

Pandemic and other emerging threats from animal and human influenza

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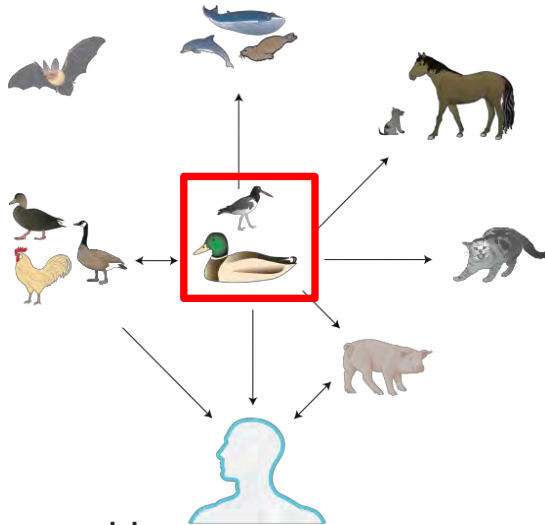
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**Where will the next
pandemic influenza
virus arise from?**



Influenza Ecology

Type A



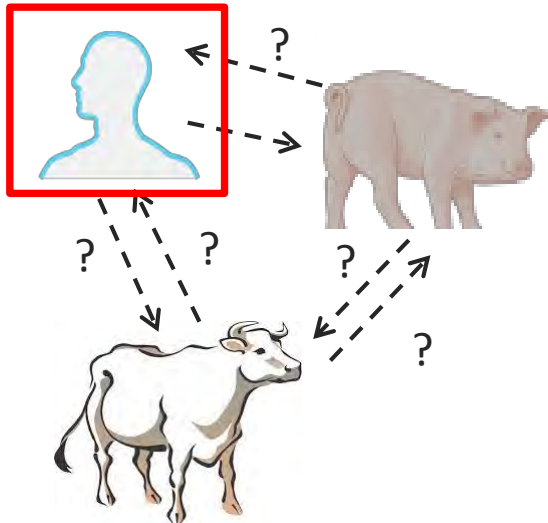
18 subtypes
Wide host range
Wild water birds natural host

