

Influenza A Viruses (Evolution and Current Status)

AND

2012 H3N2v Outbreak Update

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Influenza

□ Influenza virus

- Type A
 - Subtypes determined by surface proteins HA (1-17) and NA (1-9)
- Type B
 - Divided into 2 lineages (Victoria and Yamagata)
- Type C
 - Does not typically cause substantial human disease, not routinely tested for
- Yearly co-circulation of seasonal viruses: A (H3N2), A (H1N1), and B

□ Yearly epidemics in the U.S.

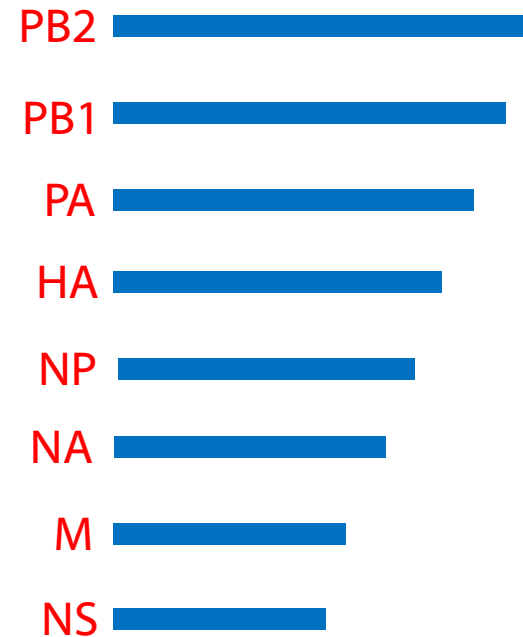
- >200,000 hospitalizations*
- Avg. 3,000 to 49,000 deaths†

*Thompson et al. Influenza-Associated Hospitalizations in the United States. *JAMA* 2004; 292(11):1333-1340.

†CDC. Estimates of Deaths Associated with Seasonal Influenza – United States, 1976 – 2007. *MMWR* 59(33):1057-1062.

Influenza Virus

- Eight RNA segments that code for 11 proteins
- Virus needs one of each of the 8 gene segments to be viable
- HA (hemagglutinin) and NA (neuraminidase) genes code for surface proteins; A subtype nomenclature
- Other genes are responsible mostly for virus structure and replication



Influenza A Virus History

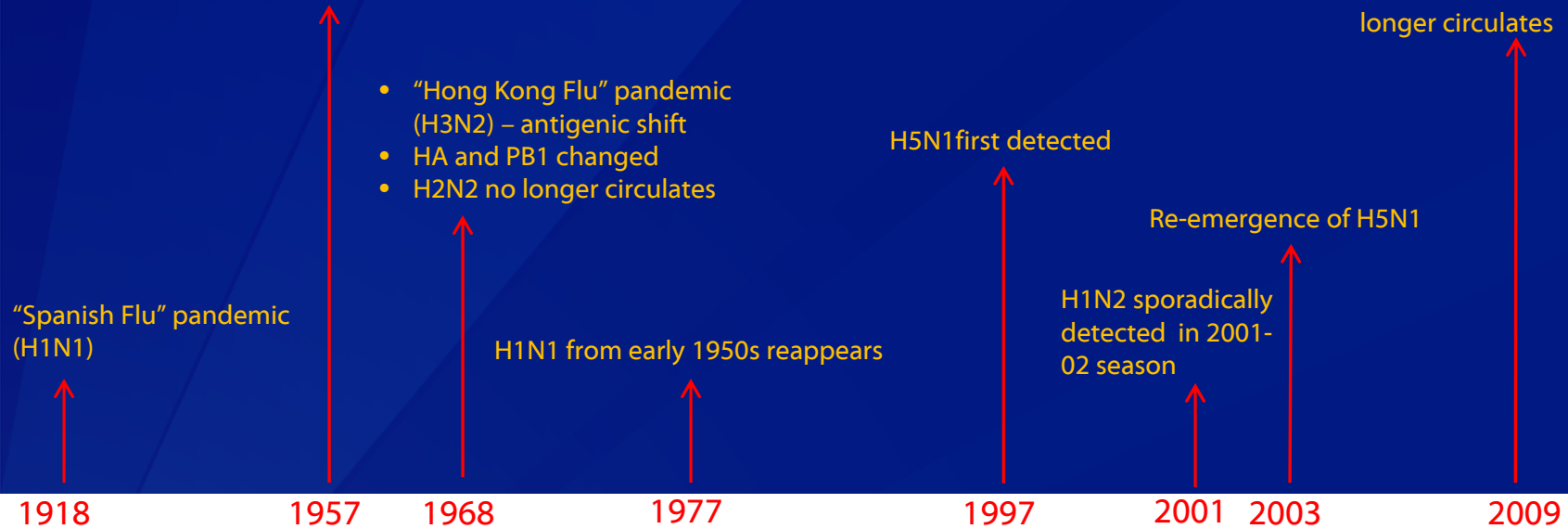
- ❑ **First full human influenza virus genome (H1N1) identified from 1918 human sample**
 - Partial sequences from 1902 and serology from late 1800's
- ❑ **First full swine influenza virus genome (H1N1) identified in 1930 pig sample**
- ❑ **These human and swine viruses are very similar antigenically suggesting a common ancestor**

Human Influenza A Timeline

- "Asian Flu" pandemic (H2N2) – antigenic shift
- HA and NA change, internal genes same as H1N1
- H1N1 no longer circulates

- "Hong Kong Flu" pandemic (H3N2) – antigenic shift
- HA and PB1 changed
- H2N2 no longer circulates

- "Swine Flu" pandemic (H1N1)
- Previous seasonal H1N1 no longer circulates



Garten et al. Antigenic and Genetic Characteristics of Swine-Origin 2009 A(H1N1) Influenza Viruses Circulating in Humans. *Science* 325, 197(2009), 197-201.

