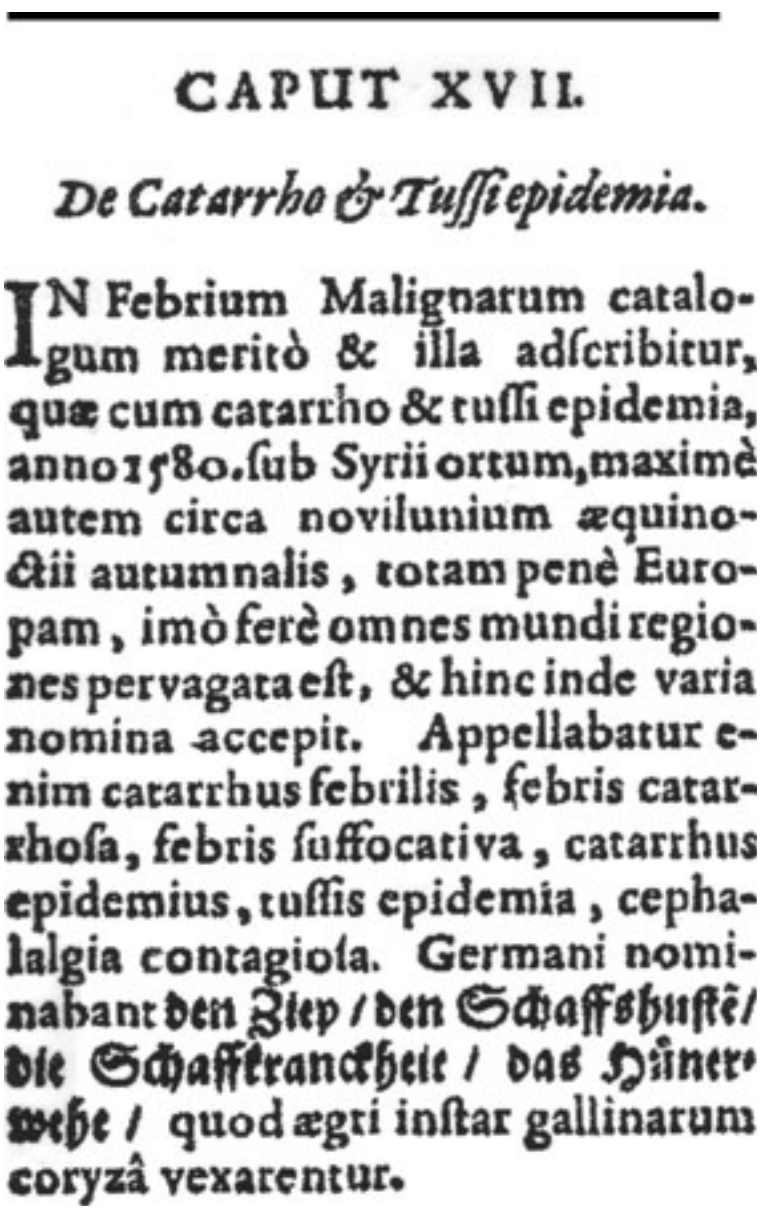
Zoonosis

Intra-species transmission

Influenza A virus is remarkable for the frequency and breadth of zoonoses: many species of birds, humans, pigs, horses, dogs

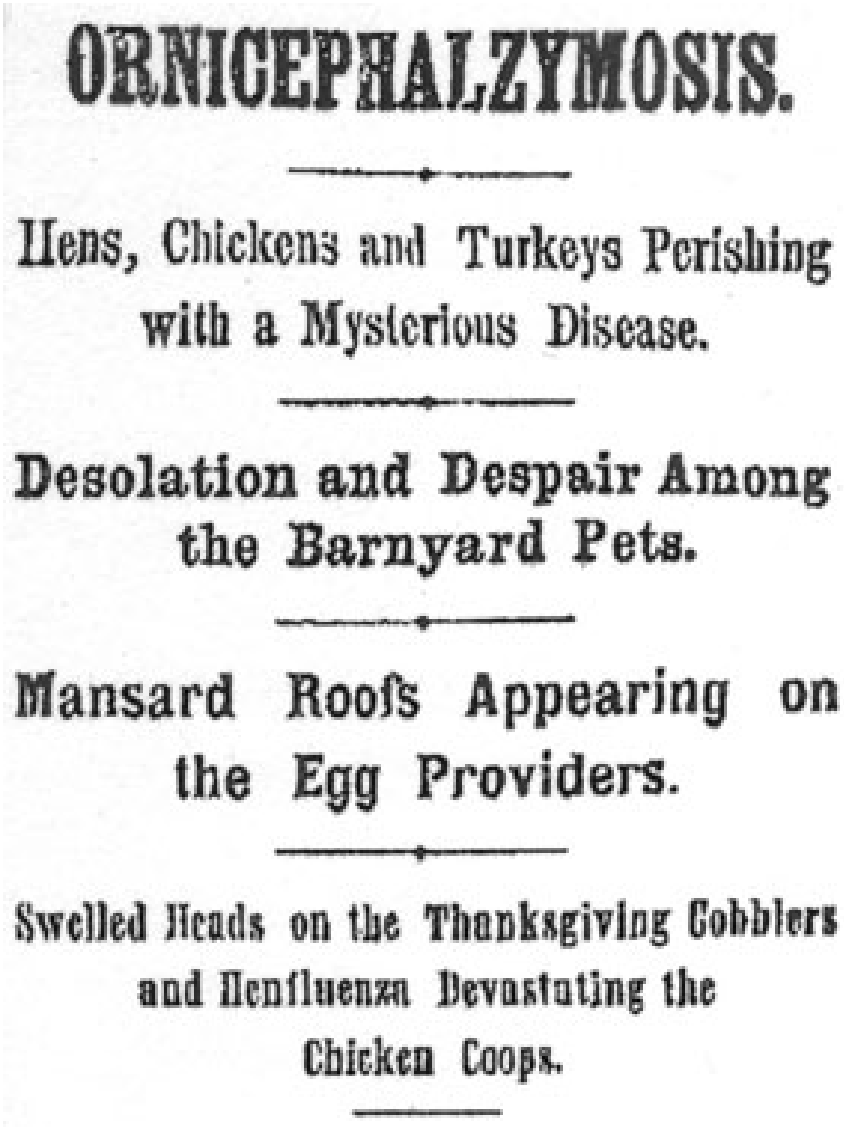


CAPUT XVII.

De Catarrho & Tussi epidemia.