Type B



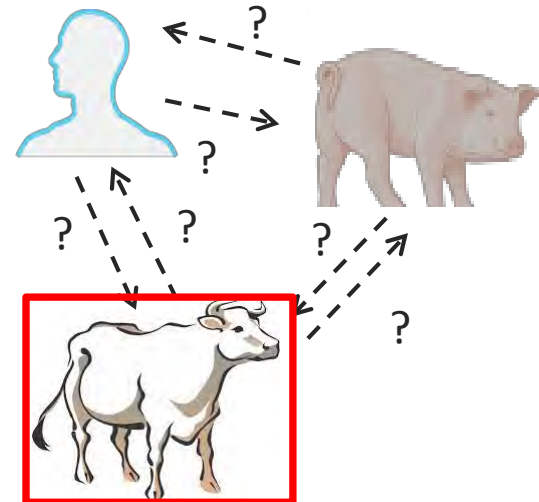
2 lineages
"Human" virus

Type C



No subtypes
Limited hosts
Mild disease

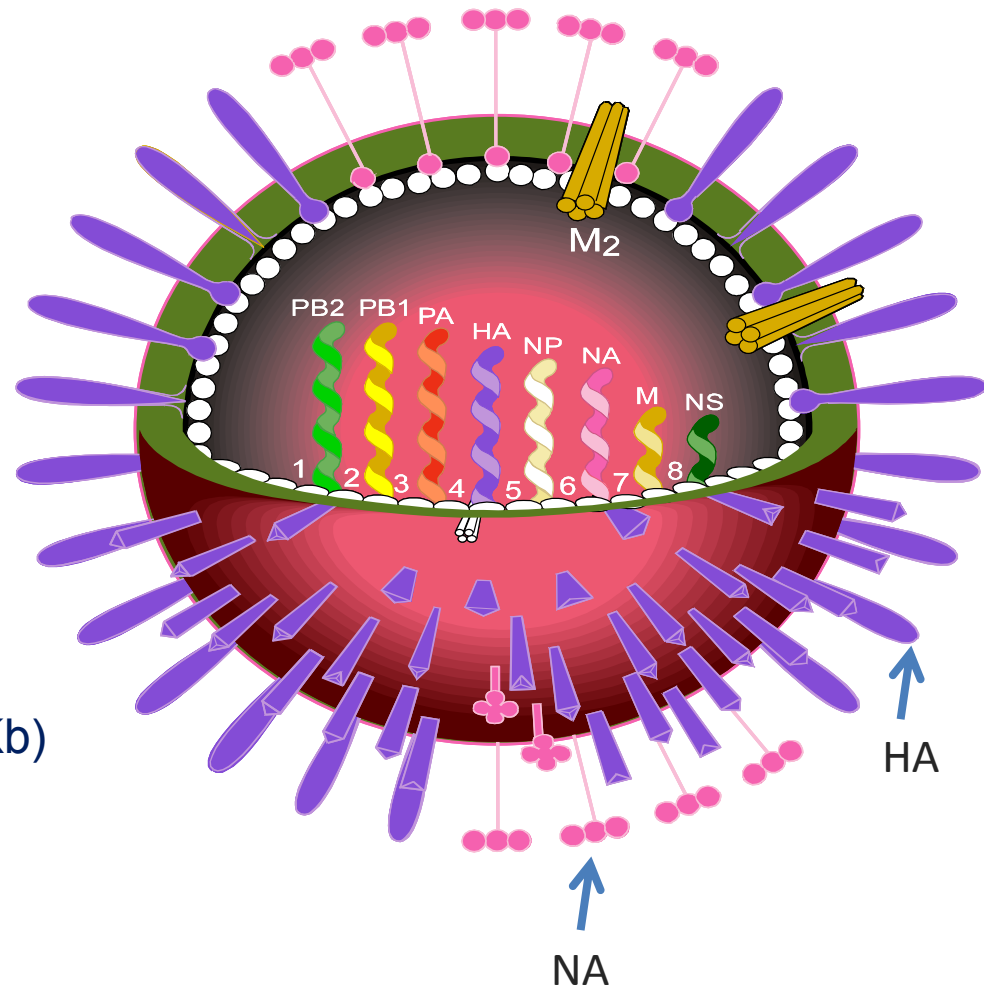
Type D



No subtypes
Limited hosts
?infect man

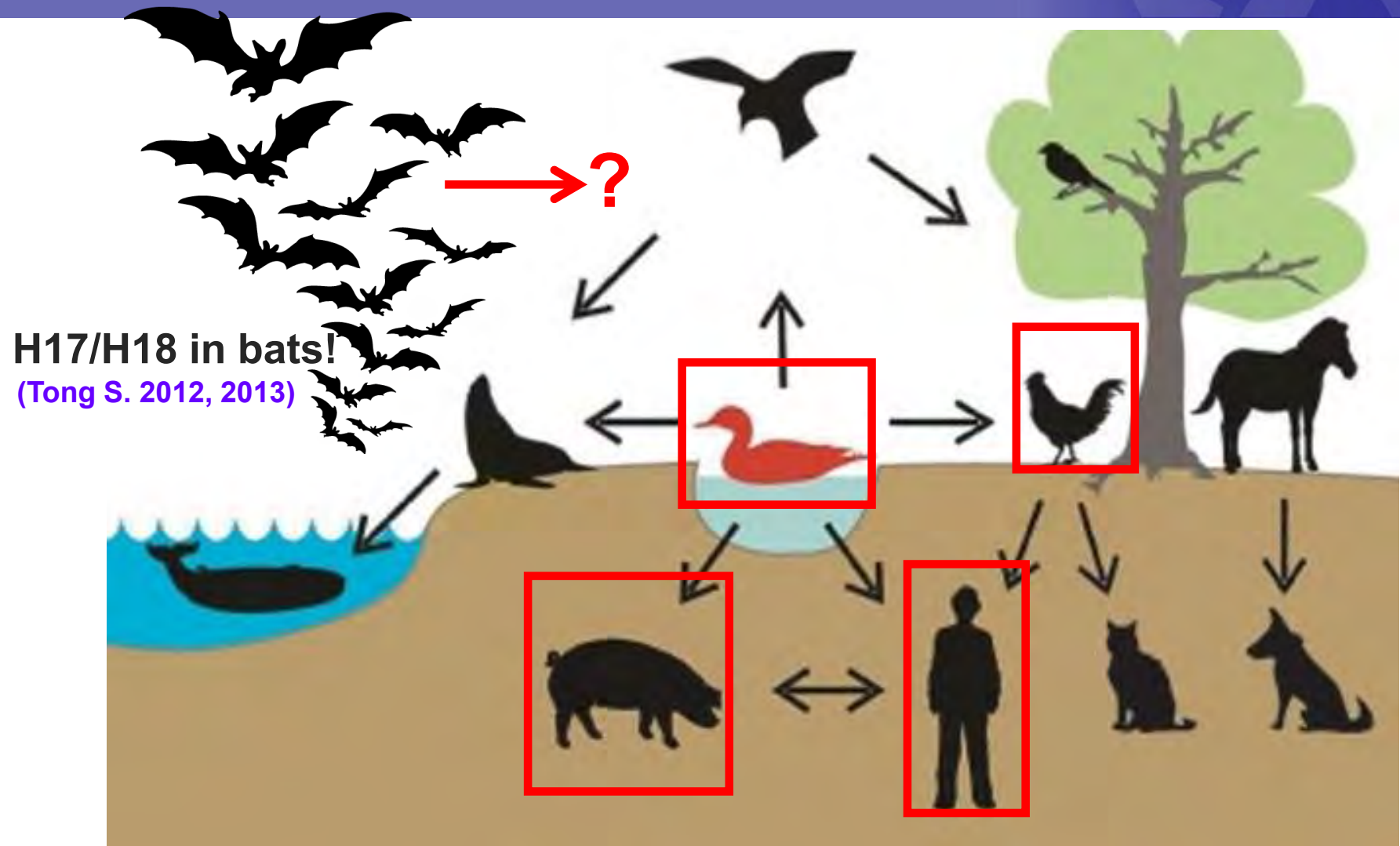


Schematic

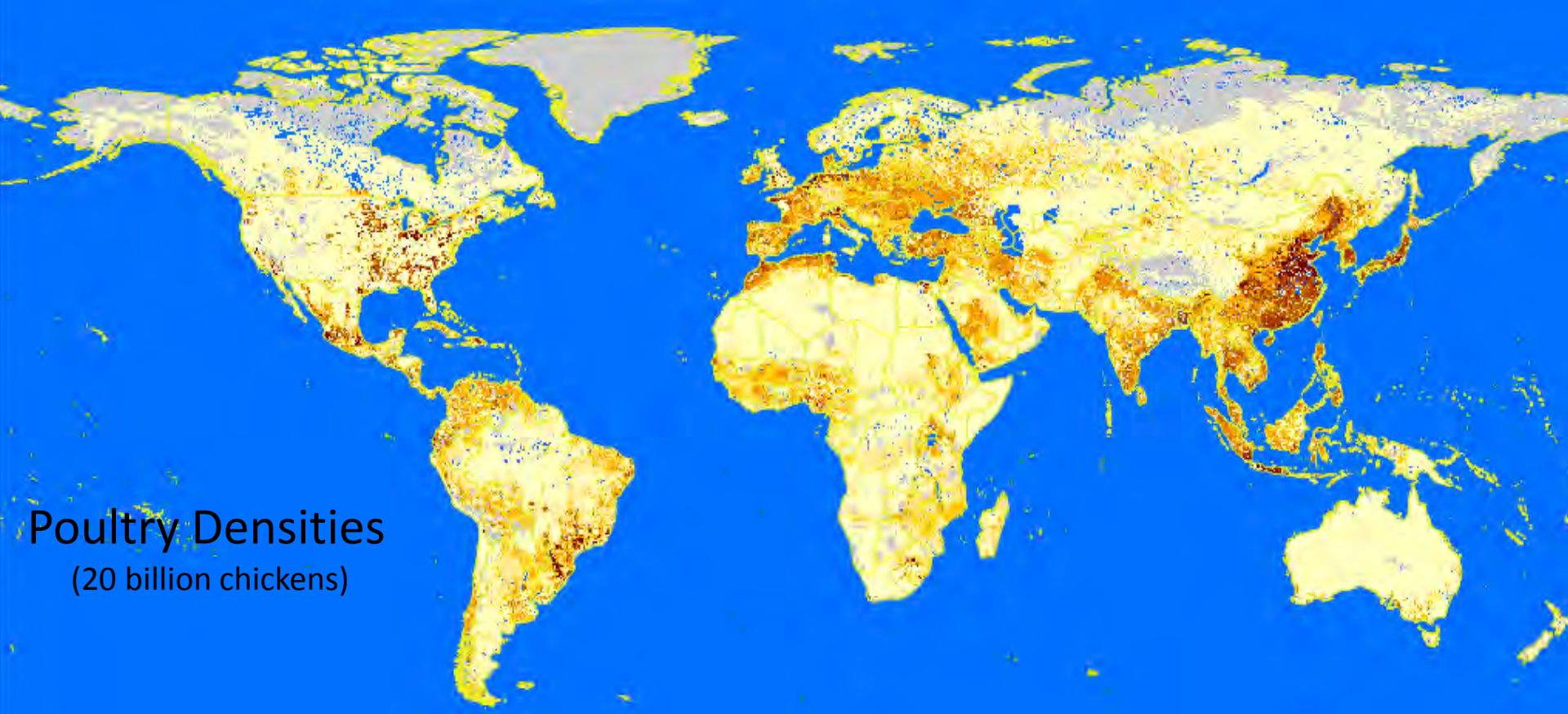


Haemagglutinin (HA), Neuraminidase (NA)

Influenza A is a zoonotic disease with many possible hosts

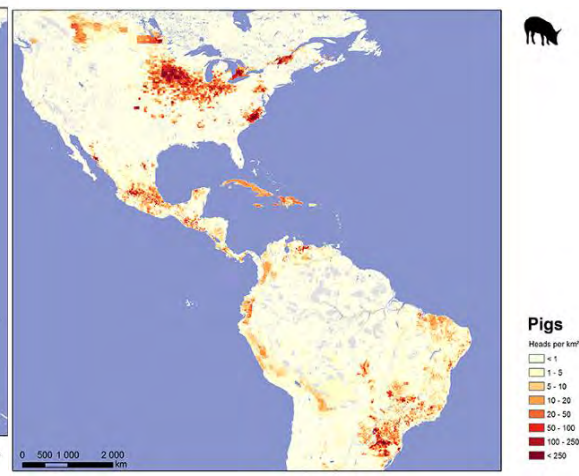
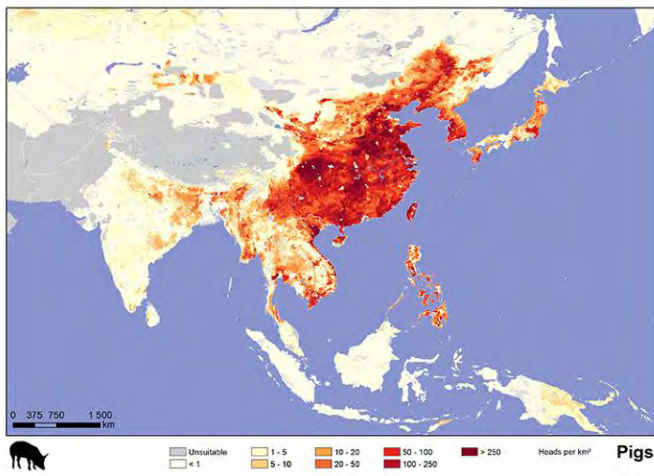
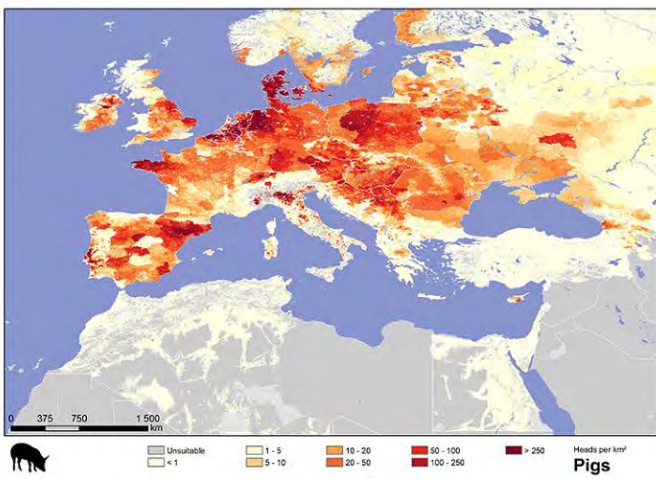


Central host are Water fowl eg. ducks, 16 Influenza A HA subtypes; most infections occur in GI tract and do not affect birds health, 2 subtypes in bats

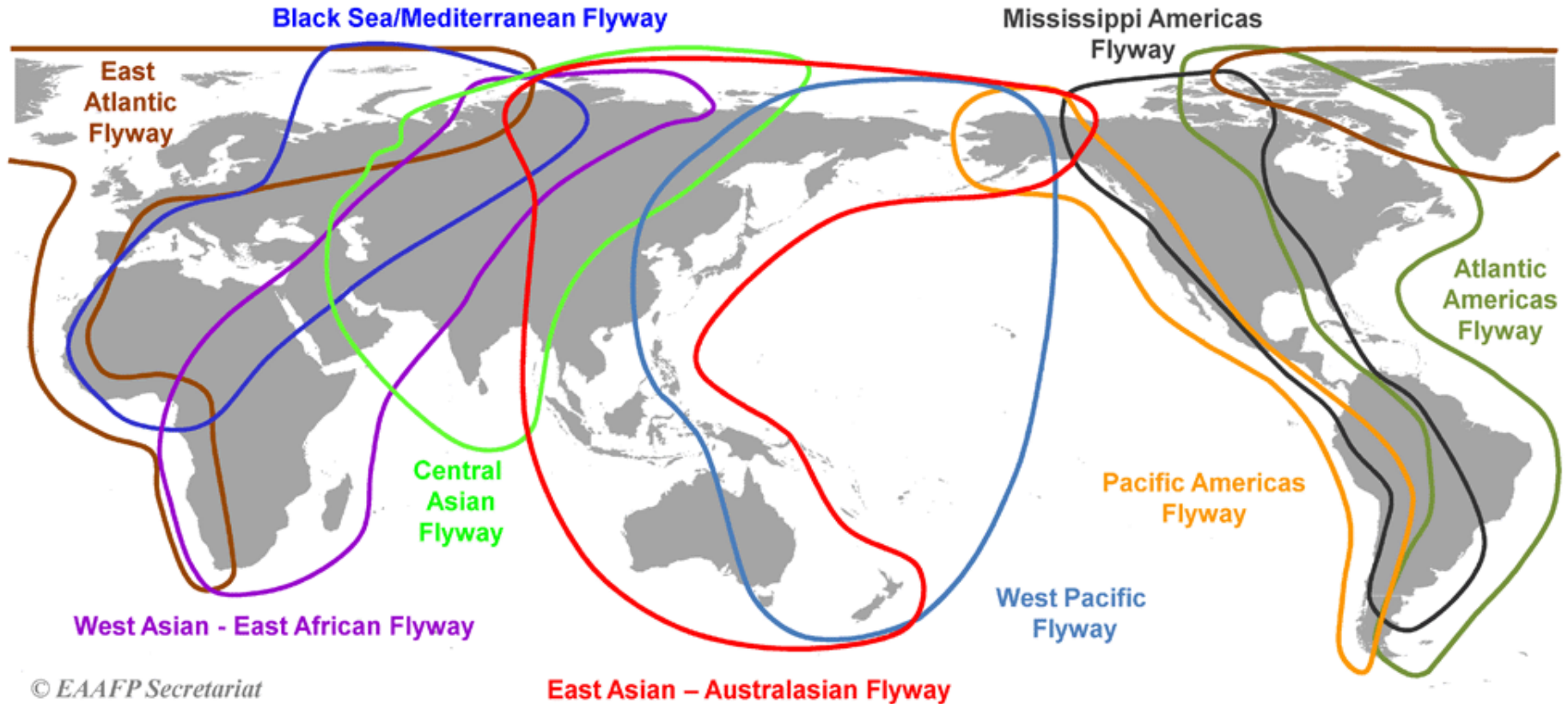


Poultry Densities
(20 billion chickens)

Swine Densities (1 billion)