Humans

Influenza A Timeline

- "Asian Flu" pandemic (H2N2) – antigenic shift
- HA and NA change, internal genes same as H1N1
- H1N1 no longer circulates

- "Hong Kong Flu" pandemic (H3N2) – antigenic shift
- HA and PB1 changed
- H2N2 no longer circulates

- "Swine Flu" pandemic (H1N1)
- Seasonal H1N1 no longer circulates

"Spanish Flu" pandemic (H1N1)



1918 1930 1957

H1N1 from early 1950s reappears



1968 1977

H5N1 first detected



1997 1998 2001

H1N2 sporadically detected in 2001-02 season



2001 2003

Re-emergence of H5N1



2003 2009

H3N2v with 2009 M gene detected in humans



2010 2011

"classical swine" (H1N1) circulating



1918 1930

- "classical swine" (H1N1) reassorts with human H3N2 and an unknown avian virus to produce triple-reassortant H3N2 (trH3N2)
- Further reassortments created trH1N1 and trH1N2



1997 1998 2001

2009 H1N1 widespread among U.S. swine



2003 2009

Nov. – H3N2v with pandemic M gene present in swine



2010 2011

Swine

Garten et al. Antigenic and Genetic Characteristics of Swine-Origin 2009 A(H1N1) Influenza Viruses Circulating in Humans. *Science* 325, 197(2009), 197-201.

Shu, et al. Genetic analysis and antigenic characterization of swine origin influenza viruses isolated from humans in the United States, 1990-2010. *Virology* 422(2012), 151-160

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Research

Multiple Reassortment between Pandemic (H1N1) 2009 and Endemic Influenza Viruses in Pigs, United States

Mariette F. Ducatez, Ben Hause, Evelyn Stigger-Rosser, Daniel Darnell, Cesar Corzo, Kevin Juleen, Randy Simonson, Christy Brockwell-Staats, Adam Rubrum, David Wang, Ashley Webb, Jeri-Carol Crumpton, James Lowe, Marie Gramer, and Richard J. Webby ✉

Author affiliations: Author affiliations: St. Jude Children’s Research Hospital, Memphis, Tennessee, USA (M.F. Ducatez, E. Stigger-Rosser, D. Darnell, C. Brockwell-Staats, A. Rubrum, D. Wang, A. Webb, J.-C. Crumpton, R.J. Webby); Newport Laboratories, Worthington, Minnesota, USA (B. Hause, R. Simonson); University of Minnesota College of Veterinary Medicine, Saint Paul, Minnesota, USA (C. Corzo, K. Juleen, M. Gramer); and Carthage Veterinary Services, Carthage, Illinois, USA (J. Lowe)

[↩ Main Article](#)

Figure 1

| | PB2 | PB1 | PA | HA | NP | NA | M | NS |
|-----------------|-----|-----|----|----|----|----|---|----|
| sw/MN/239105/09 | | | ■ | | ■ | | ■ | |
| sw/IN/240218/10 | ■ | | ■ | | | | ■ | ■ |
| sw/MN/239106/10 | ■ | ■ | ■ | | ■ | | ■ | |
| sw/NC/239108/10 | | ■ | ■ | | | | | ■ |
| sw/NC/226126/10 | | | ■ | | ■ | | ■ | ■ |
| sw/MN/226128/10 | * | * | ■ | | | | ■ | ■ |
| sw/MN/340304/10 | * | * | * | * | * | * | * | * |

Figure 1. Lineages of North American reassortant swine influenza viruses identified through phylogenetic analyses. Pandemic and endemic gene segments are represented in black and white, respectively. *Denotes partial sequences. Isolates sw/NC/226124/10 and sw/NC/226125/10 (not shown) have the same genotype as sw/NC/226126/10. PB2, polymerase basic 2; PB1, polymerase basic 1; PA, polymerase acidic; HA, hemagglutinin; NP, nucleoprotein; NA, neuraminidase; M, matrix; NS, nonstructural.

