Chronology and Evolution of Pandemic H1N1 Influenza of Man

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Chronology

- First confirmed in April 2009 in Mexico and California
- Virus has ability to induce fatal disease in at risk patients (obese – BMI ≥30, pregnant, asthma, COPD, diabetic); *Streptococcus pneumoniae* role–significance?
- Worldwide, pandemic H1N1 has rapidly displaced seasonal influenza – the second wave is ending
- First report of PB2 change to more pathogenic type of gene with the PB2 627 K (glutamic to lysine change) in The Netherlands in 2 people – Sept. 28

1918-2009, A 91 Year Pandemic?
Mortality associated with Influenza

	Excess Deaths from any cause (no. per 100,000 population)
• 1918-1919 H1N1*	598
• 1951-1953 H1N1 (intrasubtypic)	34.1
• 1957-1958 H2N2	40.6
• 1968-1969 H3N2	16.9
• 1977-1978 H3N2 and H1N1 (<26y)	21

CO-CIRCULATION BEGINS IN PEOPLE

• 1997-1999 H3N2 and H1N1	49.5

- 2009 pH1N1 cases – median age is 17 years
  (26 years for hospitalization and 45 years for fatal cases)

Morens, Taubenberger and Faucci

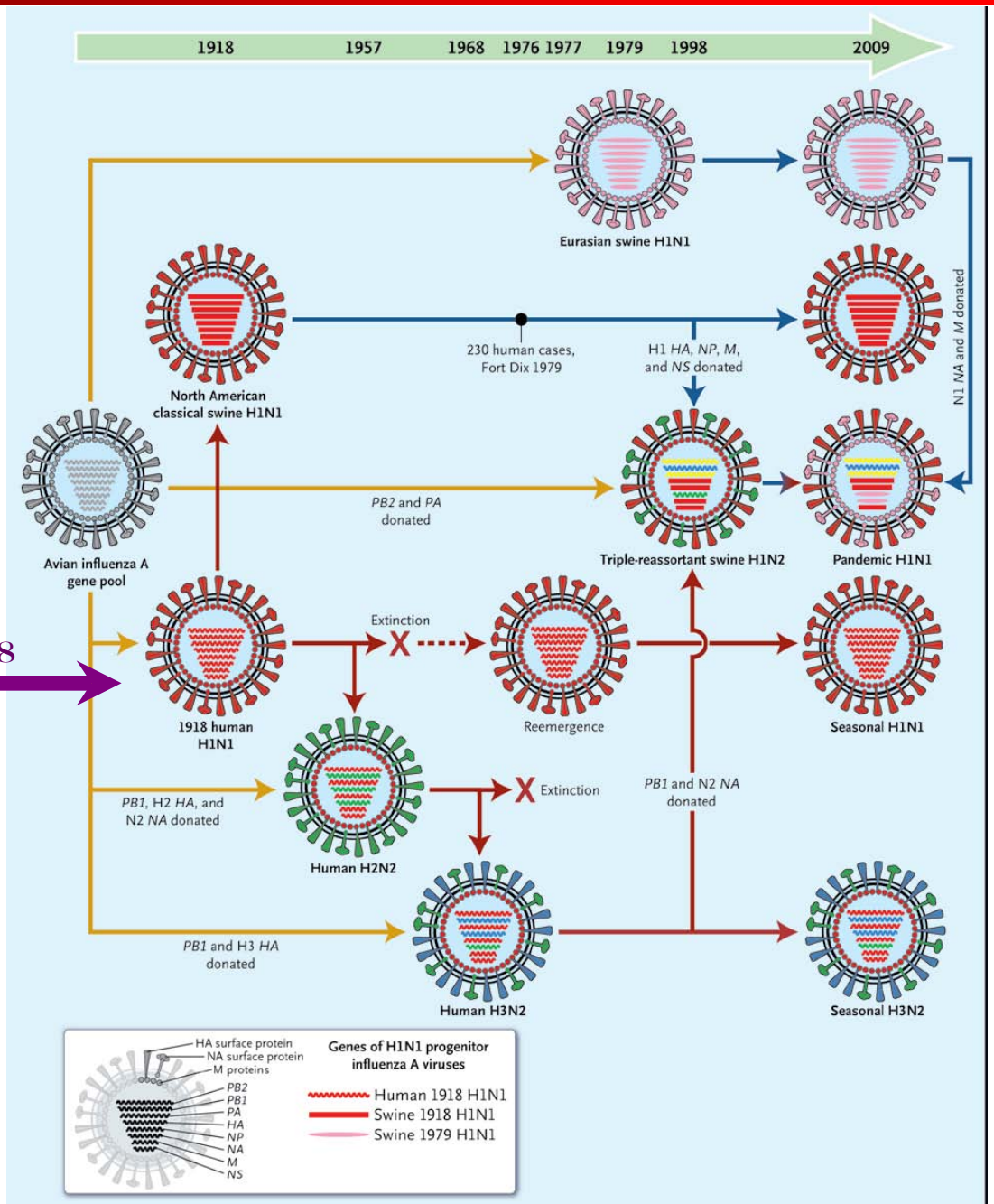
National Institute of Allergy and Infectious Diseases