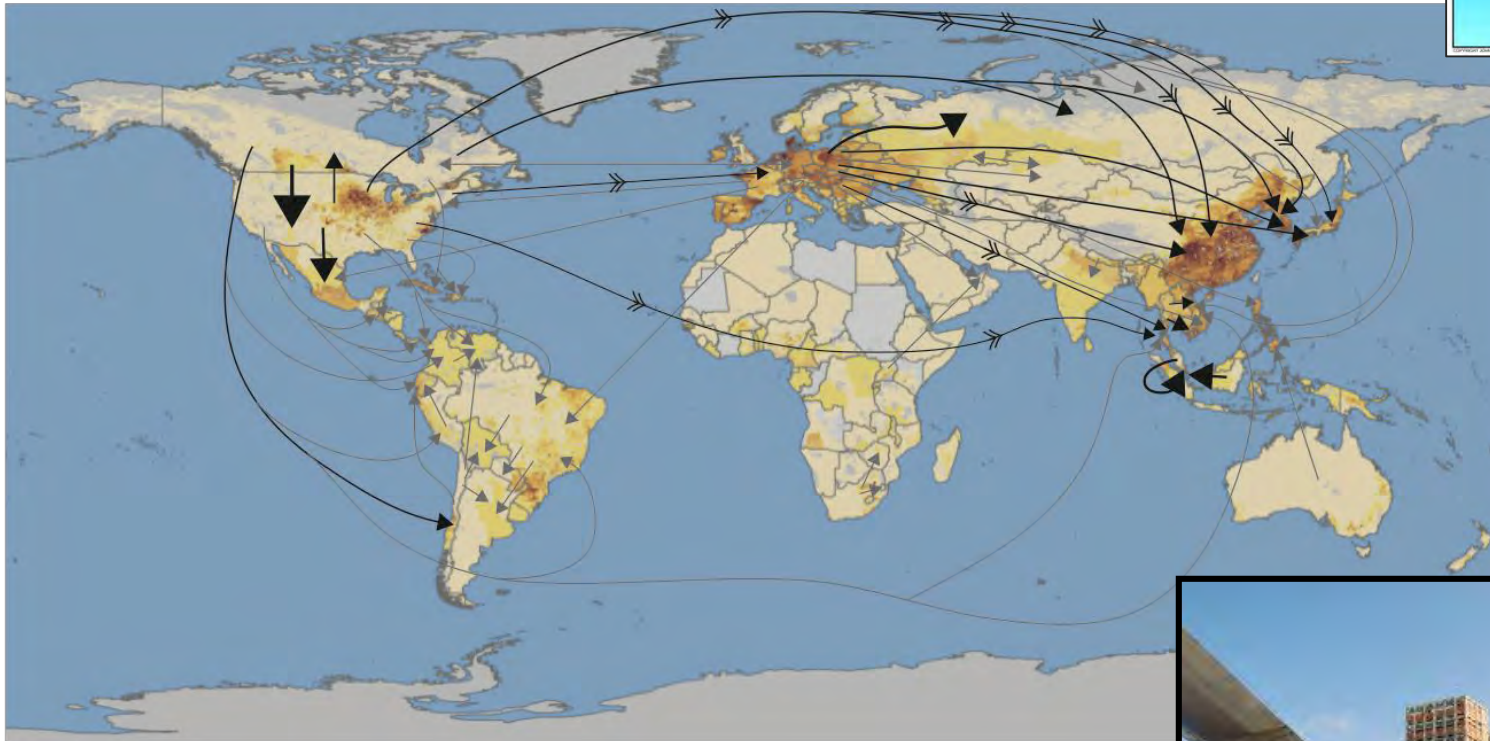
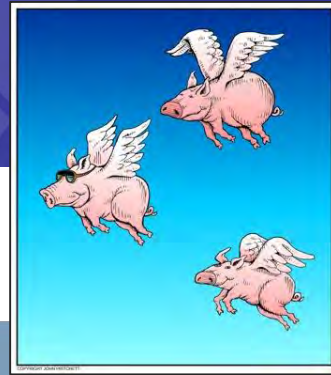


Birds travel on the wing and on bike!

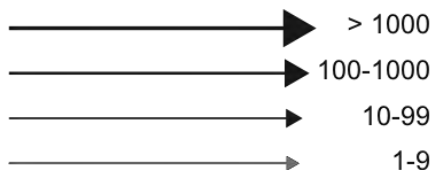


And pigs really DO fly!

Live swine trade routes



Trade value of live swine, 1996-2012, \$mil



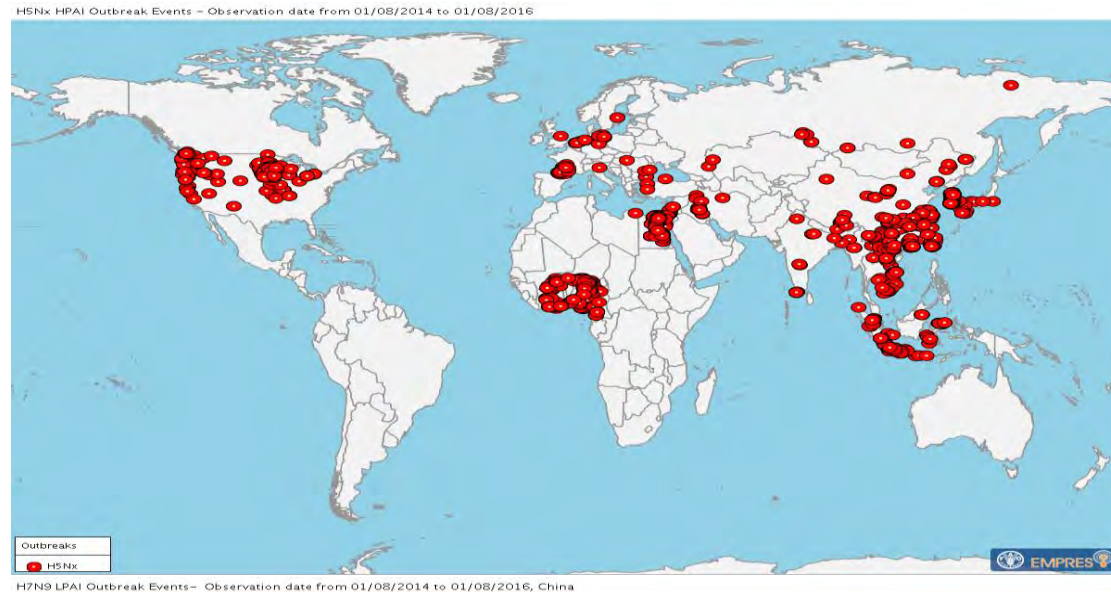
UN Commodity Trade Statistics Database



Slide courtesy of Martha Nelson,
Fogarty Institute, NIH, USA

Avian influenza outbreaks in birds reported to FAO 2014-2016

H5Nx HPAI



H7N9 LPAI



There has been no shortage of unusual influenza viruses infecting humans in recent years!

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Chinese health experts investigate two bird flu deaths

AP 1:47 p.m. EDT April 1, 2013

Experts don't yet know how a lesser-known bird flu virus crossed over to humans, but they say it is unlikely to spread

f 23 **62** **in 2**
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BEIJING (AP) — Health officials say they still don't understand how a lesser-known bird flu virus was able to kill two men and seriously sicken a woman in China, but that it's unlikely that it can spread easily among humans.

Two men in Shanghai became the first known human fatalities from the H7N9 bird flu virus after contracting it in February. A woman in the eastern city of Chuzhou remains in serious condition, China's National Health and Family Planning Commission said.

It was unclear how the three patients became infected, the health agency said. It sought to calm

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HEALTH AND WELLNESS

Cost of not caring: Stigma set in stone

Two men have died and a woman is sick with a rare strain of bird flu

The H7N9 virus is a rare strain of the virus

Health officials don't know

(Photo: AP)

April 1 2013

H7N9

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Taiwan reports first human case of H6N1 bird flu to world health body

Taiwanese woman is first person to catch H6N1 flu strain; experts search for source of infection and play down fear of human-to-human spread

Lawrence Chung in Taipei and Lo Wei

PUBLISHED : Saturday, 22 June, 2013, 12:00am
UPDATED : Saturday, 22 June, 2013, 4:57am

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H7N9 avian flu



Dr Ho Pak-leung. Photo: SCMP

Taiwan reported the world's first human case of H6N1 bird flu infection yesterday but appealed for calm, saying no sign of human-to-human transmission had been detected.

The patient, a 20-year-old woman who worked at a breakfast shop in Taipei, was admitted to hospital on May 8 with a fever and cough.

June 22 2013

H6N1

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Taiwan reports first human case of H6N1 bird flu

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Indiana reports four fair-linked H3N2v cases

Filed Under: H3N2v Influenza; Swine Influenza
Lisa Schnirring | Staff Writer | CIDRAP News | Jun 27, 2013

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Indiana health officials yesterday reported four variant H3N2 (H3N2v) influenza infections in people who attended the same county fair, which could herald a wave of similar infections that occurred last summer.

All four of the people visited the Grant County Agricultural Fair from Jun 16 to Jun 22 before they got sick, and at least two had contact with swine, according to a statement from the Indiana State Department of Health (ISDH). Grant County is in central Indiana, and the fairgrounds are located in Marion.



Thinkstock

The Indiana State Board of Animal Health said 13 pigs at the fair tested positive for H3N2 and that pigs infected with swine influenza viruses sometimes don't show any signs of illness. Flu viruses aren't transmitted by eating pork or pork products.

H3N2v was first detected in people in July 2011, and only 12 cases were detected from five states yesterday but appeared to have been detected.

The patient, a 20-year-old woman who worked at a breakfast shop in Marion, was admitted to hospital on May 8 with a

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June 27 2013

H3N2v

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China reports first H10N8 avian flu death

By Madison Park, CNN

December 18, 2013 -- Updated 1336 GMT (2136 HKT)

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Chickens are seen at a poultry farm in China.

STORY HIGHLIGHTS

- A 73-year-old woman, confirmed to have H10N8 avian flu virus, died
- Woman was from China and suffered several underlying diseases
- Chinese health authorities: Risk of human infection is low
- H7N9 outbreak said to pose greater risk to public health

Hong Kong (CNN) -- An elderly woman infected with a strain of avian flu that is rarely seen in humans died in China earlier this month -- marking the first human fatality from the H10N8 virus.

The 73-year-old woman in Jiangxi province was admitted to a hospital on November 30, suffering from several ailments including severe pneumonia, hypertension, heart disease and a muscular weakness condition. She died on December 6.

The woman had a history of contact with live poultry markets, and



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June 26, 2014 -- Updated 0334 GMT (1134 HKT)



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Dec 18 2013

H10N8

There has been no shortage of unusual influenza viruses infecting humans in recent years!

China report

By Madison Park, CNN
December 18, 2013 -- Updated 13:00

STORY HIGHLIGHTS

- A 73-year-old woman confirmed to have flu virus, died
- Woman was from Hong Kong and suffered severe diseases
- Chinese health officials say the case is a higher risk of human infection
- H7N9 outbreak in China has caused a greater risk of human infection

Done

NEWS • HONG KONG • HEALTH

Hong Kong sees first case of H9N2 avian flu in four years

Lo Wei and Ernest Kao

PUBLISHED : Monday, 30 December, 2013, 7:26pm
UPDATED : Tuesday, 31 December, 2013, 2:55am



Health authorities have confirmed a rare case of H9N2 avian flu human infection in Hong Kong. Photo: EPA

An 86-year-old Hongkonger living in Shenzhen has become infected with the H9N2 strain of bird flu - Hong Kong's first human case of the virus strain in four years.

The case, in light of the other bird flu strains hitting humans with increased frequency - including the deadly H7N9 and H10N8 subtypes - may signal a higher risk of virus mutation and genetic swapping, experts say.

The man was in a stable condition at North...