Novel Influenza A Virus Reporting

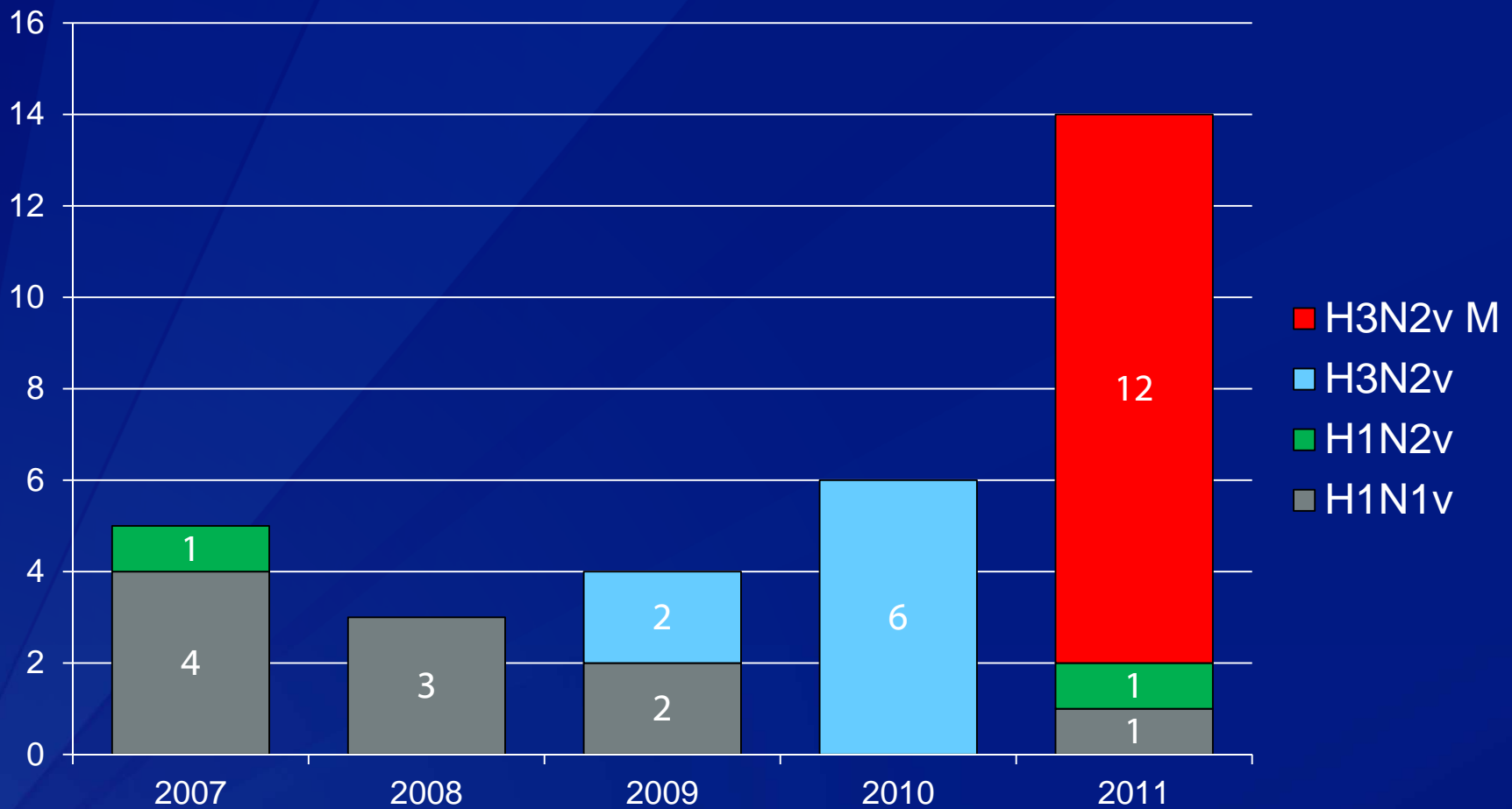
- **Human infection with a novel influenza A virus made nationally notifiable in 2007**
 - Human infection with an influenza A virus different from currently circulating seasonal influenza viruses
 - 33 cases identified from 14 states from 2007 to March 2012
 - All swine-origin viruses (variant)
 - H1N1v (10), H1N2v (2), and H3N2v (21)



Influenza A (H3N2)v

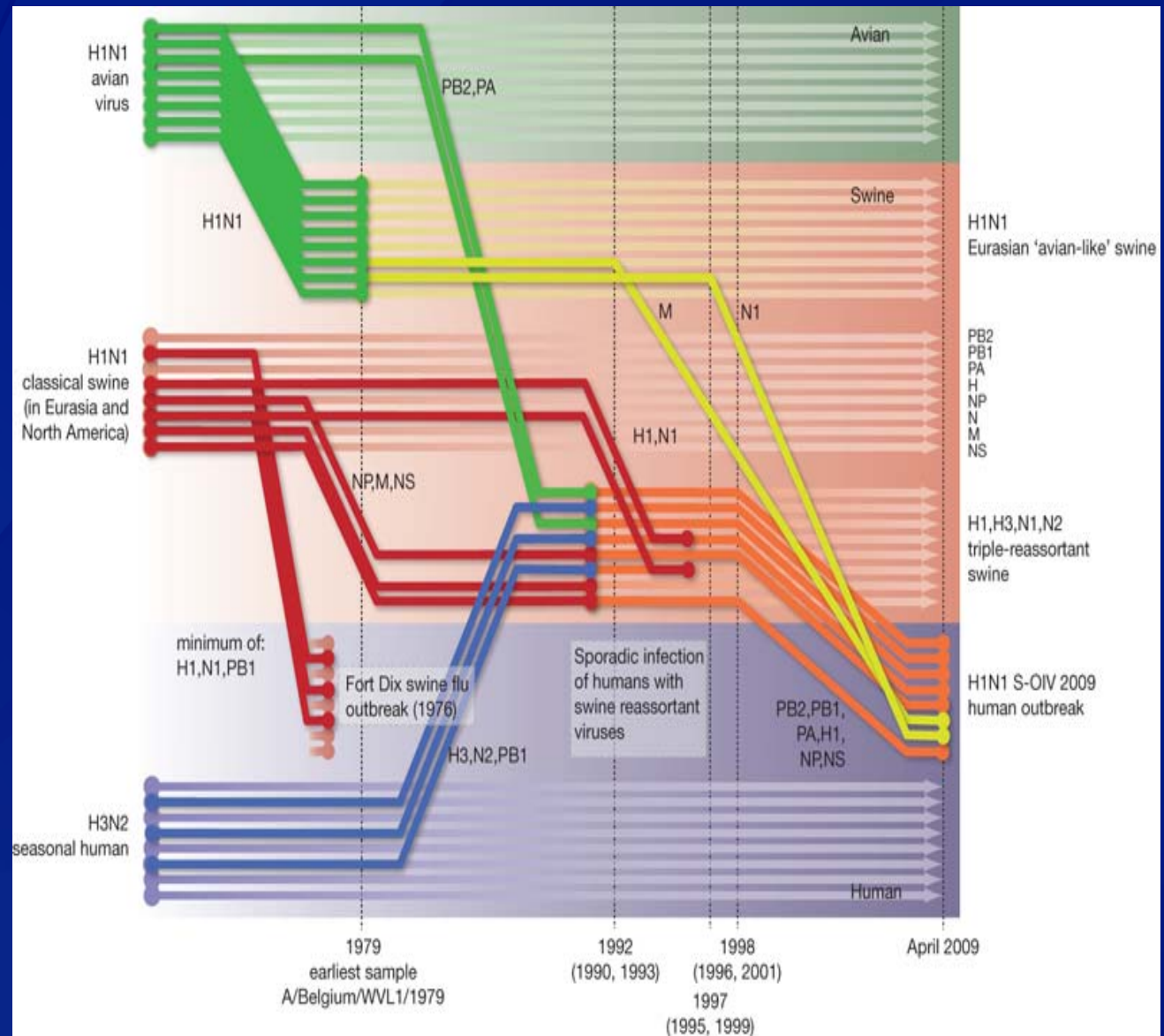
- ❑ **In August 2011 first case of triple-reassortant influenza A (H3N2) with M gene from influenza A (H1N1)pdm09 detected**
- ❑ **13 confirmed cases detected from 6 states (IN, IA, ME, PA, UT, and WV)**
 - Several cases were associated with larger outbreaks of respiratory illness in children
 - Child care settings became a particular focus