IN Febrium Malignarum catalogum meritò & illa adscribitur, quæ cum catarrho & tussi epidemia, anno 1580. sub Syrii ortum, maximè autem circa novilunium æquinoctii autumnalis, totam penè Europam, imò ferè omnes mundi regiones pervagata est, & hinc inde varia nomina accepit. Appellabatur enim catarrhus febrilis, febris catarrhosa, febris suffocativa, catarrhus epidemius, tussis epidemia, cephalalgia contagiosa. Germani nominabant den Ziep / den Schaffshuste / die Schafftranckheit / das Hünerwehe / quod ægri instar gallinarum coryzâ vexarentur.

Figure 3. The first page of Chapter 17, ''On the catarrh and coughing epidemic'', in Daniel Sennert's account of the 1580 influenza pandemic.[48] Sennert refers obliquely to a ''coryza of chickens'', but it is not known whether avian influenza occurred during the pandemic.



ORNICEPHALZYMOSIS.

Hens, Chickens and Turkeys Perishing with a Mysterious Disease.

Desolation and Despair Among the Barnyard Pets.

Mansard Roofs Appearing on the Egg Providers.

Swelled Heads on the Thanksgiving Cobblers and Henfluenza Devastating the Chicken Coops.

Figure 2. *New York Herald* headline (Monday, November 18, 1872, page 3, column 6), reporting outbreaks of fatal avian disease in birds brought from surrounding areas into New York City and elsewhere.[30]

Pandemics since 1700

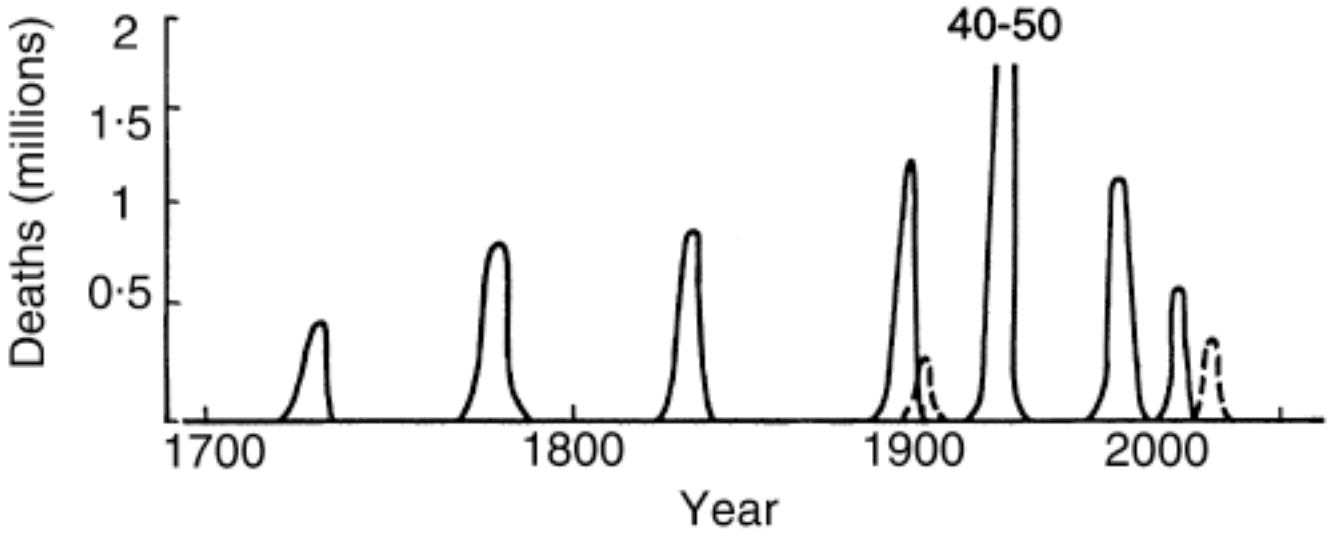


Fig. 2 History of influenza pandemics 1700–2000. Not to exact scale

The 1918 pandemic was totally out of scale and has been called `the greatest medical holocaust in history.' 40-50 million deaths but that was only a few percent of the infected (20% of the world's population).

The 1918 “Spanish flu” pandemic

Policemen in Seattle during the 1918 pandemic

Your Pastor Speaks to You Here

Missoula Clergymen, Barred From Pulpits by Epidemic, Talk to Their Parishioners Through the Columns of This Morning's Missoulian.

We Need a Faith That Casts Out All Fears

BY REV. J. N. MACLEAN, D. D.
of the Presbyterian Church.

"There stood by me this night the angel of God whose I am and whom I serve, saying, Fear not." Acts 27:23.

These words were spoken in circumstances that gave no opportunity for camouflage. They represent genuine human experience. They were spoken on board a storm-driven ship, when all hope of being saved, except the hope of one man, was taken away. For fourteen days and nights the storm prevailed, "neither sun nor stars appearing" through the clouds and darkness. There were seventy-six souls on board, consisting of ship's crew and passengers and some soldiers in charge of a few prisoners on the way to Rome for trial before the emperor. It was the climax of the storm, and the roar of