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Dec 30 2013

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China report Hong Kong

H5N1 bird flu death confirmed in Alberta, 1st in North America

Officials say no risk of human-to-human transmission

By Laura Payton, CBC News | Posted: Jan 08, 2014 3:15 PM ET | Last Updated: Jan 09, 2014 7:29 AM ET



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H5N1 flu death confirmed in Alberta 32:50

Jan 8 2014

H5N1

Woman was first to suffer severe diseases

Chinese health of human infection

H7N9 outbreak greater risk

The case, in light of the other bird flu strains hitting humans with increased frequency - including the deadly H7N9 and H10N8 subtypes - may signal a higher risk of virus mutation and genetic swapping, experts say.

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after crossing the border...

become infected with the virus strain in

first human case of the virus strain in

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China's human H5N6 infection an individual case

(Xinhua)
Updated: 2014-05-09 16:20

BEIJING, May 9 (Xinhua) -- A human H5N6 virus infection that was reported on Tuesday and resulted in the death of the patient was an individual case, a National Health and Family Planning Commission spokeswoman said on Friday.

Speaking at a press conference, Song Shuxin said people who had close contact with the patient have shown no symptoms, and health experts found that the risk of human infection is low.

Song said people should maintain good personal hygiene habits and not contact ill or dead poultry to prevent and control respiratory infectious diseases.

The case is believed to be the world's first human H5N6 infection. The virus had previously been isolated to waterfowls and wild ducks, said Ni Daxin, a Chinese Center for Disease Control and Prevention official, citing reports of Germany, Sweden and the United States as well as Taiwan.

The H5N6 patient was a 49-year-old man from Nanbu County of Nanchong City in Southwest China's Sichuan Province. He died in hospital after being treated for several days, experts say.

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- Woman was found to have suffered severe diseases
- Chinese health officials say human infection risk is higher
- H7N9 outbreak poses greater risk to humans

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May 9 2014

H5N6

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Genesis and Spread of Newly Emerged Highly Pathogenic H7N9 Avian Viruses in Mainland China

Lei Yang^a, Wenfei Zhu^a, Xiyan Li^a, Minmei Chen^c, Jie Wu^d, Pengbo Yu^e,
Shunxiang Qi^f, Yiwei Huang^g, Weixian Shi^h, Jie Dong^a, Xiang Zhao^a,
Weijuan Huang^a, Zi Li^a, Xiaoxu Zeng^a, Hong Bo^a, Tao Chen^a, Wenbing Chen^a,
Jia Liu^a, Ye Zhang^a, Zhenli Liang^c, Wei Shi^e, Yuelong Shu^{a,b} and Dayan Wang^a

Stacey Schultz-Cherry, Editor

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ABSTRACT

The novel low-pathogenic avian influenza A H7N9 viruses (LPAI H7N9 viruses) have been a threat to public health since their emergence in 2013 because of the high rates of mortality and morbidity that they cause. Recently, highly pathogenic variants of these avian influenza A H7N9 viruses (HPAI H7N9 viruses) have emerged and caused human infections and outbreaks among poultry in mainland China. However, it is still unclear how the HPAI H7N9 virus was generated and how it evolved and spread in China. Here, we show that the ancestor virus of the HPAI H7N9 viruses originated in the Yangtze River Delta region and spread southward to the Pearl River Delta region, possibly through live poultry trade. After introduction into the Pearl River Delta region, the origin LPAI H7N9 virus acquired four amino acid insertions in the hemagglutinin (HA) protein cleavage site and mutated into the HPAI H7N9 virus in late May 2016. Afterward, the HPAI H7N9 viruses further reassorted with LPAI H7N9 or H9N2 viruses locally and generated multiple different genotypes. As of 14 July 2017, the HPAI H7N9 viruses had spread from Guangdong Province to at least 12 other provinces. The rapid geographical expansion and genetic evolution of the HPAI H7N9 viruses pose a

May 2016

HPAI H7N9

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International Edition +

World's first human case of H7N4 avian flu reported in China

By Mark Lieber, CNN
Updated 2018 GMT (0418 HKT) February 15, 2018

China re
H5N1
Am
Officials
By Laura Paj



Source: CNN

What is bird flu? 01:12

Story highlights

H5N1 flu

- Woman who suffered severe diseases
- Chinese health officials report human infection
- H7N9 outbreak causes greater risk

The 68-year-old woman was hospitalized in January

Wild aquatic birds are the natural hosts for most influenza type A viruses

H7 virus infections in humans are not common and typically cause mild to moderate illnesses

treatment January 22

(CNN) — The first human case of the H7N4 strain of avian influenza has been reported in China, Hong Kong's Centre for Health Protection announced Wednesday.

A 68-year-old woman living in Jiangsu Province in eastern China, near Shanghai, had contact with live poultry before she began developing pneumonia-like symptoms December 25. She was admitted to a hospital January 1 and was discharged.

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H7N4

Outcomes from these zoonotic infections



- **Outcomes from H5N1 human cases**

- Since 2003; 860 cases detected, 454 deaths; HFR 53%
- But in 2017; 4 cases with 2 deaths; 2018 (up to March) 0 cases

- **Outcomes from H7N9 (Chinese) human cases**

- Since 2013 a total of 1565 cases with 620 deaths (HFR 39%)
- 5th wave 2016-7 766 cases (incl. HPAI); 6th wave 2017-8 only 3 cases reported, ?deaths

- **Outcomes from other isolated human avian influenza infections**

- H6N1, single case, hospitalized, recovered, no evidence of person-person transmission
- H10N8, 3 cases, 2 deaths, no evidence of transmission
- H9N2, several cases, few hospitalized, recovered, no evidence of person-person transmission
- H5N6, 17 cases (1 in 2017) – all in China, 11 deaths, no evidence of person-person transmission

- **Outcomes from other isolated human swine (variant) influenza infections**

- In US 468 cases since 2005, small number of hospitalizations and 1 death
- Other isolated human cases in several countries eg. Switzerland 2017; mild disease

Clinical syndromes in human infections of novel subtypes of influenza A viruses

	Avian source		Swine source
	LPAI viruses	HPAI viruses	Variant viruses*
Conjunctivitis	H7N2, H7N3, H7N7, H10N7	H7N3, H7N7	H1N1v, H3N2v
Upper respiratory tract illness	H6N1, H7N2, H7N3, H7N9, H9N2, H10N7	H5N1, H5N6, H7N7	H1N1v, H1N2v, H3N2v
Lower respiratory tract disease, pneumonia	H7N2, H7N9, H9N2, H10N8	H5N1, H5N6, H7N7, H7N9	H1N1v, H3N2v
Respiratory failure, acute respiratory distress syndrome	H7N9, H10N8	H5N1, H5N6, H7N7, H7N9	H1N1v, H3N2v
Multiorgan failure	H7N9, H10N8	H5N1, H5N6, H7N7, H7N9	..
Encephalopathy or encephalitis	H7N9	H5N1	..
Fatal outcomes†	H7N9, H9N2, H10N8	H5N1, H5N6, H7N7, H7N9	H1N1v, H3N2v

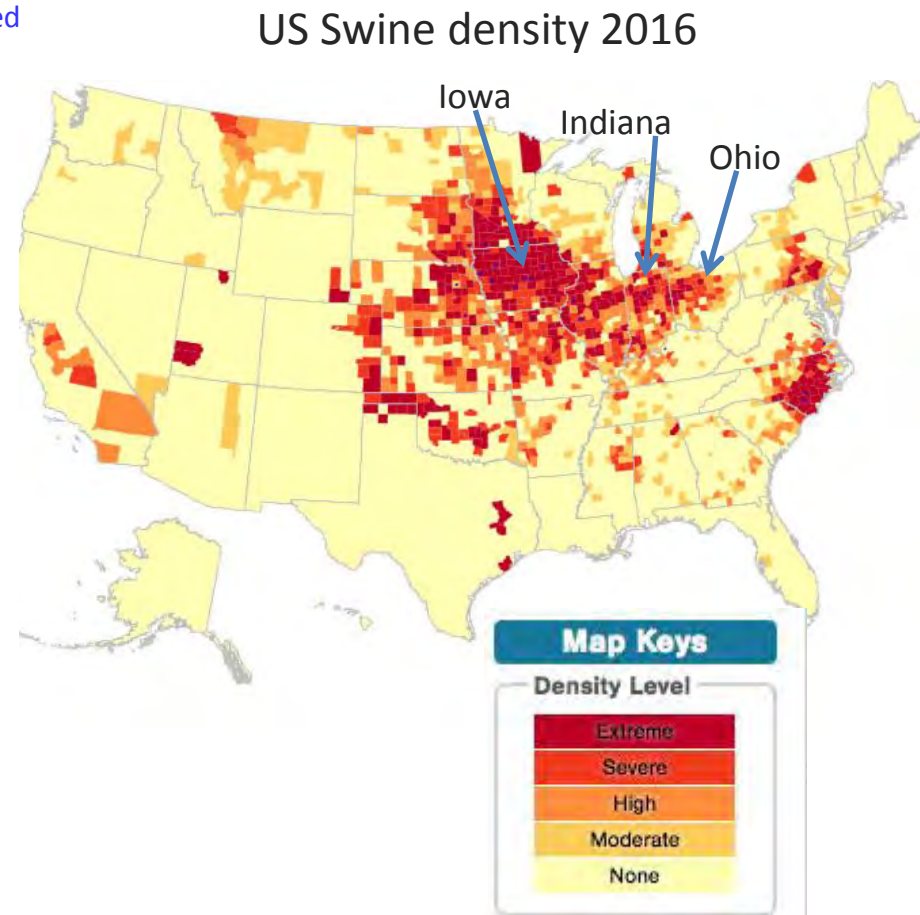
Uyeki T et al. Lancet 2017

*Variant viruses of swine origin

†High mortality in reported cases: about 40% for LPAI H7N9, about 50% for HPAI H5N1, and about 70% for HPAI H5N6.