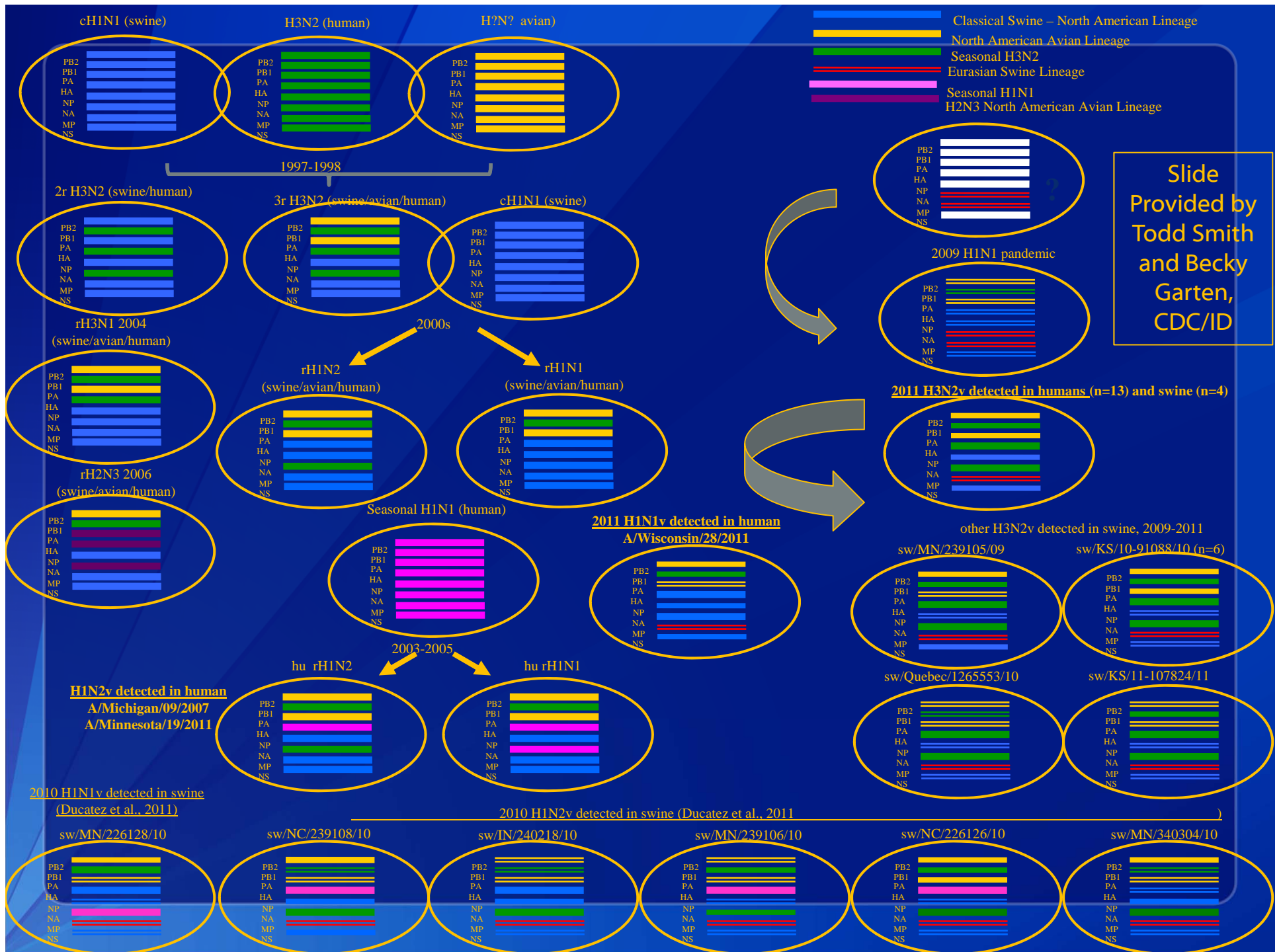
Subtypes of Variant Influenza A Cases, U.S., 2005 – 2011

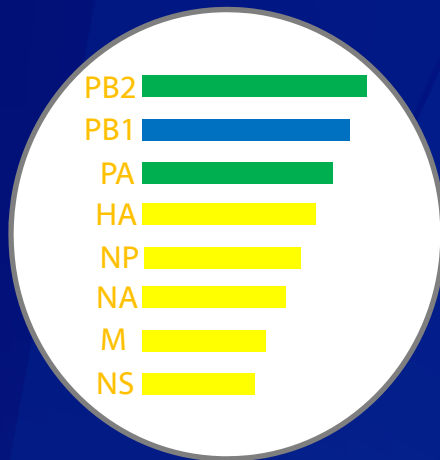


Reconstruction of the sequence of reassortment events leading up to the emergence of 2009 pdm