NEJM Online First June 30 2009

North Carolina Veterinary Diagnostic Laboratory System

***Cedar Rapids Swine Show, September 30-October 5, 1918**

Genetic Origin of H1N1 Viruses of Man



1918

2009 PANDEMIC

WILL THEY BECOME EXTINCT?

Morens, Taubenberger and Faucci

National Institute of Allergy and Infectious Diseases

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Genetic Origins of Pandemic H1N1

- HA – North American Swine-like – A/Sw/IN/00-like

- NA –Eurasian Swine-like
- M – Eurasian Swine-like

- NP – classical Swine-like
- NS – classical Swine-like
- PA – avian-like
- PB1 – human-like
- PB2 – avian like

Triple Reassortant Core of TX 98 H3N2

Newton Grove, NC herd was not the origin for Pandemic H1N1 Influenza Virus

- H3N2 isolated August 1998 – Newton Grove
- That virus was a double reassortant virus, with 5 classical swine H1N1 genes and human HA, NA and PB1 genes
- Pandemic H1N1 strain was derived from triple reassortant virus like TX 98 prototype isolated by NVSL at the same time as the NC isolate

A/Sw/NC/35992/98 vs. A/Sw/TX/4199-2/98

- Newton Grove isolate SWNC98
  - 1995 era human HA, NA and PB1
  - Remaining genes classical H1N1 SIV origin
- SW TX, IA, MN 98
  - 1995 era human HA and NA, 1997 era human PB1
  - PA (Avian origin – A/Sw/HK/81/78 H3N2 isolate)
  - PB2 (Avian origin – A/Seal/MA/133/82 H4N5 isolate)

(Zhou, et al. J Virology 73:8851-8856. 1999)

Viral origin of current pandemic H1N1

- North America, Europe and Asia –

  (Gibbs, et. al, Virology Journal Nov 2009)

  - North American SIV triple reassortant strains – 1999 era – for 6 of the genes, excluding NA and M (A/Sw/IN/9K035/1999, A/Sw/IN/P12439/2000, A/Sw/MN/55551/2000 H1N2 SIV)
  - NA closest to 1991-1993 European H1N1 SIV (A/Sw/Spain/WVL6/1991, A/Sw/England/WVL7/1992, A/Sw/England/WVL10/1993)
  - M closest to 1999-2000 Asian H3N2 SIV (A/Sw/Hong Kong/5200/1999, A/Sw/Hong Kong/5190/1999, A/Sw/Hong Kong/5212/1999)