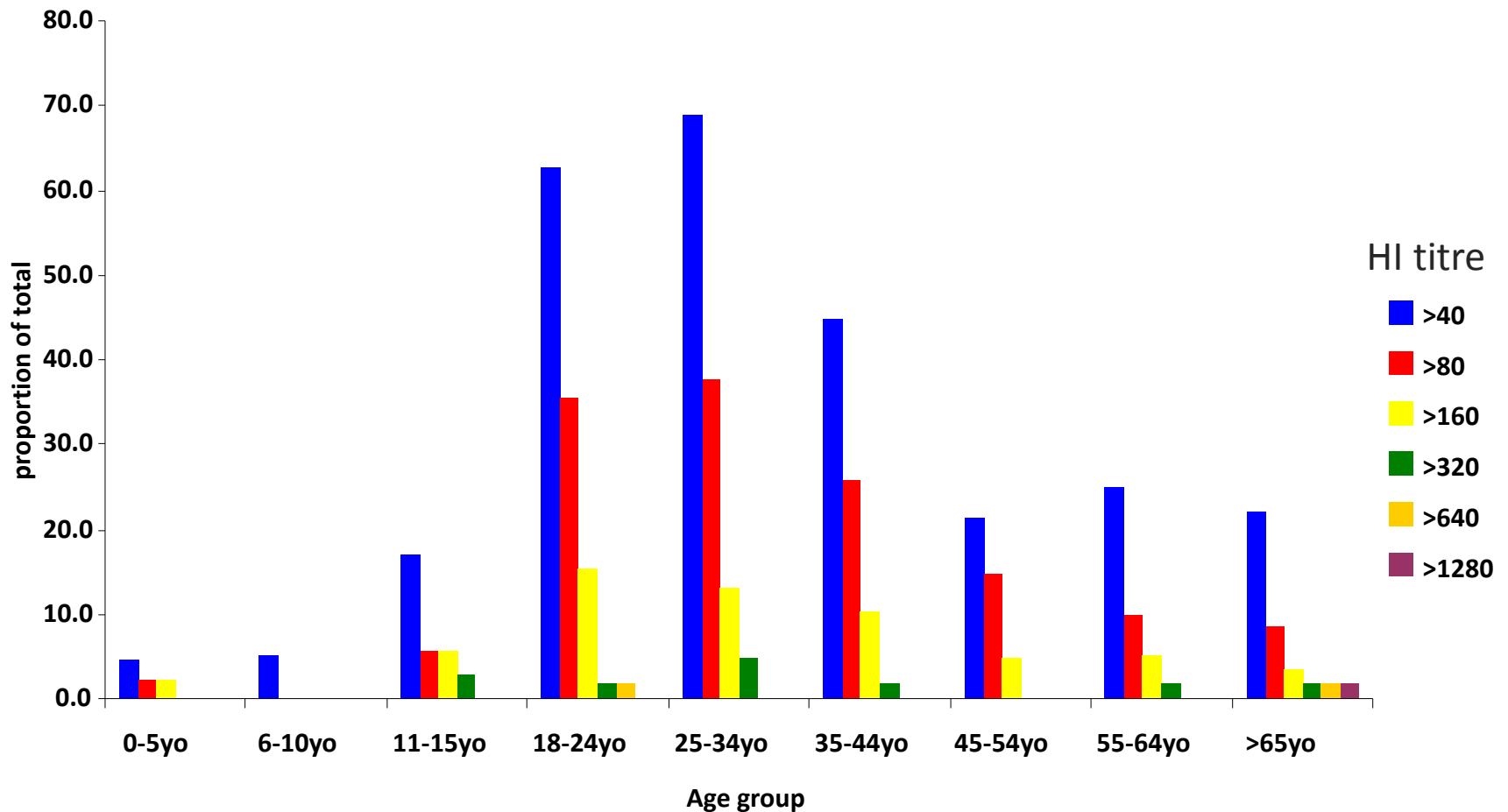
U.S. Human infections with Variant swine influenza Viruses by State (since December 2005)

Reporting State	H3N2v	H1N1v	H1N2v	Total Detected
Arkansas		2		
Colorado			1	
Delaware	1			
Hawaii	1			
Illinois	5	1		
Indiana	154			
Iowa	7	5	1	
Kansas	1			
Maine	2			
Maryland	51			
Michigan	23		1	
Minnesota	9	4	6	
Missouri		2		
Nebraska	1			
New Jersey	1			
North Dakota	1			
Ohio	131	3	3	
Pennsylvania	17			
South Dakota		1		
Texas	1	1		
Utah	1			
West Virginia	5			
Wisconsin	22	2	1	
Total	434** (93%)	21 (5%)	13 (2%)	468



**The majority of H3N2v human cases occurred in 2012 with 309 lab confirmed cases (71% H3N2v cases); with 16 hospitalizations and 1 death

Age dependent serum antibody levels to A/Minnesota/11/2010 H3N2v of Australians by MN titre (sera sampled end 2011)



Data generated by Karen Laurie @ WHO CC Melbourne

Swine influenza in Australia



Apart from incidental H1N1pdm infections, Australian swine thought to be influenza free
2 outbreaks detected in July/August 2012 in pigs in Western Australia and Queensland

Virus subtype	Source	Gene Segment							
		PB2	PB1	PA	HA	NP	NA	MP	NS
H1N2*	WA pigs	Red	Red	Red	Blue	Red	Green	Red	Red
H3N2*	WA pigs	Green	Green	Blue	Green	Green	Green	Green	Green
H1N2*	Qld pigs	Red	Red	Red	Blue	Red	Green	Red	Red
H1N2	Qld pigs	Red	Red	Red	Red	Red	Green	Red	Red
H1N1pdm	Qld pigs	Red	Red	Red	Red	Red	Red	Red	Red



H1N1pdm (post 2009)



Human H1N1 (~1983-96)

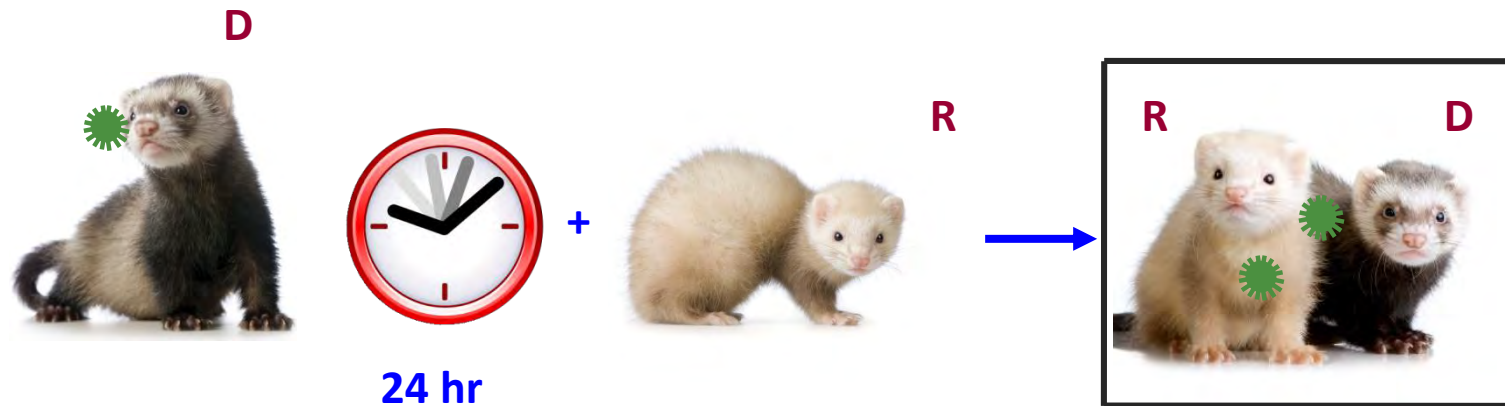


Human H3N2 (~1970-2003)

Virus isolation and sequencing work performed with CSIRO, AAHL, Geelong

Ferret contact transmission model

- ❖ Infect donors intranasally
- ❖ 24 hr's post infection, naïve ferret is placed in the same cage
- ❖ Transmission from donor to recipient ferret measured (RT-PCR + TCID₅₀)
- ❖ Actually a combination between contact/aerosol transmission

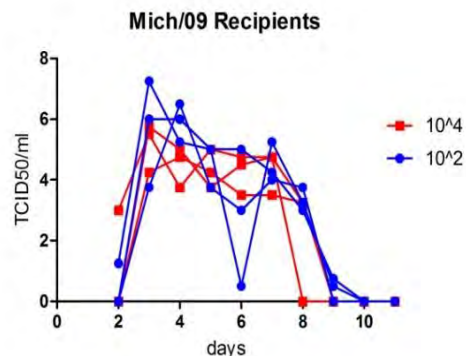
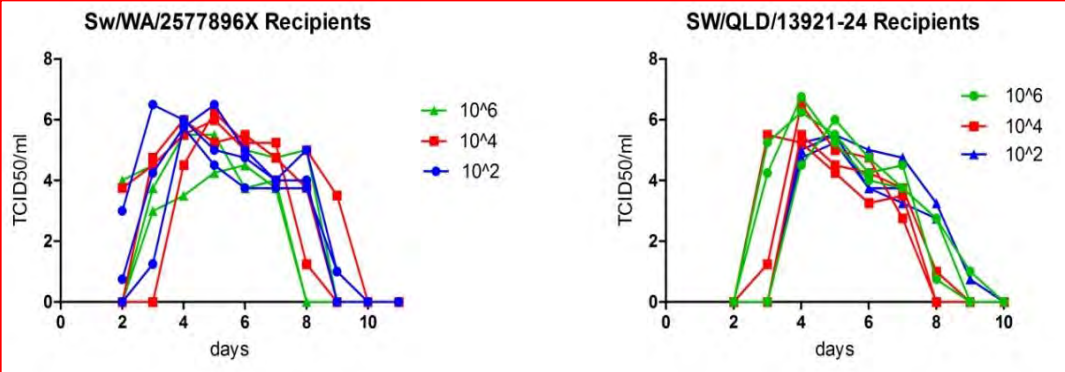
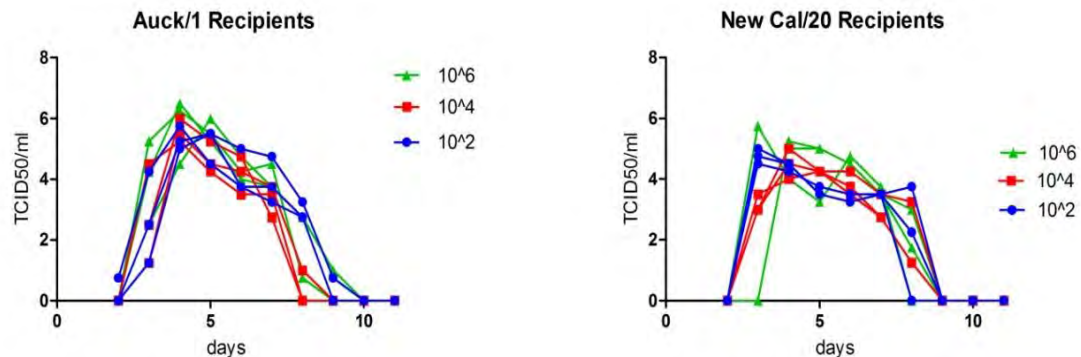


Work performed by Chantal Baas

- Hurt et al, 2010 J Virol 84(18): 9427-9438
- Laurie et al, 2010 J Infect Dis 202(7):1011-1020

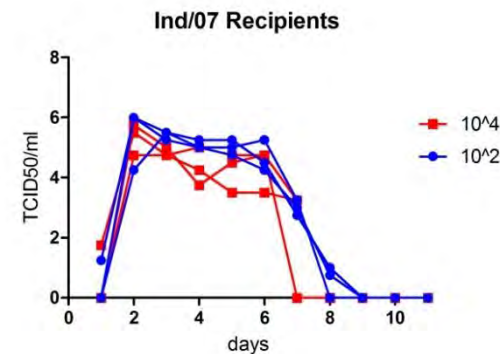
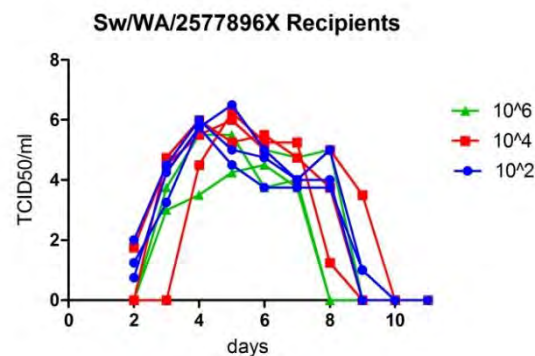
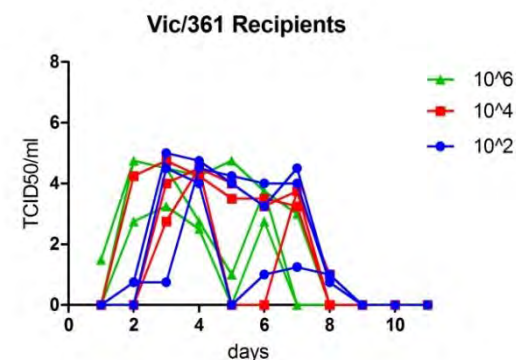
Australian swine H1 & H3 viruses readily transmit & replicate in ferret contact model (C. Baas)

A(H1) viruses



Conclusion: Both the Australian H1N2v and the H3N2v were capable of close contact transmission in ferrets and probably ?humans

A(H3) viruses



Can we learn from past influenza pandemics?