- Gaps in surveillance
- Indicative of a long period of unsampled ancestry before the pandemic
- Suggests reassortment of swine lineages may have occurred years before emergence in humans
- Phylogenetic analysis of individual genes indicates that nearest ancestors are at least 10 years old



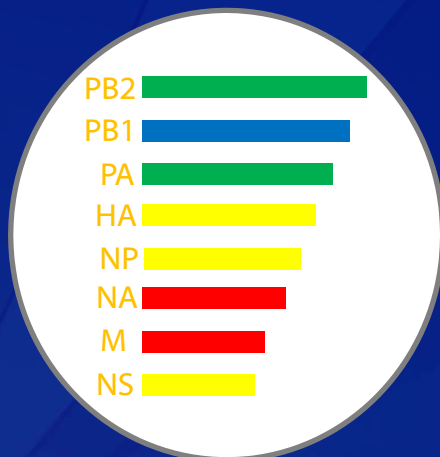




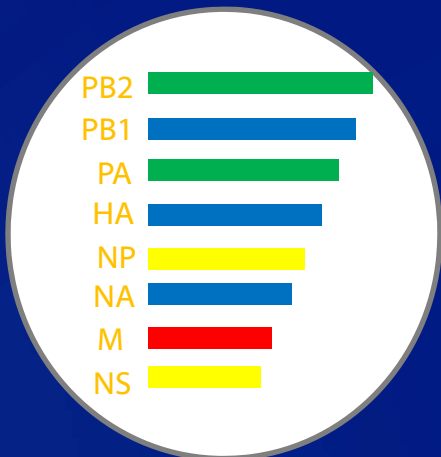
trH1N1



trH1N2



2009 H1N1



2011-12 H3N2



trH3N2

Origin of Swine and Variant virus Gene Segments

| | HA | NA | M* | NP [†] | NS | PB1 | PA | PB2 |
|--------------|----|-----|-----|-----------------|----|-----|----|-----|
| trH1N2 | H | H | CS | CS | CS | H | A | A |
| trH1N1 | CS | CS | CS | CS | CS | H | A | A |
| trH3N2 | H | H | CS | CS | CS | H | A | A |
| 2009 H1N1 | CS | EAS | EAS | CS | CS | H | A | A |
| 2011-12 H3N2 | H | H | EAS | CS | CS | H | A | A |