it

Churchless Sundays May Revive the Family Altar

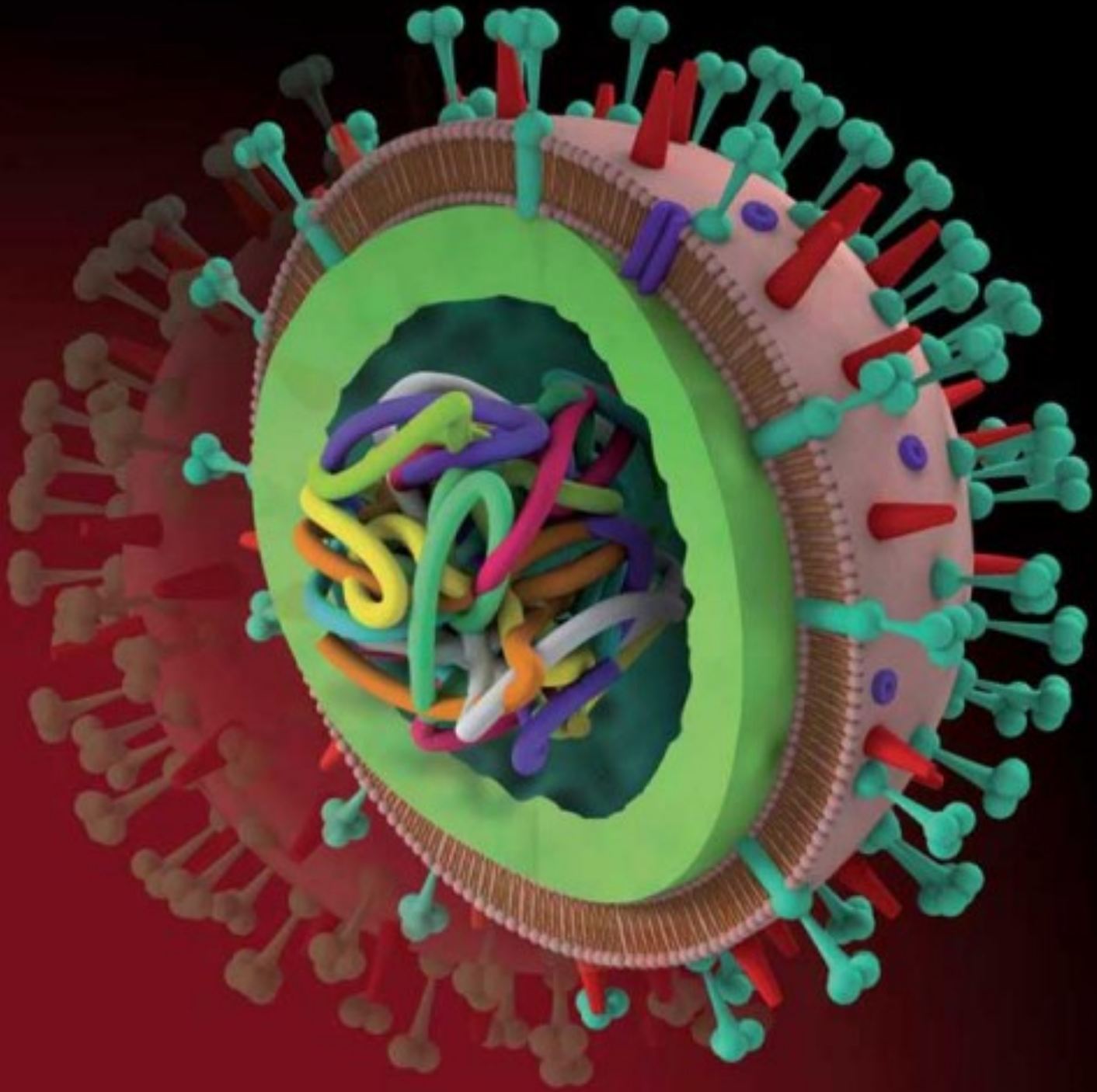
BY. REV. CHARLES D. CROUCH
of First Methodist Episcopal Church.

"For I know Him that He will command His children, and His household after Him." (Genesis 18:19).

At noon, as Abram sat in the door of his tent three men dressed in shining garments stood before him. They were angels. The home, where God loves to dwell is the truly happy home. His angels visit homes where husbands love their wives and where wives love their husbands, and where children honor their parents. Such a home is in harmony with God's will and God's law. Angels can go wherever God, the Father, the great head of the family in Heaven, is respected.

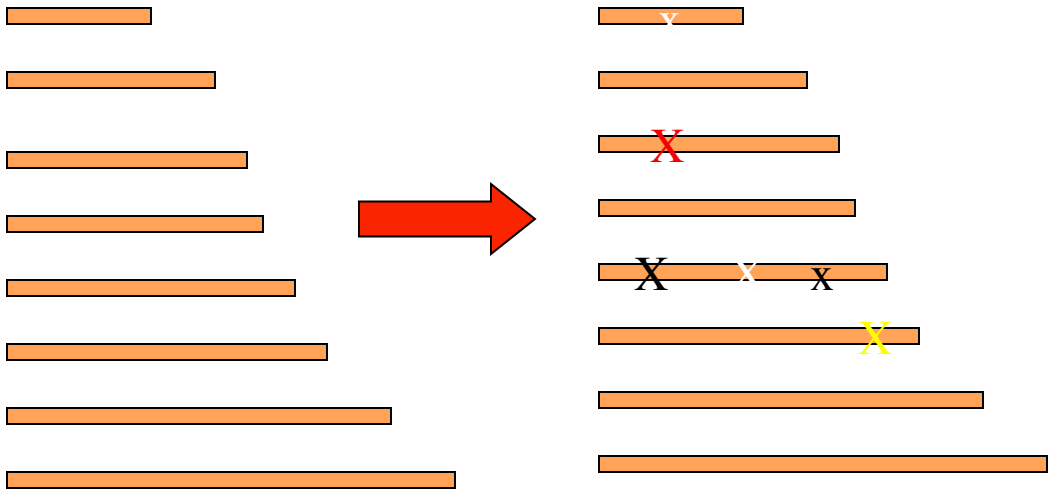
All over our great land the epidemic of Spanish influenza is raging, followed by a deadly form of pneumonia. Obedient to the orders of the public

DM 10/27/18 P8.4

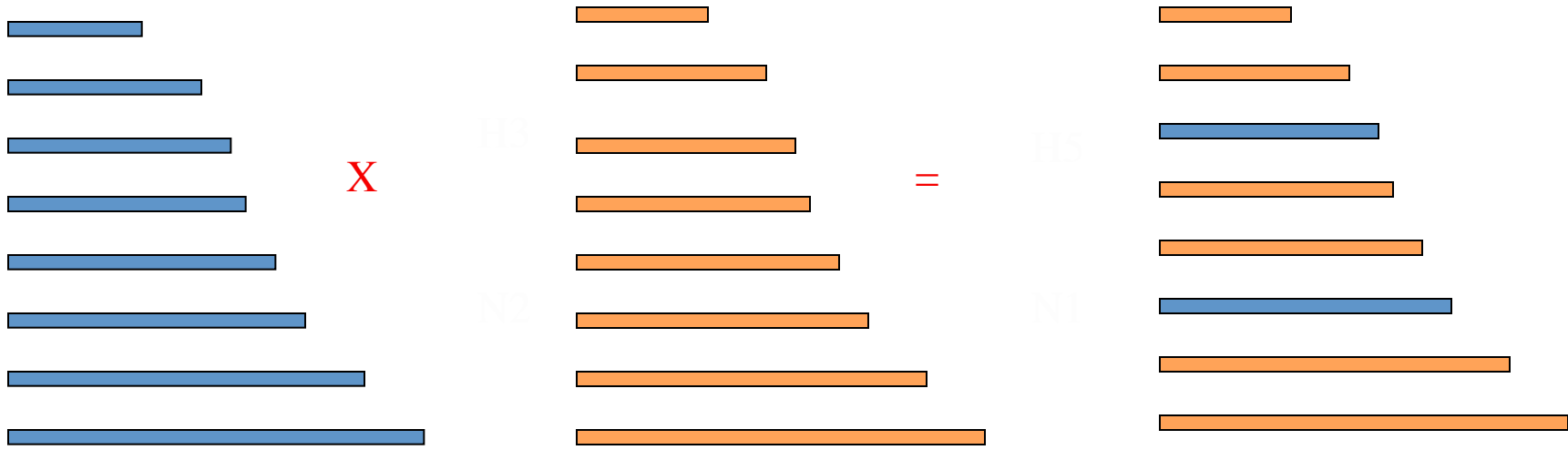


Genetic Changes Among Influenza Viruses:
DRIFT
Associated with human EPIDEMIC

Mutations



Genetic Changes Among Influenza Viruses: REASSORTMENT=SHIFT Associated with human PANDEMIC