1918: “Spanish Flu”

40 to 50 million deaths

A(H1N1)

CFR 2-3%

Original source: ?

1957: “Asian Flu”

1 to 4 million deaths

A(H2N2)

CFR <0.2%

Original source: ?

1968: “Hong Kong Flu”

1 to 4 million deaths

A(H3N2)

CFR <0.2%

Original source: ?

2009: “Swine Flu”

<0.1 million deaths

A(H1N1)swl

CFR <0.005%

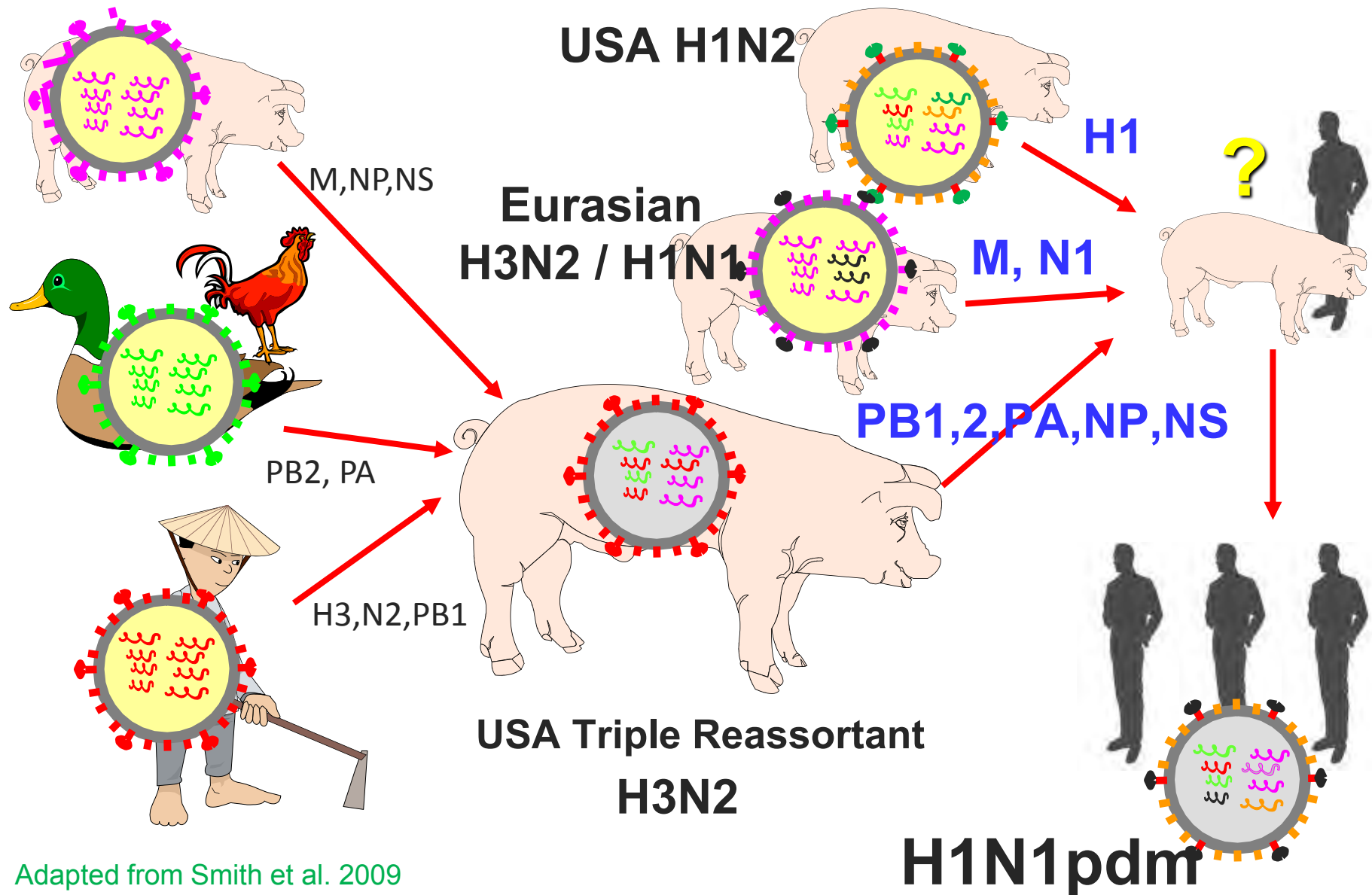


1977
Re-emergence
of A(H1N1)

Original source: swine?

How did the Pandemic (H1N1) 2009 arise?

No swine H1N1pdm09 virus; phylogenetic reconstruction only!



IRAT (CDC) and TIPRA (WHO)

- IRAT (Influenza Risk Assessment Tool) for pandemic preparedness
 - Developed by US CDC (began 18-19 October 2011)
 - CANNOT predict a future pandemic
 - Intended to prioritize and maximize investments in pandemic preparedness by helping to determine which novel (new) influenza viruses to develop vaccines
 - Identify key gaps in information and knowledge which can be the basis to prompt additional studies
 - Document in a transparent manner the data and scientific process used to inform management decisions associated with pandemic preparedness
 - Provide a flexible means to easily and regularly update the risk assessment of novel influenza viruses as new information becomes available
 - Be an effective communications tool for policy makers/influenza community
 - Be a measure (**by using 10 scientific criteria**) of the ability of an influenza virus to “emerge” as a pandemic capable virus (i.e., become capable of efficient human-to-human spread) or “impact” the human population if it did emerge

The 10 evaluation criteria of IRAT

Properties of the Virus

1. **Genomic variation** is a measure of the extent of genetic diversity or presence of known molecular signatures important for human infections and disease.
2. **Receptor binding** refers to the host preference (e.g., animal or human) of an influenza virus as well as the types of tissues and cells the virus is best suited to infecting (e.g., nose tissue and cells vs. deep lung tissue and cells)
3. **Transmission in lab animals** is a measure of the ability of an influenza virus to transmit efficiently in animals in laboratory studies (transmit through the air via small infectious droplets /direct contact with an infected host)
4. **Antiviral treatment susceptibility/resistance** is a measure of how well an influenza virus responds to treatment with influenza antiviral drugs, such as oseltamivir, zanamivir and M2 blockers.

Attributes of the Population

5. **Existing population immunity** does the human population has any existing immune protection against the novel influenza virus being evaluated. Susceptibility/severity may depend on age, geographic area, or genetic factors
6. **Disease severity and pathogenesis** measures the severity of illness caused by a particular influenza virus in people and/or animals.
7. **Antigenic relationship to vaccine candidates** is a measure of how similar a novel influenza virus is when compared to a current or previously manufactured influenza vaccine strain.

Ecology and Epidemiology

8. **Global distribution (animals)** measures of how widespread an influenza virus is in animals. For example, is the virus found in animals in a limited area or is it found in animals from many different areas?
9. **Infection in animal species** refers to what kinds of animals are impacted by the influenza virus and the likelihood of human contact with these animals. For example, are influenza infections occurring in wild birds or domestic birds?
10. **Human Infections** are human infections with a novel influenza virus are occurring. If so, how? Eg Has human-to-human transmission or clusters of disease occurred? or how frequently/easily does transmission occur after direct/prolonged contact between humans/ infected animals?

Information on H7N4 case provided by CNIC on 15.2.2018

(original H7N4 diagnosis by Jiangsu Provincial CDC)

58y female farmer from Jiangsu province, developed cough on 25/12/2017, local clinic 27/12/2017, County level hospital 30/12/2017, ICU city hospital 1/1/2018 (severe pneumonia), Discharged 22/1/2018

Full genome analysis based on the throat swab of the patient

BLAST result of each segment showed that all segments sharing high identity with avian influenza viruses (Table 1). It contained PKGR↓G at the cleavage site of HA, indicating low pathogenic to poultry. Phylogenetic analysis of HA gene indicated it was distinct from the A(H7N9) virus which caused outbreaks since 2013 in China (figure 1). Internal genes are not from H9N2 virus (Table 1).

Key molecular makers:

- ✓ Mutations that reduced sensitivity to Neuraminidase inhibitors were NOT found in this virus.
- ✓ Mutations that reduced sensitivity to amantadine and rimatadine were NOT found in this virus.
- ✓ It contained the 186G, 226Q and 228G (H3 numbering) in HA1, indicating avian-type receptor specificity.
- ✓ The sequence of patient sample carried 627K in PB2, reported as mammalian adaption. Sequence from chicken and duck samples showed E in 627 position of PB2.

Next.....

Influenza subject matter experts evaluate novel influenza viruses based on each of these 10 criteria “low risk” scored 1-10; 1-3; “moderate risk” scored 4-7; “high risk” scored 8-10 then elements multiplied by set weightings for BOTH “Emergence” and “Impact” then graphed.