H – Human

CS – Classical Swine

EAS – Eurasian Swine

A – Avian

* CDC Influenza PCR assay: infA

† CDC Influenza PCR assay : pdminfA



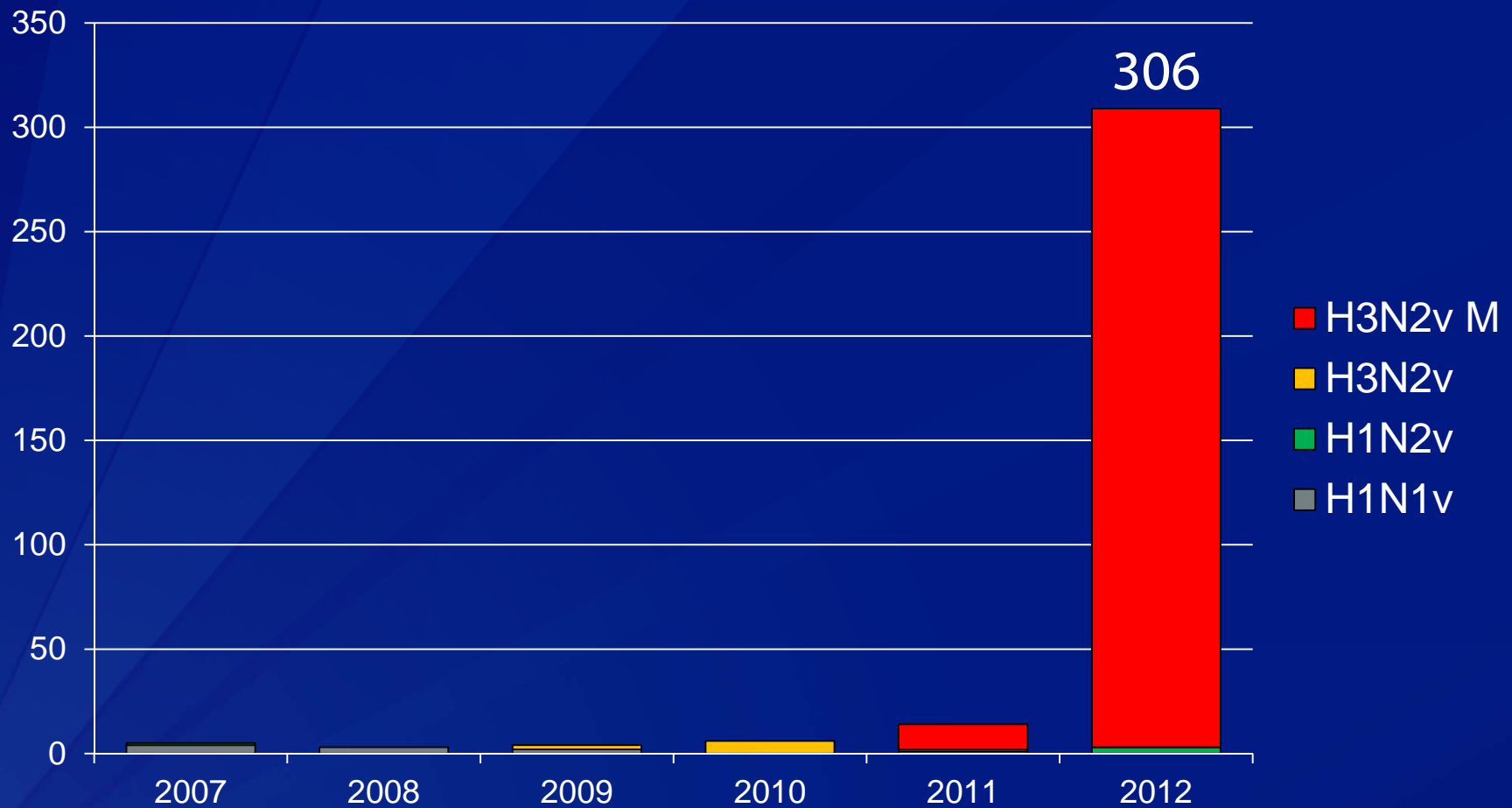
2012 H3N2v OUTBREAK

H3N2v Case Count

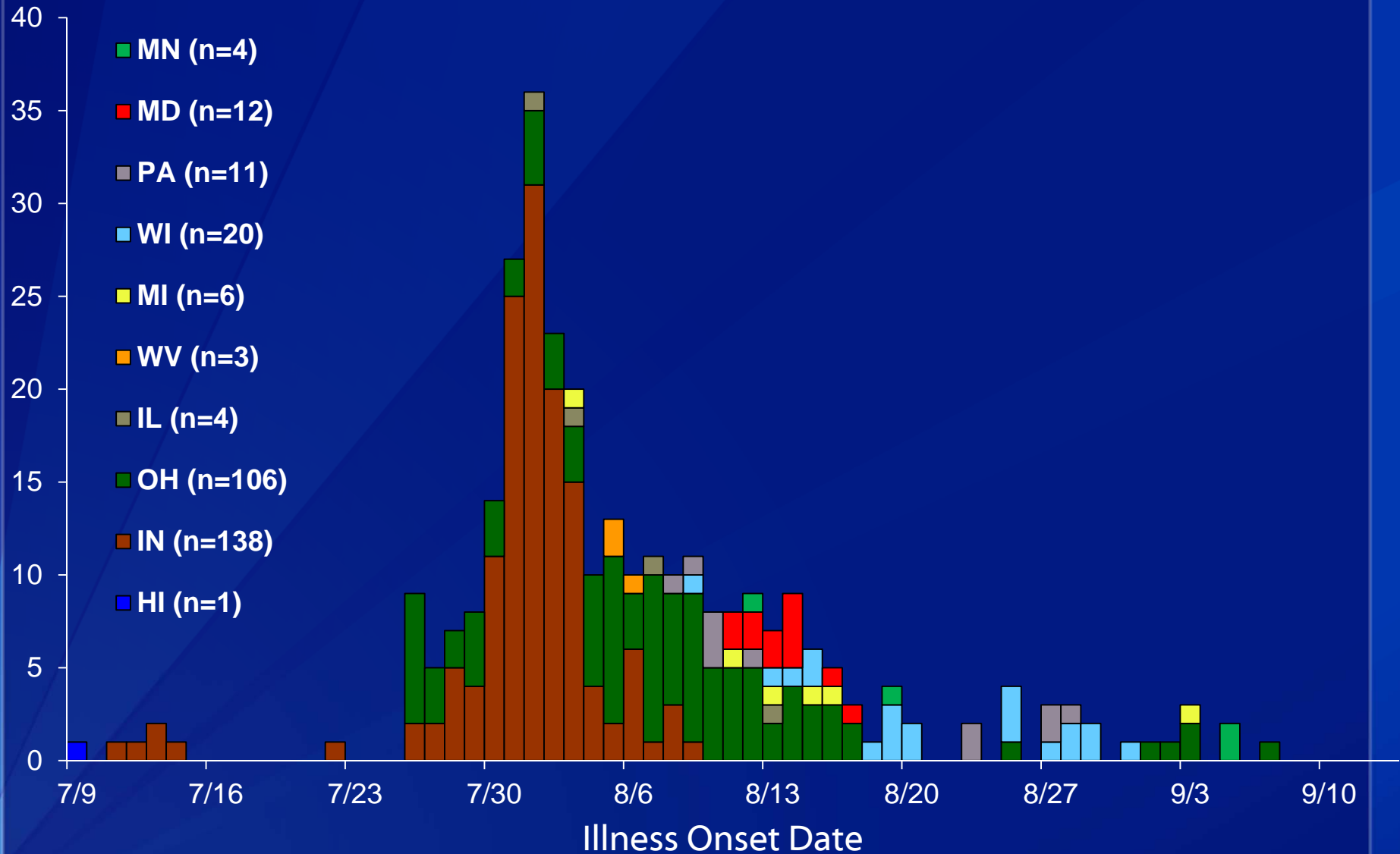
July – October 11, 2012

| | |
|---|-----|
| Cumulative counts since July 12, 2012 | |
| Number of states with confirmed cases | 10 |
| Number of confirmed cases* | 306 |
| Number of confirmed cases hospitalized | 16 |
| Number of fatal confirmed cases | 1 |
| Confirmed cases with presumed human to human transmission** | 15 |