Preparedness of NC Swine Industry

- Farm personnel are vaccinated with seasonal human influenza vaccine – adopted across almost all farms
- Pandemic H1N1 vaccine has not been available to vaccinate farm personnel due to lack of vaccine supply
- No H1N1 SIV isolate to date from NC hogs has the pH1N1 HA (6.1 – 10.2% HA sequence divergence from A/CA/2009)

Cumulative Impacts on Pork Production

- From 2007– 2008, ethanol from corn resulted in $14.7 loss per head marketed, and in 10% less pork producers on a national basis
- **Post pH1N1**: April through mid August 2009, US pork producers have lost an average of $25 per hog marketed for a total loss of $991 million in 4.5 months
- Pandemic H1N1 resulted in a double digit drop in fresh pork consumption ($590m), which has now recovered
- Since 2007 US pork producers have lost >70% of their equity (2008 = $680m for MB)
- Four NC producers are now bankrupt – Coharie, Coastal Plains, Perfect Pig, and Bunting Swine

Biosecurity risks to industry

- On farm and service personnel, visitors
- As of 11/27/09, WHO reports pH1N1 activity in >207 countries; CDC 11/30 reports the end of second wave; 1714 deaths since April (mostly pediatric in second wave)
- Location of human index case still unknown
- Strict ILI policy for farm personnel – If symptomatic, remain off farm for 7 days

Milestone –pH1N1 vs. HPAI H5N1 June 26, 2009

	pH1N1	H5N1
Year of identification	2009	1996
Months since discovery	3	150 (approx)
As of current WHO report	26 Jun	02 Jun
Countries affected	112	64
Human cases	59,814	433
Human deaths	**263**	262
Case Fatality Rate	0.4%	60.5%

Courtesy: Barrett Slenning, NCSU CVM June 29 2009

Detection and Differentiation of Novel H1N1 Influenza Virus by NCVDLS

- NP rRT-PCR will detect the pandemic H1N1
- NAHLN pH1N1 Matrix rRT-PCR will detect pandemic H1N1 if it occurs in NC swine
- NAHLN N1 rRT-PCR confirms pH1N1

Vaccine availability for pigs

- A large (60 pig) vaccination and challenge trial at NADC has confirmed that existing USDA-licensed SIV vaccines will not protect against pH1N1

- USDA CVB has produced and released master seed virus to US SIV vaccine manufacturers for a conditional license vaccine – several are pursuing