Average risk point scores and ranked weighting applied to risk scoring of influenza A(H7N9) virus isolate A/Shanghai/1/2013 for emergence and impact questions, May 2013*

Emergence question

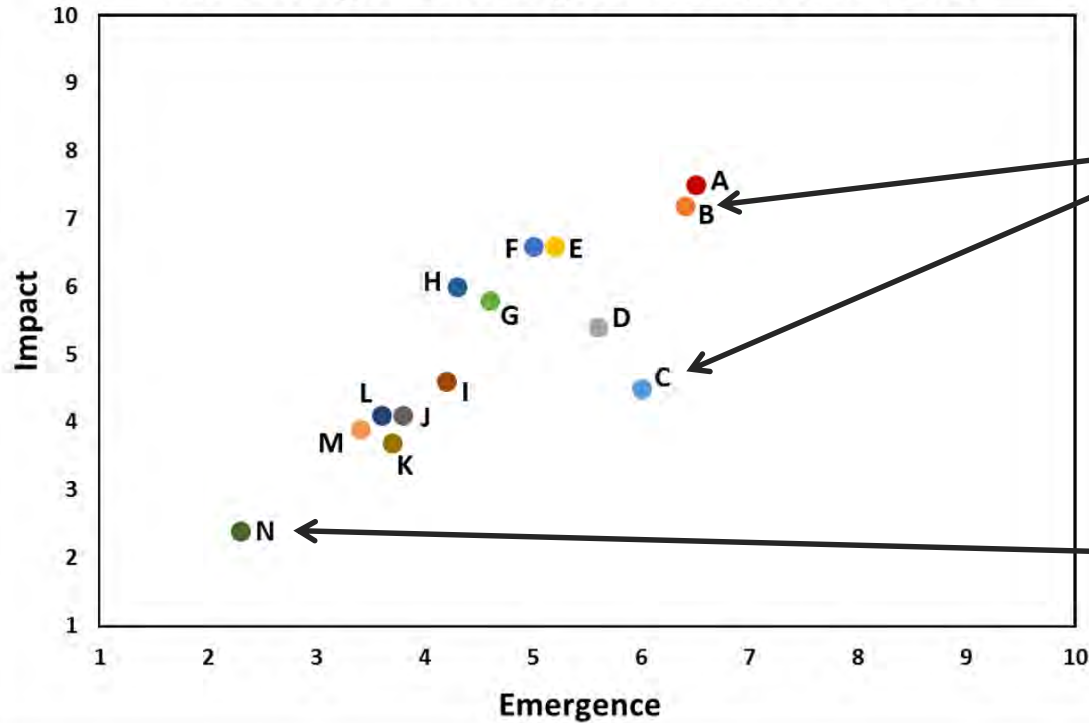
		Average point scores
Element	Weight	May 2013
Human infections	0.2929	5.0
Transmission (laboratory animals)	0.1929	7.0
Receptor binding	0.1429	6.3
Population immunity	0.1096	9.0
Infections in animals	0.0846	4.7
Genomic variation	0.0646	8.6
Antigenic relationship	0.0479	3.7
Global distribution (animals)	0.0336	4.7
Disease severity	0.0211	8.5
Antivirals/treatment options	0.001	5.8
Weighted IRAT aggregate score		6.2

Impact question

		Average point scores
Element	Weight	May 2013
Disease severity	0.2929	8.5
Population immunity	0.1929	9.0
Human infections	0.1429	5.0
Antivirals/treatment options	0.1096	5.8
Antigenic relationship	0.0846	3.7
Receptor binding	0.0646	6.3
Genomic variation	0.0479	8.6
Transmission(laboratory animals)	0.0336	7.0
Global distribution (animals)	0.0211	4.7
Infections in animals	0.001	4.7
Weighted IRAT aggregate score		7.0

And the output

IRAT Emergence and Impact - Average Risk Scores



	Virus	Emergence Score	Impact Score
● A	H7N9 [A/Hong Kong/125/2017]	6.5	7.5
● B	H7N9 [A/Shanghai/02/2013]	6.4	7.2
● C	H3N2 variant [A/Indiana/08/2011]	6.0	4.5
● D	H9N2 G1 lineage [A/Bangladesh/0994/2011]	5.6	5.4
● E	H5N1 Clade 1 [A/Vietnam/1203/2004]	5.2	6.6
● F	H5N6 [A/Yunnan/14584/2015] – like	5.0	6.6
● G	H7N7 [A/Netherlands/2019/2003]	4.6	5.8
● H	H10N8 [A/Jiangxi-Donghui/346/2013]	4.3	6.0
● I	H5N8 [A/gyrfalcon/Washington/41088/2014]	4.2	4.6
● J	H5N2 [A/Northern pintail/Washington/40964/2014]	3.8	4.1
● K	H3N2 [A/canine/Illinois/12191/2015]	3.7	3.7
● L	H5N1 [A/American green-winged teal/Washington/1957050/2014]	3.6	4.1
● M	H7N8 [A/turkey/Indiana/1573-2/2016]	3.4	3.9
● N	H1N1 [A/duck/New York/1996]	2.3	2.4

WHO CC's/ERL makes seed viruses against the most prevalent/concerning/different viruses currently circulating

H5Nx

Table 4. Status of influenza A(H5) candidate vaccine virus development

Candidate vaccine viruses	Clade	Institution*	Available
A/Viet Nam/1203/2004 (CDC-RG; SJRG-161052)	1	CDC and SJCRH	Yes
A/Viet Nam/1194/2004 (NIBRG-14)	1	NIBSC	Yes
A/Cambodia/R0405050/2007 (NIBRG-88)	1.1	NIBSC	Yes
A/Cambodia/X0810301/2013 (IDCDC-RG34B)	1.1.2	CDC	Yes
A/duck/Hunan/795/2002 (SJRG-166614)	2.1.1	SJCRH/HKU	Yes
A/Indonesia/5/2005 (CDC-RG2)	2.1.3.2	CDC	Yes
A/Indonesia/NIHRD11771/2011 (NIIDRG-9)	2.1.3.2a	NIID	Yes
A/bar-headed goose/Qinghai/1A/2005 (SJRG-163222)	2.2	SJCRH/HKU	Yes
A/chicken/India/NIV33487/2006 (IBCDC-RG7)	2.2	CDC/NIV	Yes
A/whooper swan/Mongolia/244/2005 (SJRG-163243)	2.2	SJCRH	Yes
A/Egypt/2321-NAMRU3/2007 (IDCDC-RG11)	2.2.1	CDC	Yes
A/turkey/Turkey/1/2005 (NIBRG-23)	2.2.1	NIBSC	Yes
A/Egypt/N03072/2010 (IDCDC-RG29)	2.2.1	CDC	Yes
A/Egypt/3300-NAMRU3/2008 (IDCDC-RG13)	2.2.1.1	CDC	Yes
A/Egypt/N04915/2014 (NIBRG-306)	2.2.1.2	NIBSC	Yes
A/common magpie/Hong Kong/5052/2007 (SJRG-166615)	2.3.2.1	SJCRH/HKU	Yes
A/Hubei/1/2010 (IDCDC-RG30)	2.3.2.1a	CDC	Yes
A/duck/Bangladesh/19097/2013 (SJ007)	2.3.2.1a	SJCRH	Yes
A/barn swallow/Hong Kong/D10-1161/2010 (SJ003)	2.3.2.1b	SJCRH/HKU	Yes
A/duck/Viet Nam/NCVD-1584/2012 (NIBRG-301)	2.3.2.1c	NIBSC	Yes
A/chicken/Hong Kong/AP156/2008 (SJ002)	2.3.4	SJCRH/HKU	Yes
A/Anhui/1/2005 (IBCDC-RG6)	2.3.4	CDC	Yes
A/duck/Laos/3295/2006 (CBER-RG1)	2.3.4	FDA	Yes
A/Japanese white eye/Hong Kong/1038/2006 (SJRG-164281)	2.3.4	SJCRH/HKU	Yes
A/chicken/Bangladesh/11rs1984-30/2011 (IDCDC-RG36)	2.3.4.2	CDC	Yes
A/Guizhou/1/2013 (IDCDC-RG35)	2.3.4.2	CDC/CCDC	Yes
A/Sichuan/26221/2014 (IDCDC-RG42A) (H5N6)	2.3.4.4	CDC/CCDC	Yes
A/Hubei/29578/2016 (H5N6)	2.3.4.4	CCDC	Yes
A/gyrfalcon/Washington/41088-6/2014 (IDCDC-RG43A) (H5N8)	2.3.4.4	CDC	Yes
A/duck/Hyogo/1/2016 (NIID-001) (H5N6)	2.3.4.4	NIID	Yes
A/goose/Guizhou/337/2006 (SJRG-165396)	4	SJCRH/HKU	Yes
A/chicken/Viet Nam/NCVD-016/2008 (IDCDC-RG12)	7.1	CDC	Yes
A/chicken/Viet Nam/NCVD-03/2008 (IDCDC-RG25A)	7.1	CDC	Yes

Candidate vaccine viruses in preparation	Clade	Institution	Availability
A/chicken/Guizhou/1153/2016	2.3.2.1c	SJCRH/HKU	Pending
A/chicken/Ghana/20/2015-like	2.3.2.1c	CDC	Pending
A/chicken/Viet Nam/NCVD-15A59/2015 (H5N6)	2.3.4.4	SJCRH	Pending
A/Fujian-Sanyuan/21099/2017-like (H5N6)	2.3.4.4	CCDC	Pending
A/environment/Hubei/950/2013	7.2	CDC/CCDC	Pending

* Institutions developing and/or distributing the candidate vaccine viruses:

CDC - Centers for Disease Control and Prevention, United States of America

NIV - National Institute of Virology, India

CCDC - Chinese Center for Disease Control and Prevention

FDA - Food and Drug Administration, United States of America

HKU - University of Hong Kong, Hong Kong Special Administrative Region, China.

NIBSC - National Institute for Biological Standards and Control, a centre of the Medicines and Healthcare products Regulatory Agency (MHRA), United Kingdom

NIID - National Institute of Infectious Diseases, Japan

SJCRH - St Jude Children's Research Hospital, United States of America

H7N9

Table 5. Status of influenza A(H7N9) candidate vaccine virus development

Candidate vaccine virus	Type	Institution*	Available
IDCDC-RG33A (A/Anhui/1/2013)	Reverse genetics	CDC	Yes
NIBRG-268 (A/Anhui/1/2013)	Reverse genetics	NIBSC	Yes
NIIDRG-10.1 (A/Anhui/1/2013)	Reverse genetics	NIID	Yes
SJ005 (A/Anhui/1/2013)	Reverse genetics	SJCRH	Yes
NIBRG-267 (A/Shanghai/2/2013)	Reverse genetics	NIBSC	Yes
CBER-RG4A (A/Shanghai/2/2013)	Reverse genetics	FDA	Yes
IDCDC-RG32A (A/Shanghai/2/2013)	Reverse genetics	CDC	Yes
IDCDC-RG32A.3 (A/Shanghai/2/2013)	Reverse genetics	CDC	Yes
IDCDC-RG56B (A/Hong Kong/125/2017-like)	Reverse genetics	CDC	Yes
CNIC-GD003 (A/Guangdong/17SF003/2016-like)	Reverse genetics	CCDC	Yes
IDCDC-RG56N (A/Guangdong/17SF003/2016-like)	Reverse genetics	CDC	Yes
NIBRG-375 (A/Guangdong/17SF003/2016-like)	Reverse genetics	NIBSC	Yes
CBER-RG7C (A/Guangdong/17SF003/2016-like)	Reverse genetics	FDA	Yes
CNIC-HN02650 (A/Hunan/02650/2016-like)	Reverse genetics	CCDC	Yes