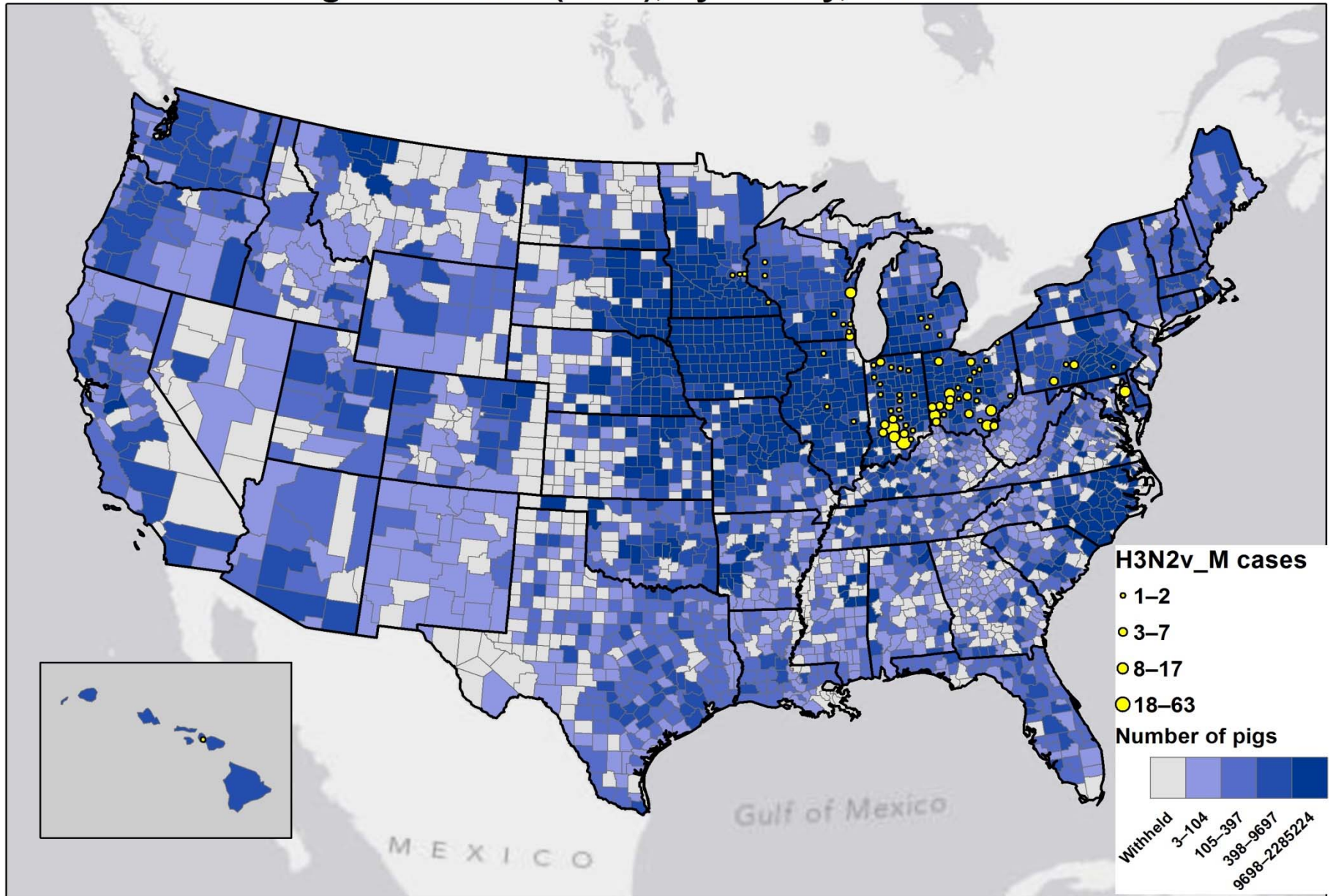
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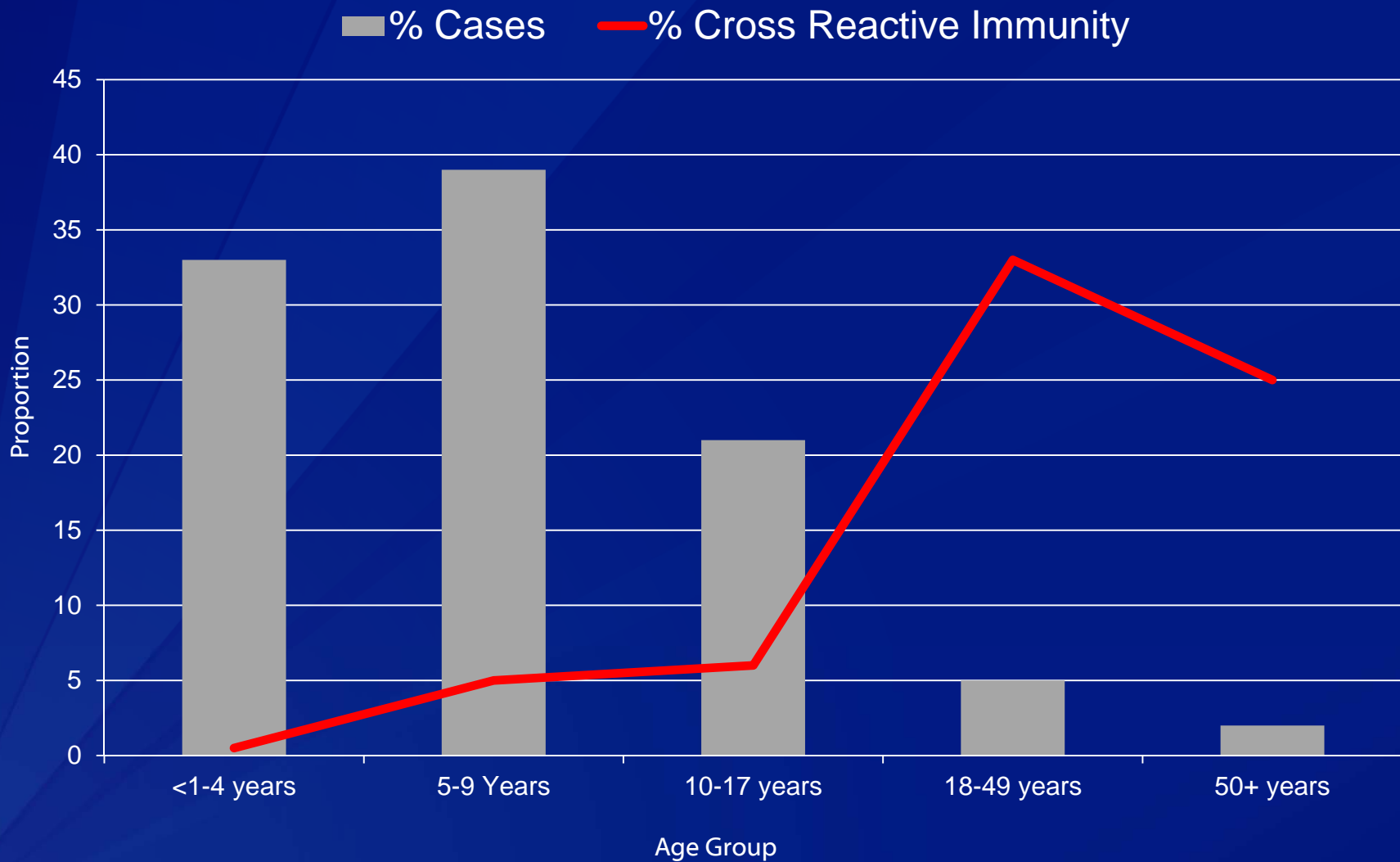
Epi-Curve for Confirmed Cases of H3N2v, July 12 - October 11, 2012 (N=306)