The First North American Farm →

US – world status

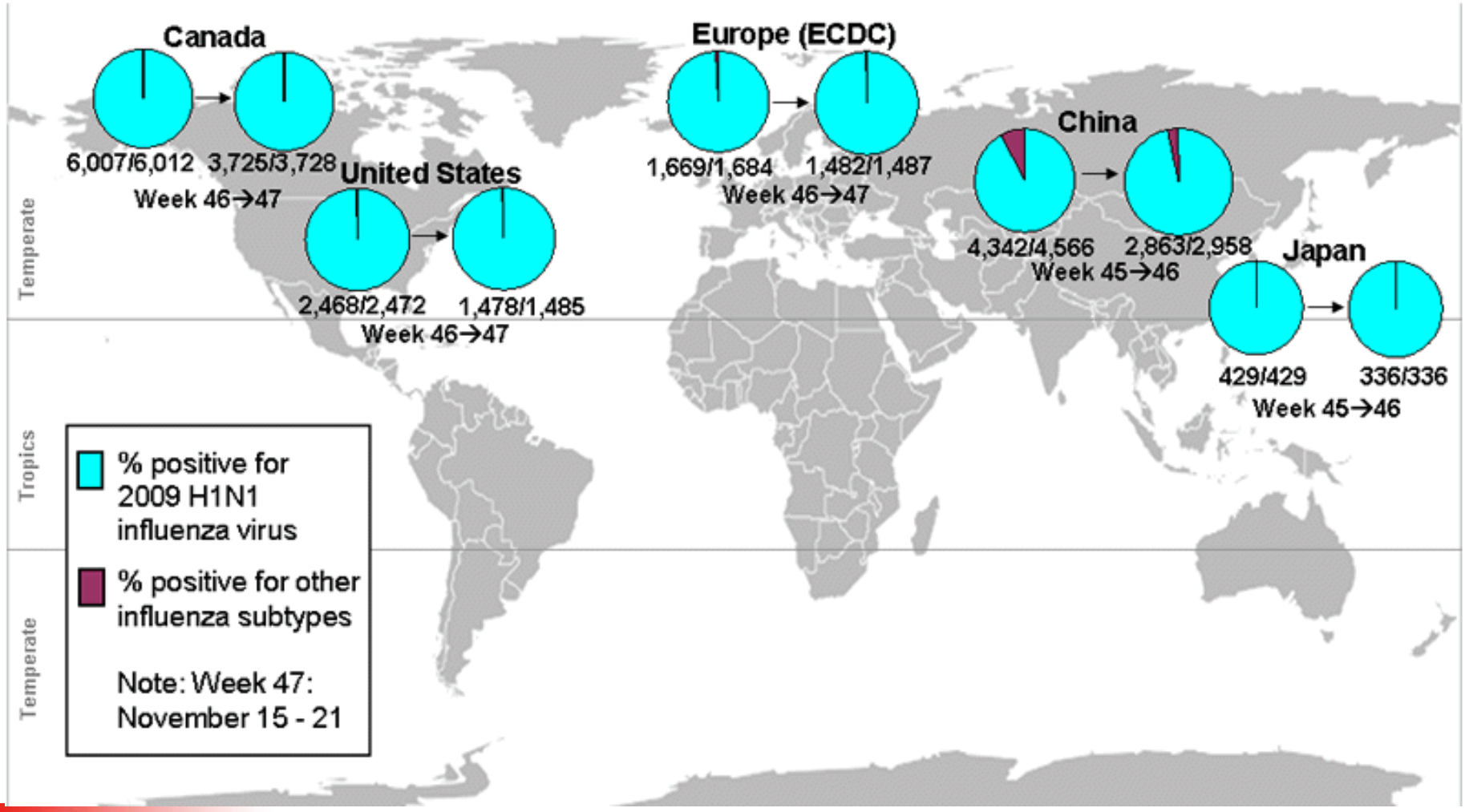
- Canadian herd had about 20% morbidity and NADC and UK experimental infection confirm similar clinical disease
- Sept 2009-MN state fair pigs; Nov-first farm-3000 sows
- Pig farms are no longer quarantined (Argentina, Australia, Canada, Finland, N. Ireland, Indonesia, Norway, Japan, Iceland, China, Taiwan, UK-Norfolk)

Response to pH1N1 infected swine herds

- USDA does not quarantine infected herds
- Controlled movement plan if herds are infected with pH1N1
  - No marketing until 14 days after last clinical signs
  - More problematic in continuous flow farms/areas

So where are we?

- Will a third wave of pH1N1 occur in January?
- Pandemic H1N1 has displaced seasonal influenza, and has infected US pigs, cats, ferrets, and turkeys (dogs in China)
- The southern hemisphere winter flu season revealed the greater ability of pH1N1 to penetrate deeply into lung, resulting in severe viral pneumonia
- Will Tamiflu-contaminated municipal plant wastewater may create a reservoir of resistant AIV strains in waterfowl?


Canada
6,007/6,012
3,725/3,728
Week 46→47
United States
2,468/2,472
1,478/1,485
Week 46→47
Europe (ECDC)
1,669/1,684
1,482/1,487
Week 46→47
China
4,342/4,566
2,863/2,958
Week 45→46
Japan
429/429
336/336
Week 45→46
Temperate
Tropics
Temperate
% positive for 2009 H1N1 influenza virus
% positive for other influenza subtypes
Note: Week 47: November 15 - 21

Questions?