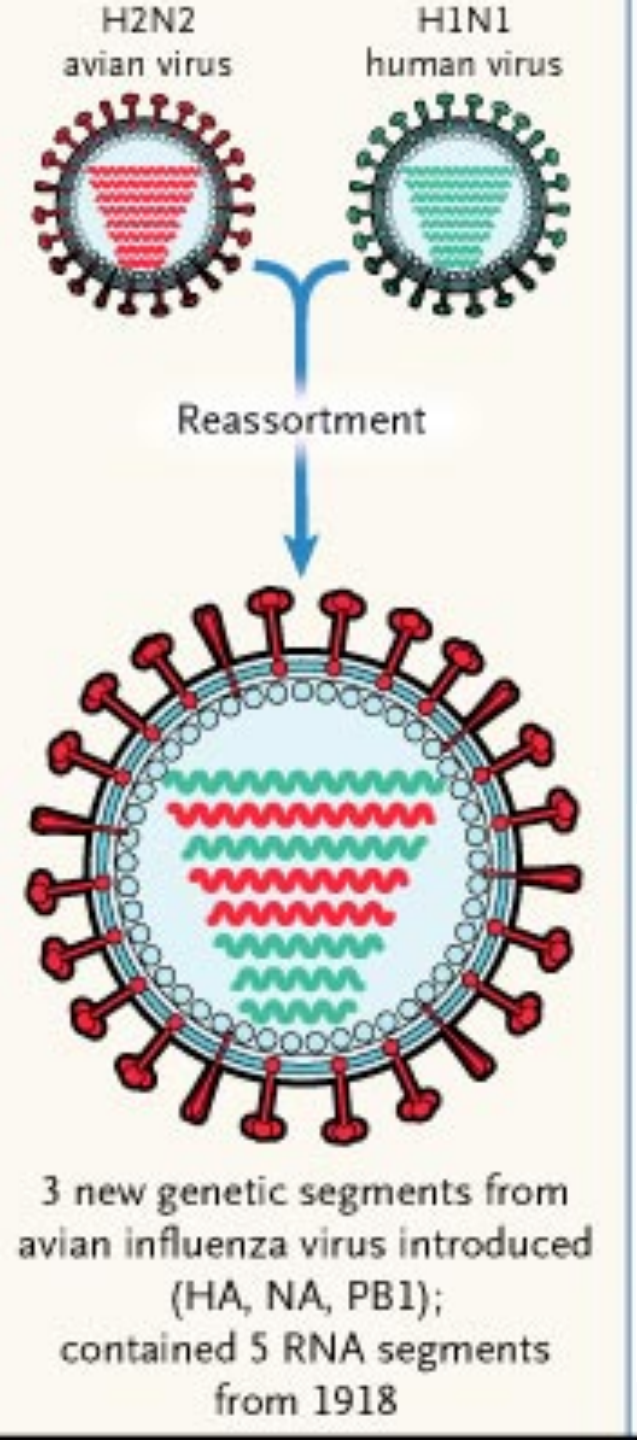


The 1918 “Spanish flu” pandemic

Table 1. Age-specific excess mortality related to influenza A (H1N1), United States.

Season	Influenza subtype	P&I data source*	Excess mortality rate/100,000† for: All ages	Persons ⩾65 years old	Persons <65 years old
1918–1919	**H1N1**	[16]	529 (546,000)	166 (8000)	546 (538,000)
1919–1920	H1N1	[16]	93 (96,000)	175 (8000)	89 (88,000)
1921–1922	H1N1	[16]	16 (17,000)	93 (5000)	12 (12,000)
1922–1923	H1N1	[16]	37 (41,000)	280 (16,000)	24 (25,000)
1925–1926	H1N1	[16]	26 (30,000)	221 (14,000)	15 (16,000)
1928–1929	H1N1	[16]	84 (102,000)	594 (39,000)	55 (63,000)
1936–1937	H1N1	[16]	18 (23,000)	101 (8000)	12 (15,000)
1943–1944	H1N1	[15]	14 (19,000)	123 (13,000)	4.8 (6000)
1977–1978§	H1N1		3.8 (8300)	30 (7100)	0.6 (1200)
	H3N2	[19]	3.7 (8200)	31 (7400)	0.4 (800)
		[4]	3.3 (7300)	26 (6300)	0.5 (1000)
1983–1984	H1N1, B		1.5 (3500)	16 (4400)	0 (0)
1986–1987	H1N1		0.7 (1800)	5.7 (1700)	0 (0)
1988–1989	H1N1, B		2.1 (5100)	15 (4400)	0.1 (200)

Table from Simonsen *et al*, *The Journal of Infectious Diseases*, 178:53 (1998)



