Human cases of swine H1
Seasonal H1

(Garten, et al Science 2009)
Possible Pathways for Generation of Pandemic Influenza A Viruses

Avian virus → Avian virus → Avian reassortant virus → Human virus

Avian reassortant virus → Reassortment in swine

Reassortment in humans

Avian-human pandemic reassortant virus
April 23 Mexican Cases of Severe Respiratory Illness are Confirmed as Novel H1N1
April 25  First Cases of the Novel Influenza A H1N1 Virus Recognized in Canada
April 25  First Cases of the new Influenza A H1N1 Virus Recognized Outside of North America
April 29  WHO Raises Pandemic Alert Level to **Phase 5**
June 11 WHO Declares **Phase 6** Level of Pandemic Influenza Alert
This map indicates geographic spread and does not measure the severity of influenza activity.
Seasonality
Weekly Frequency of Influenza Virus Isolation

Impact of Pandemic H1N1 in 2009-2010???