H3N2 M variant influenza virus infections in humans, July–October 11, 2012, and number of hogs and swine (2007), by county, United States of America.



Distribution of H3N2v Cases and Proportion of Persons with H3N2v HI Antibody Titer ≥ 40 by Age-Group*



*CDC, Morb Mortal Wkly Report 61:237-241, 2012

Public Health Prevention and Control

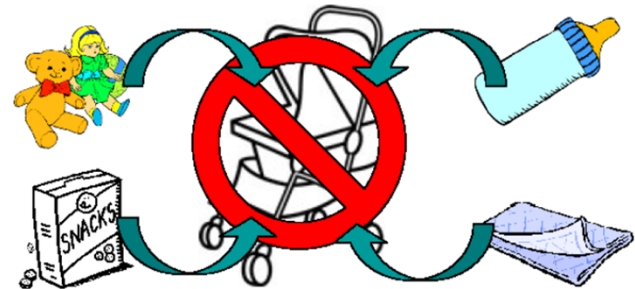
- ❑ Continue strong collaboration with USDA and animal health community
- ❑ Aggressively investigate all cases and contacts
- ❑ Focus on identification of cases with human to human transmission
- ❑ Surveillance guidance for state and local public health
 - Consider increasing collection of PCR quality specimens from patients presenting with influenza-like illness (ILI) in the following high priority areas:
 - All ILINet sentinel health care providers statewide.
 - ILI outbreaks statewide, particularly among children in child care and school settings
 - Unusual or severe presentations of ILI, hospitalized persons.
 - Medically attended ILI and acute respiratory infection (ARI), especially in children in counties or states where confirmed H3N2v cases have occurred

Prevention of Variant Influenza at Fairs

- ❑ Infectious animals can look healthy
- ❑ Avoid eating, drinking, and smoking in animal areas
- ❑ Cover pacifiers, bottles, and sippy cups before entering animal areas
- ❑ Supervise small children
- ❑ Wash hands before exiting
- ❑ Wash clothes when you get home
- ❑ Limit stroller and wheelchair use in animal areas if possible



For your health and safety, please stow strollers here before entering



Please also store your child's toys, food, drinks, and blankets in the stroller

What Might Happen?

- Hard to predict – cooler weather is approaching
- Likely that additional cases of H3N2v will be identified in the coming weeks
- Possible that sporadic infections or even localized outbreaks may occur in parts of the country that are yet unaffected
 - USDA has identified infection in pigs in different parts of the US
- Possible that we could see isolated cases of H3N2v virus infection and even localized outbreaks in schools or day cares as we did last year
 - Perhaps on a larger scale
- Influenza viruses are constantly changing
 - We need to continue to monitor the situation and investigate all cases aggressively

CONCLUSIONS

Conclusions (General)

- The genetics are complicated
 - Reassortment is common in pigs
 - Many different combinations of genes from different sources
- Surveillance in humans **AND** pigs is **ESSENTIAL** to understand the spread of these viruses in both species

Conclusions (H3N2v)

- Fairs are places that pigs come together and if one are more pigs are infected there is transmission among pigs and sometimes to people
- People with direct and prolonged exposure have been those at risk of H3N2v infection to date
- Risk of H3N2v infection is low in exhibitors
 - 11-14% in “hot” fairs where pigs are sick
 - less in other fairs
- Risk of H3N2v infection is very low in casual visitors
- No H3N2v cases arising from general population without exposure to pigs or to sick people
- No significant person to person transmission
- No community transmission
- In most people illness is short and self limited , few are hospitalized and there has been one death and there could be more

Questions??



For more information please contact Centers for Disease Control and Prevention

1600 Clifton Road NE, Atlanta, GA 30333

Telephone: 1-800-CDC-INFO (232-4636)/TTY: 1-888-232-6348

E-mail: cdcinfo@cdc.gov Web: <http://www.cdc.gov>

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

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