1957 "Asian flu" H2N2 pandemic

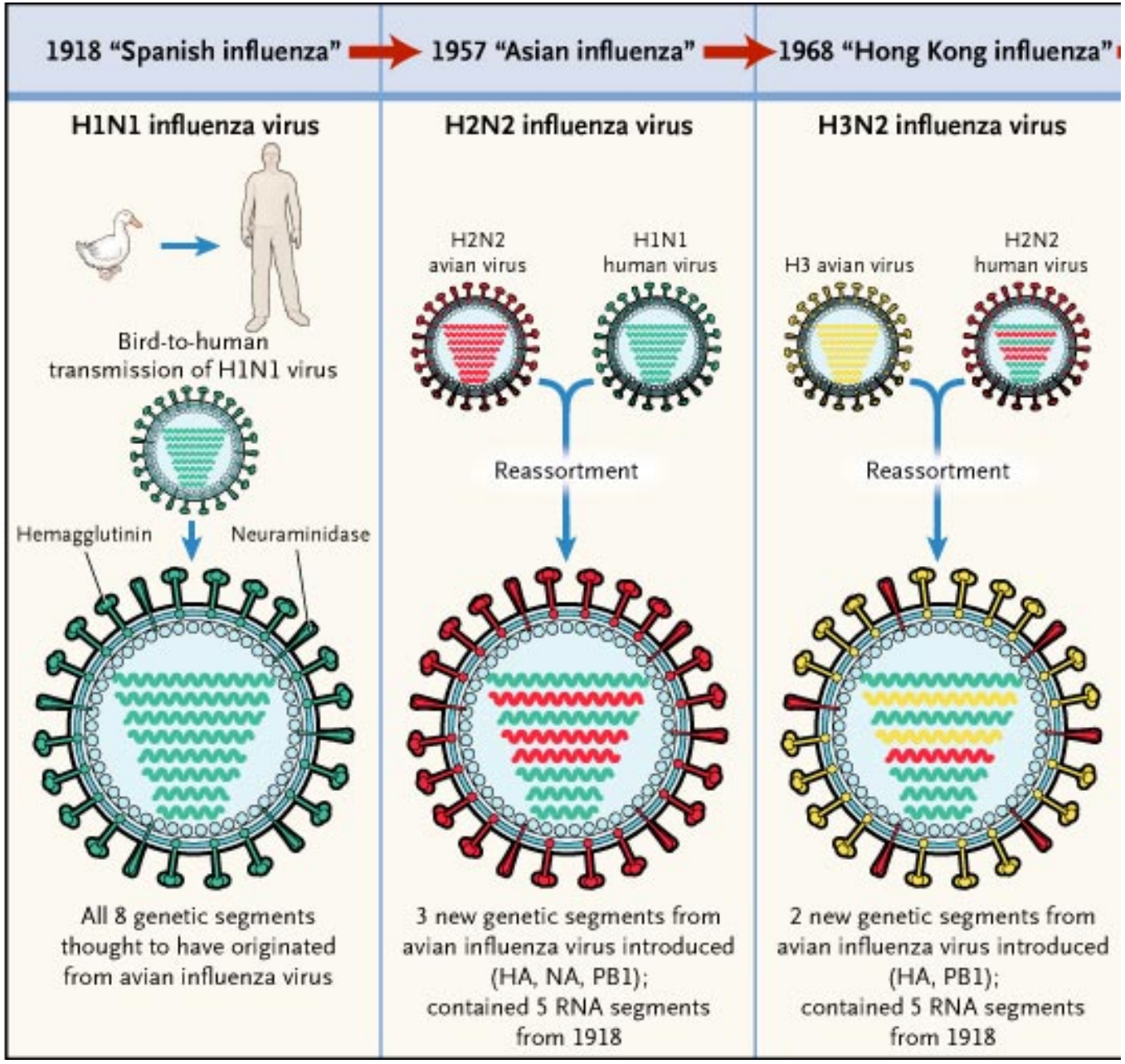
Thought to have originated in Southeast Asia. Less lethal than the 1918 pandemic. H2N2 replaced the circulating H1N1.

Table 2. Age-specific excess mortality related to influenza A (H2N2), U

Season	Influenza subtype	All-cause data source*	Excess mortality rate/100,000† for: All ages	Persons ⩾65 years old	Persons <65 years old
1957–1958	**H2N2**	[18]	39 (66,000)	273 (42,000)	15 (24,000)
1959–1960	H2N2	[18]	18 (32,000)	145 (23,000)	5.6 (9000)
1962–1963	H2N2	[18]	25 (46,000)	198 (35,000)	7.0 (12,000)
1967–1968	H2N2	[18]	11 (22,000)	113 (21,000)	0.6 (1000)

Table from Simonsen *et al*, *The Journal of Infectious Diseases*, 178:53 (1998)

The 1968 “Hong Kong flu” H3N2 pandemic



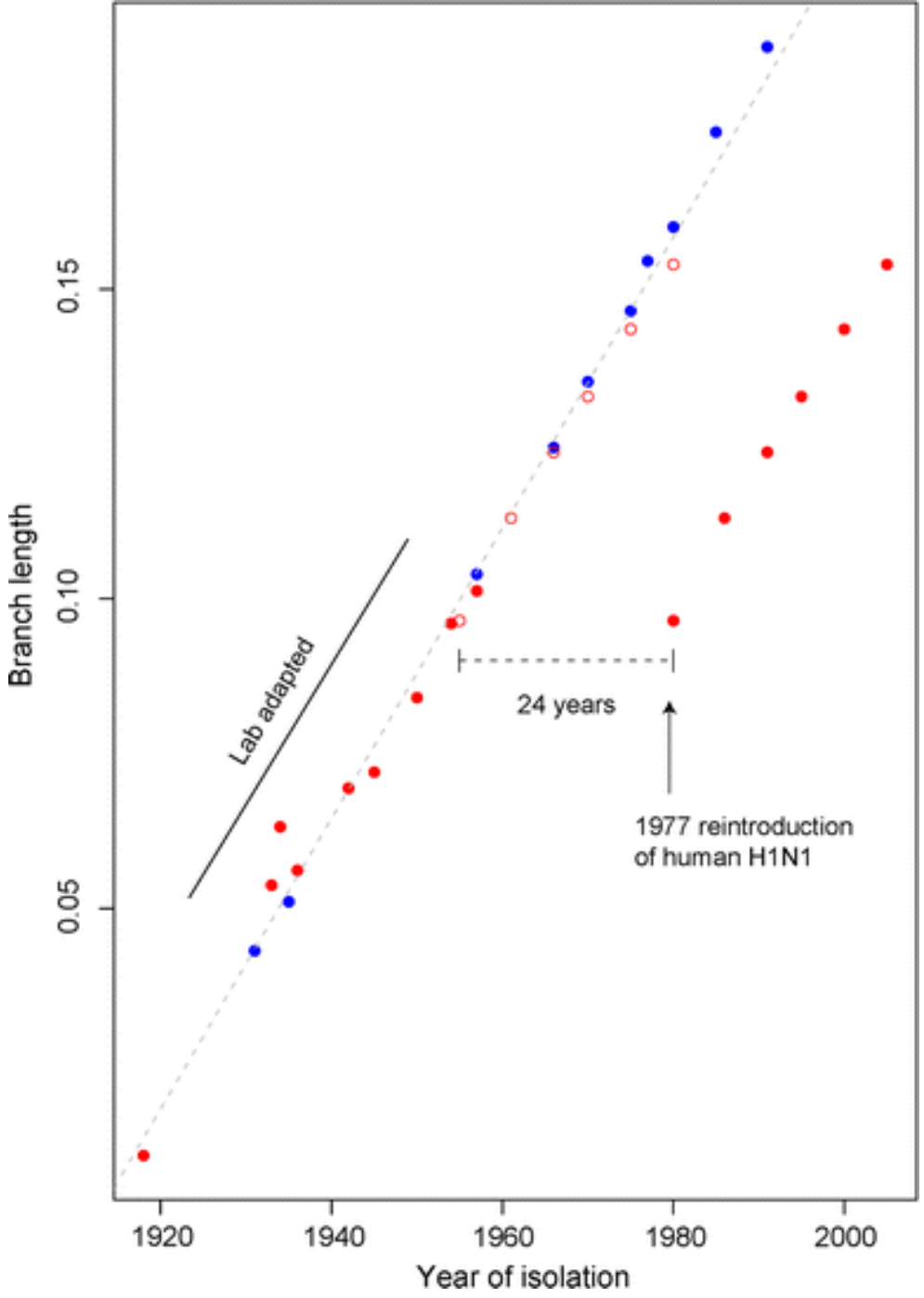
H3N2 pandemic was even less lethal than the H2N2 pandemic