H7Nx

Table 6. Status of influenza A(H7) candidate vaccine virus development (excluding A(H7N9))

Candidate vaccine virus	Subtype	Type	Institution*	Available
A/mallard/Netherlands/12/2000 (NIBRG-63)	H7N1	Reverse genetics	NIBSC	Yes
A/turkey/Italy/3889/99	H7N1	Wild type	NIBSC	Yes
A/turkey/Virginia/4529/2002 (IBCDC-5)	H7N2	Reverse genetics	CDC	Yes
A/New York/107/2003 (NIBRG-109)	H7N2	Reverse genetics	NIBSC	Yes
A/Canada/rv444/2004 (SJRG-161984)	H7N3	Reverse genetics	SJCRH	Yes
A/mallard/Netherlands/12/2000 (NIBRG-60)	H7N3	Reverse genetics	NIBSC	Yes
A/mallard/Netherlands/12/2000 (IBCDC-1)	H7N7	Conventional	CDC	Yes

H9

Table 7. Status of influenza A(H9N2) candidate vaccine virus development

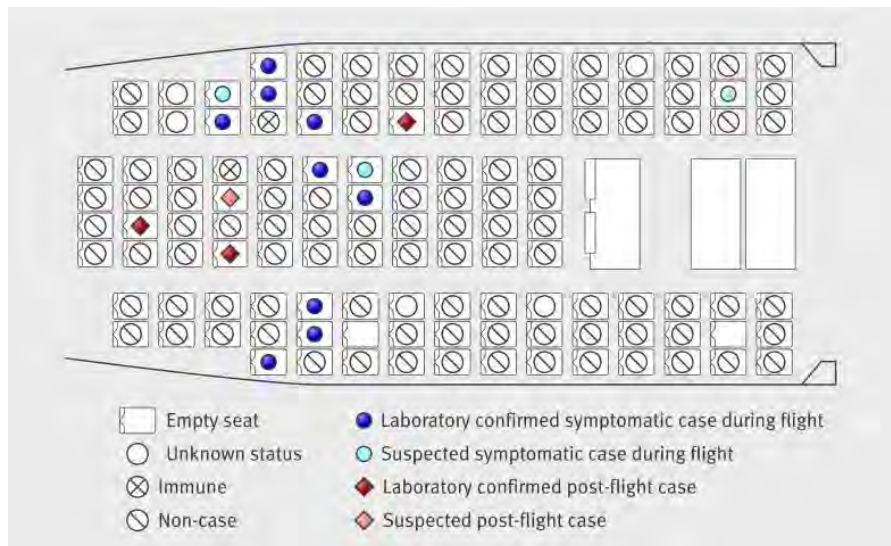
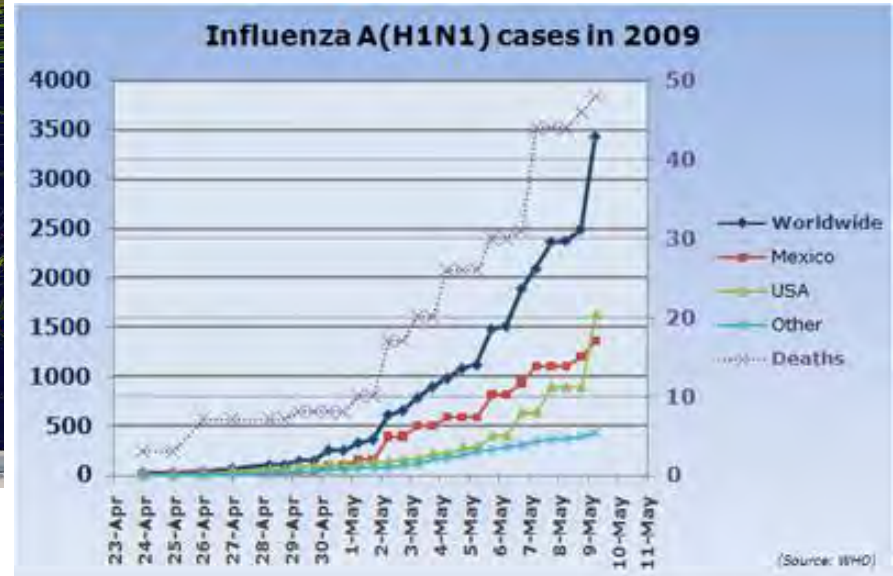
Candidate vaccine viruses	Type	Clade	Institution*	Available
A/Hong Kong/1073/99	Wild type	G1	NIBSC	Yes
A/chicken/Hong Kong/G9/97 (NIBRG-91)	Reverse genetics	Y280/G9	NIBSC	Yes
A/chicken/Hong Kong/G9/97 (IBCDC-2)	Conventional	Y280/G9	CDC	Yes
A/Hong Kong/33982/2009 (IDCDC-RG26)	Reverse genetics	G1	CDC	Yes
A/Bangladesh/994/2011 (IDCDC-RG31)	Reverse genetics	G1	CDC	Yes
A/Hong Kong/308/2014 (SJ008)	Reverse genetics	Y280/G9	SJCRH	Yes

http://www.who.int/influenza/vaccines/virus/201802_zoonotic_vaccinevirusupdate.pdf?ua=1

Global interconnectivity in 21st Century – airline routes

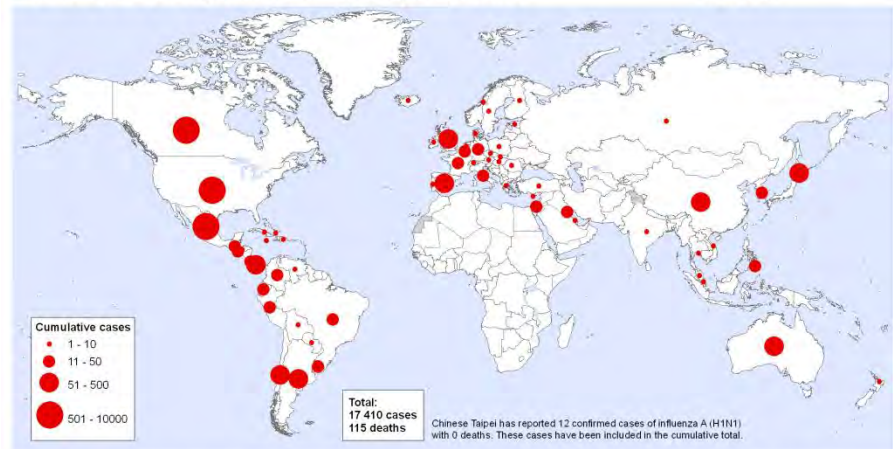


Swine H1N1 human pandemic in 2009



New Influenza A (H1N1),
Number of laboratory confirmed cases as reported to WHO

Status as of 01 June 2009
06:00 GMT



BMJ. 2010 May 21;340:c2424. doi: 10.1136/bmj.c2424.

Transmission of pandemic A/H1N1 2009 influenza on passenger aircraft: retrospective cohort study.

Baker MG, Thornley CN, Mills C, Roberts S, Perera S, Peters J, Kelso A, Barr I, Wilson N.

The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.

Map produced: 01 June 2009 06:46 GMT

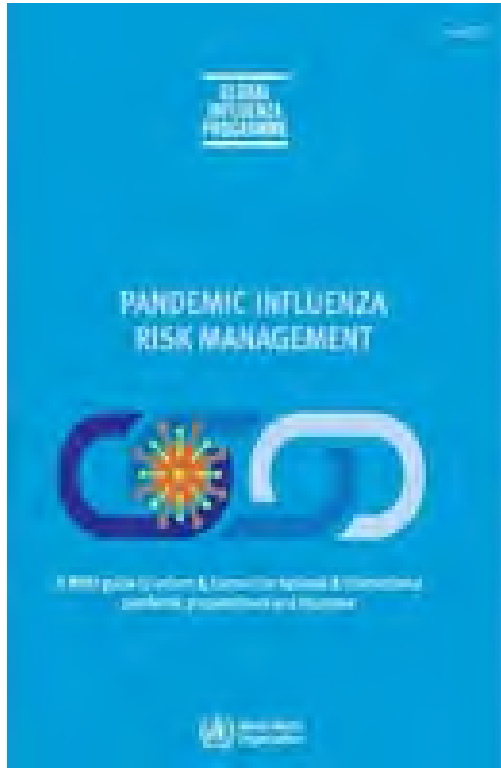
Data Source: World Health Organization
Map Production: Public Health Information
and Geographic Information Systems (GIS)
World Health Organization

World Health Organization
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Summary

- The source and subtype of the next pandemic influenza virus is unknown
- At this point in time:
 - H5Nx viruses are still prevalent in wild birds, less so in poultry, even less so in humans
 - H7N9 viruses in man and poultry in China are vastly reduced in 2017-8 vs 2016-7
 - Swine viruses (eg H1N1v, H1N2v, H3N2v) cases persist in USA (+ elsewhere) but reduced
- But.....
 - Avian influenza viruses are still quite prevalent
 - Avian surveillance (especially poultry) is heavily focused on HPAI viruses
 - Influenza surveillance in swine is very limited (USA/Europe)
 - Extensive reassorting of viruses occurs at all interfaces b/w **av/av, sw/sw, av/sw, sw/human**
 - A small number of amino acid changes (HA/NA/PB2) can change transmission efficiency
- Evaluation tools, animal models and NGS give us insights into novel viruses
 - CDC IRAT and WHO TIPRA “rank” potential pandemic viruses by “emergence” & “severity”
 - WHO has a bank of seed viruses prepared that can be rapidly used for vaccine production
 - WHO has developed a series of processes for use in a pandemic eg PISA, PIRM etc.
- Need to remain flexible
 - May get another 2009 pandemic (mild) or a more severe pandemic (1968, moderate)
 - Source wont matter once the pandemic occurs but can try to reduce current potential sources

Updated and new WHO pandemic documents



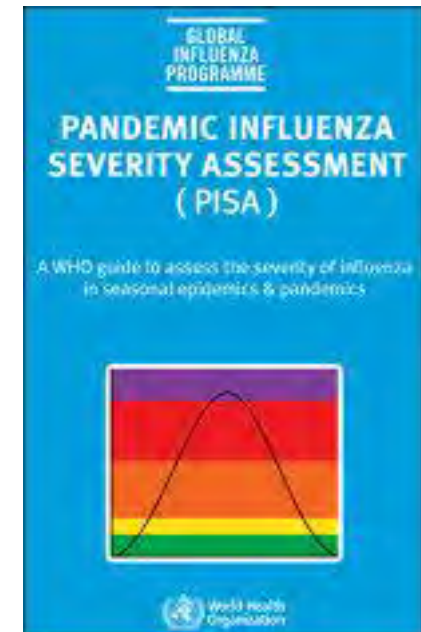
May 2017



Jan 2018



Mar 2018



May 2017



Mar 2017



The End

Yes, you can clap now!!