Table 3. Age-specific excess mortality related to influenza A (H3N2), United States.

Season	Influenza subtype	Type of data, source*	Excess mortality rate/100,000 for: All ages†	Persons ≥65 years old	Persons <65 years old
1968–1969	**H3N2**	P&I	8.1 (16,400)	44 (8600)	4.3 (7800)
		P&I [19]	7.4 (14,800)	45 (8700)	3.4 (6100)
		All-cause [18]	14 (28,100)	85 (16,500)	6.4 (11,600)
1969–1970	H3N2	P&I	3.3 (6600)	16 (3100)	1.9 (3500)
		P&I [19]	2.4 (4800)	12 (2400)	1.3 (2400)
		All-cause [18]	9.1 (18,400)	51 (10,100)	4.6 (8400)
1970–1971	H3N2	P&I	0.7 (1300)	2.8 (600)	0.4 (800)
1971–1972	H3N2	P&I	4.2 (8700)	29 (5800)	1.5 (2900)
		P&I [19]	0.6 (1200)	4.9 (1000)	0.1 (200)
1972–1973	H3N2	P&I	3.8 (7900)	21 (4500)	1.4 (2600)
		P&I [19]	4.3 (9100)	31 (6500)	1.4 (2600)
		P&I [4]	2.3 (4800)	19 (3800)	0.5 (1000)
1974–1975	H3N2	P&I	3.0 (6500)	19 (4200)	0.8 (1600)
		P&I [19]	3.3 (7100)	26 (5600)	0.8 (1500)
		P&I [4]	1.8 (3800)	15 (3000)	0.4 (800)

Table from Simonsen *et al*, *The Journal of Infectious Diseases*, 178:53 (1998)

1977 “Russian Flu” H1N1 pandemic



Emerged on the Soviet / Chinese border in 1977, was identical to H1N1 from the 1950’s.

This H1N1 did not replace the H3N2 virus. Instead, they co-circulated in the human population.

dos Reis *et al*. *Journal of Molecular Evolution*, 69:333 (2009)

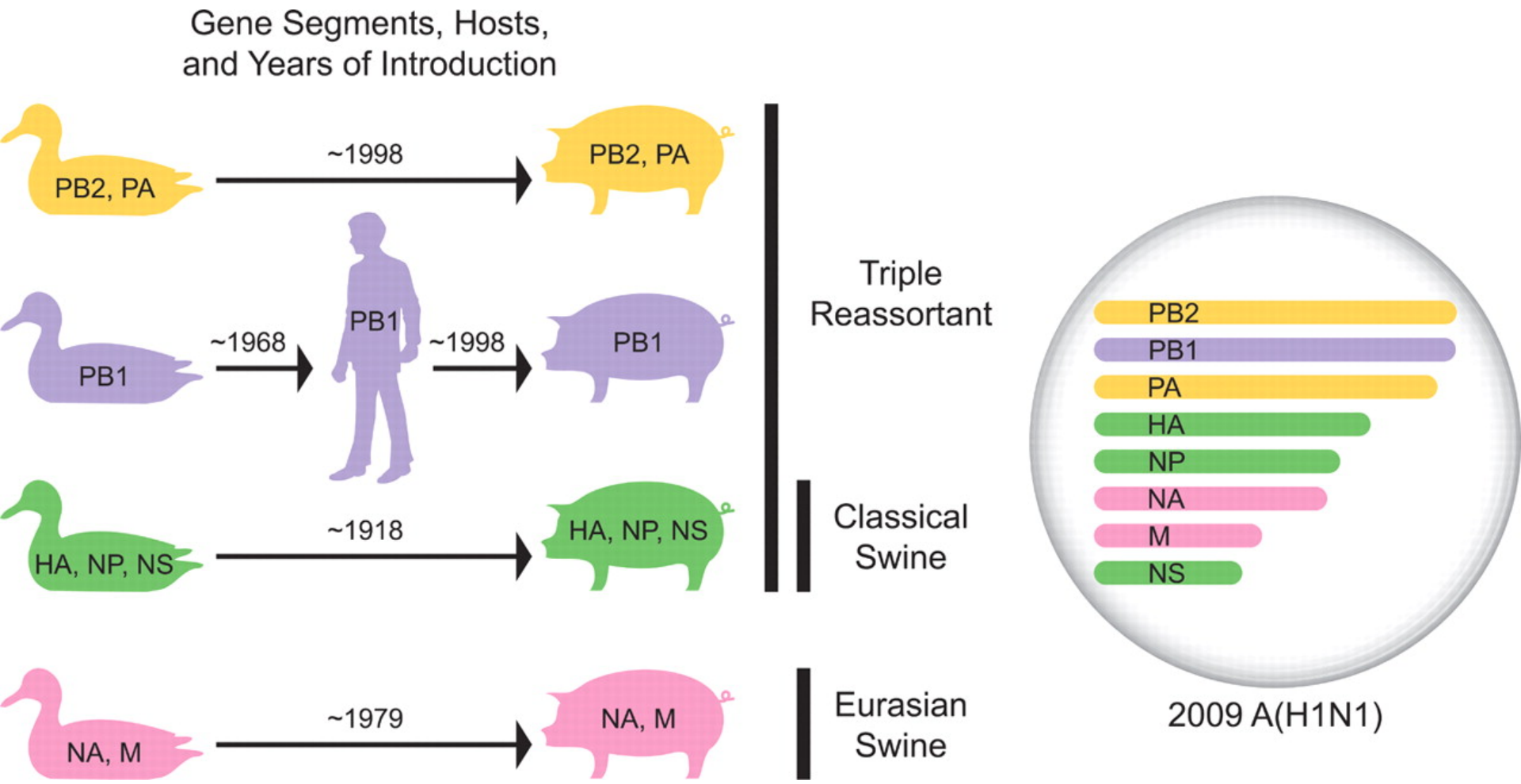
BRITISH MEDICAL JOURNAL 4 MARCH 1978

EPIDEMIOLOGY

Influenza in a boarding school

The Easter term began on 10 January, with boys returning from all over Britain and some from Europe and the Far East. One boy from Hong Kong had a transient febrile illness from 15 to 18 January. On Sunday 22 January three boys were in the college infirmary. The graph shows the daily total number confined to bed or convalescent during the epidemic: 512 boys (67%) spent between three and seven days away from class, and 83% of the boys in the junior house were affected. Of about 130 adults who had some contact with the boys, only one, a house matron, developed similar symptoms.

The 2009 swine-origin H1N1 strain



Garten *et al*, *Science,* 2009

highly pathogenic H5N1 avian influenza: deadly but not (at least yet) transmissible in humans

Cumulative number of confirmed human cases for avian influenza A(H5N1) reported to WHO, 2003-2012

Country	2003		2004		2005		2006		2007		2008		2009		2010		2011		2012		Total	
	cases	deaths	cases	deaths	cases	deaths	cases	deaths	cases	deaths	cases	deaths	cases	deaths	cases	deaths	cases	deaths	cases	deaths	cases	deaths
Azerbaijan	0	0	0	0	0	0	8	5	0	0	0	0	0	0	0	0	0	0	0	0	8	5
Bangladesh	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	2	0	3	0	6	0
Cambodia	0	0	0	0	4	4	2	2	1	1	1	0	1	0	1	1	8	8	2	2	20	18
China	1	1	0	0	8	5	13	8	5	3	4	4	7	4	2	1	1	1	1	1	42	28
Djibouti	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0
Egypt	0	0	0	0	0	0	18	10	25	9	8	4	39	4	29	13	39	15	9	5	167	60
Indonesia	0	0	0	0	20	13	55	45	42	37	24	20	21	19	9	7	12	10	6	6	189	157
Iraq	0	0	0	0	0	0	3	2	0	0	0	0	0	0	0	0	0	0	0	0	3	2
Lao People's Democratic Republic	0	0	0	0	0	0	0	0	2	2	0	0	0	0	0	0	0	0	0	0	2	2
Myanmar	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	0
Nigeria	0	0	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	1	1
Pakistan	0	0	0	0	0	0	0	0	3	1	0	0	0	0	0	0	0	0	0	0	3	1
Thailand	0	0	17	12	5	2	3	3	0	0	0	0	0	0	0	0	0	0	0	0	25	17
Turkey	0	0	0	0	0	0	12	4	0	0	0	0	0	0	0	0	0	0	0	0	12	4
Viet Nam	3	3	29	20	61	19	0	0	8	5	6	5	5	5	7	2	0	0	4	2	123	61
Total	**4**	**4**	**46**	**32**	**98**	**43**	**115**	**79**	**88**	**59**	**44**	**33**	**73**	**32**	**48**	**24**	**62**	**34**	**25**	**16**	**603**	**356**

Total number of cases includes number of deaths
WHO reports only laboratory cases
All dates refer to onset of illness

356 / 603 = 59% case fatality rate

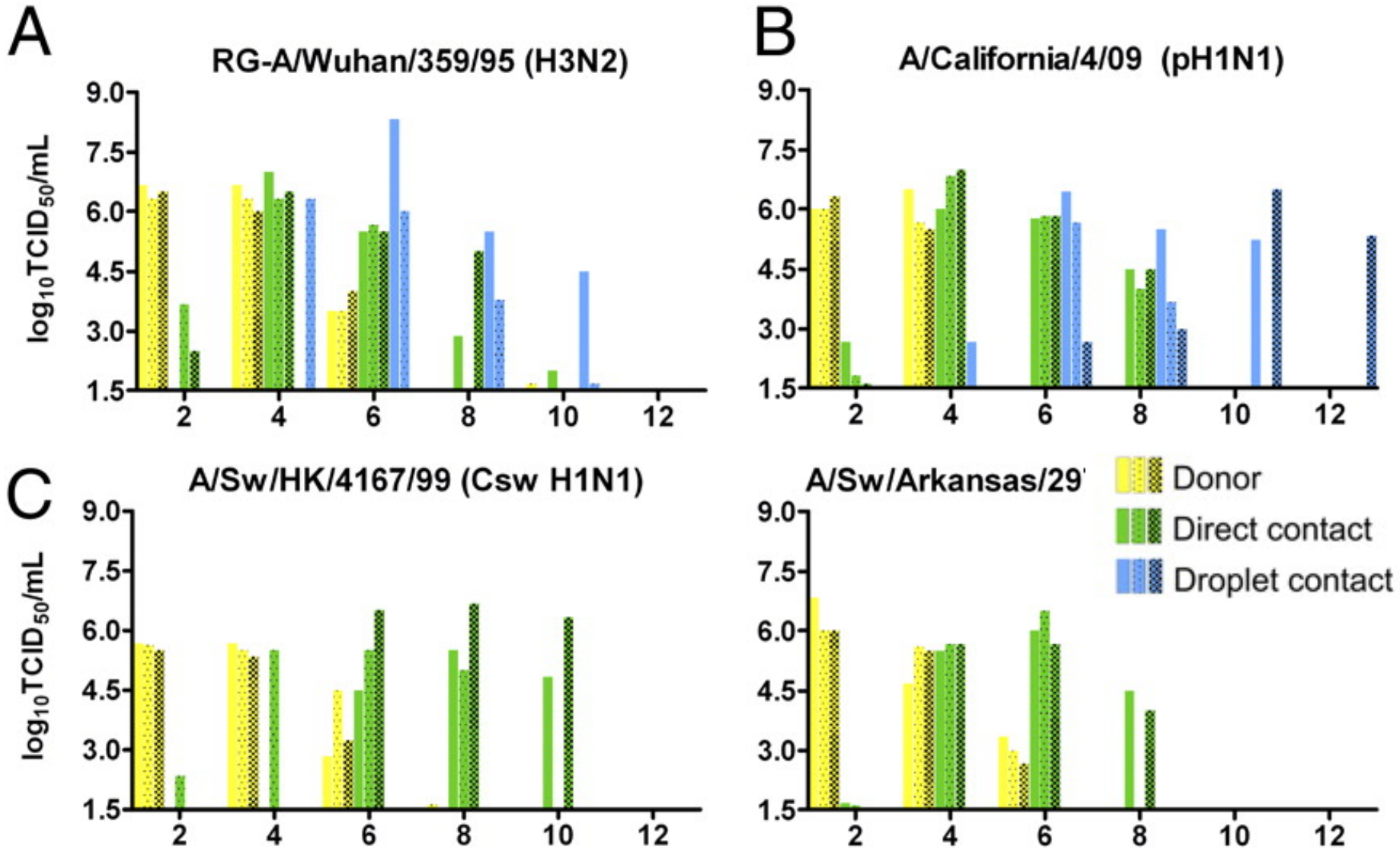
May be an overestimate due to under-reporting of non-lethal infections.

Source: WHO/GIP, data in HQ as of 02 May 2012

World Health Organization

Could H5N1 become transmissible in humans?

Ferrets as a model for airborne transmissibility. Example: the 2009 swine-origin pandemic transmits by respiratory droplets in ferrets, but its immediate swine precursor viruses do not.

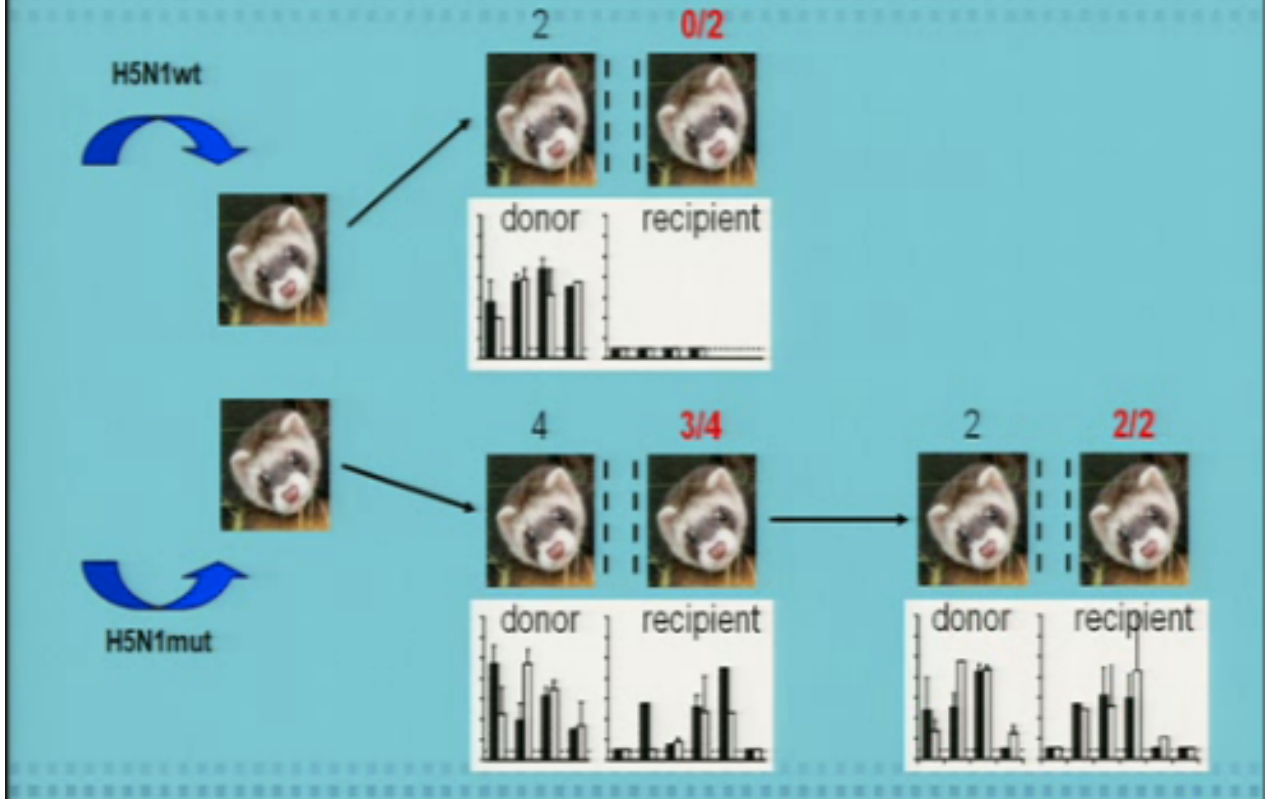


Yen *et al*, *PNAS*, 108:14264-14269 (2011)

Laboratory-modified H5N1 virus

- Aerosol transmission in ferrets -

Erasmus MC



LETTER

doi:10.1038/nature10831

Experimental adaptation of an influenza H5 HA confers respiratory droplet transmission to a reassortant H5 HA/H1N1 virus in ferrets

Masaki Imai[1], Tokiko Watanabe[1,2], Masato Hatta[1], Subash C. Das[1], Makoto Ozawa[1,3], Kyoko Shinya[4], Gongxun Zhong[1], Anthony Hanson[1], Hiroaki Katsura[5], Shinji Watanabe[1,2], Chengjun Li[1], Eiryo Kawakami[2], Shinya Yamada[5], Maki Kiso[5], Yasuo Suzuki[6], Eileen A. Maher[1], Gabriele Neumann[1] & Yoshihiro Kawaoka[1,2,3,5]

REPORT

Airborne Transmission of Influenza A/H5N1 Virus Between Ferrets

Sander Herfst,[1] Eefje J. A. Schrauwen,[1] Martin Linster,[1] Salin Chutinimitkul,[1] Emmie de Wit,[1]* Vincent J. Munster,[1]* Erin M. Sorrell,[1] Theo M. Bestebroer,[1] David F. Burke,[2] Derek J. Smith,[1,2,3] Guus F. Rimmelzwaan,[1] Albert D. M. E. Osterhaus,[1] Ron A. M. Fouchier[1]†

Benefits

1. Now we know that H5N1 has the potential to become airborne transmissible in mammals.

2. Now we know some of the specific mutations that might enable this to happen.

3. This information might aid in surveillance of the viruses ongoing evolution.

4. This information might aid in vaccine development against specific H5N1 strain lineages.

5. This information increases our mechanistic understanding of the basis for influenza transmissibility.

Risks

1. Someone could recreate the virus using reverse genetics, and then release it intentionally or accidentally.

2. There is the potential for accidental release of the virus (currently all authorized work is restricted to BSL3).

3. Controversy about this research could impede other important types of inquiry into influenza and other diseases.

Zoonosis

Intra-species transmission

Influenza A virus is remarkable for the frequency and breadth of zoonoses: many species of birds, humans, pigs, horses, dogs