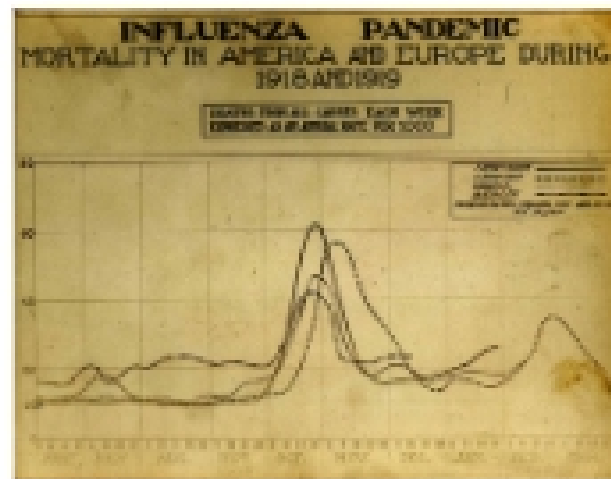




Pandemic Influenza

October 9, 2006

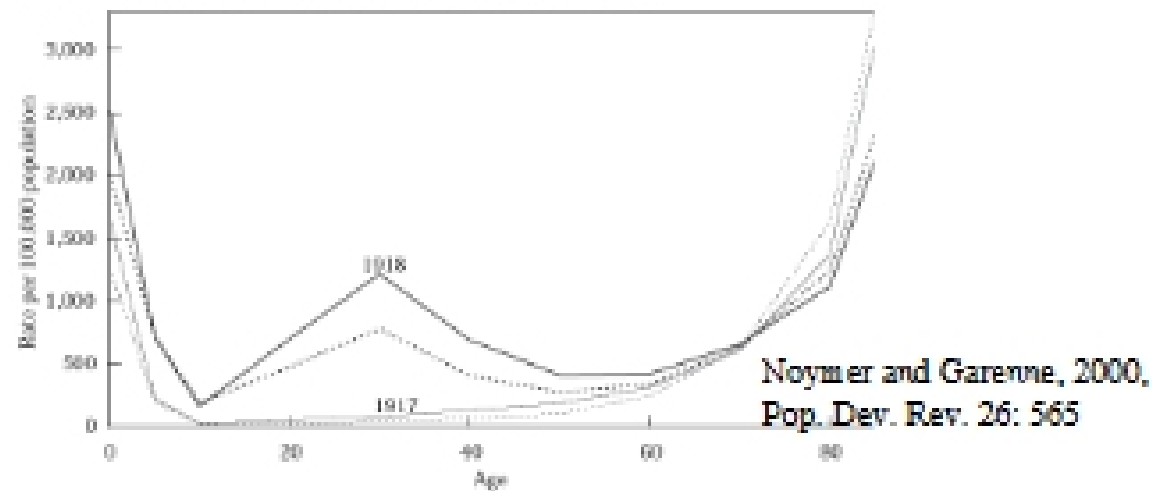
1918 influenza epidemic: realization of a worst-case scenario



First case: Albert Mitchell, Camp Funston, KS, March 11, 1918
Up to 20% of all humans infected
20-50 million deaths worldwide, 650,000 in the US
2.5% average case mortality rate; up to 16% in some cities

1918 death rate unusually high in males and people ages 20-40

FIGURE 1 Age-specific death rates for influenza and pneumonia combined, males (solid) and females (dotted), 1917 and 1918



SOURCE: U.S. Department of Health, Education, and Welfare 1954.

Damage due to overzealous immune response?

Kash et al., 2006 *Nature* epub ahead of print doi:10.1038/nature05181

Influenza A

Pleiomorphic enveloped virus,
80-120 nm

Orthomyxoviridae family,
isolated from ferrets in 1933

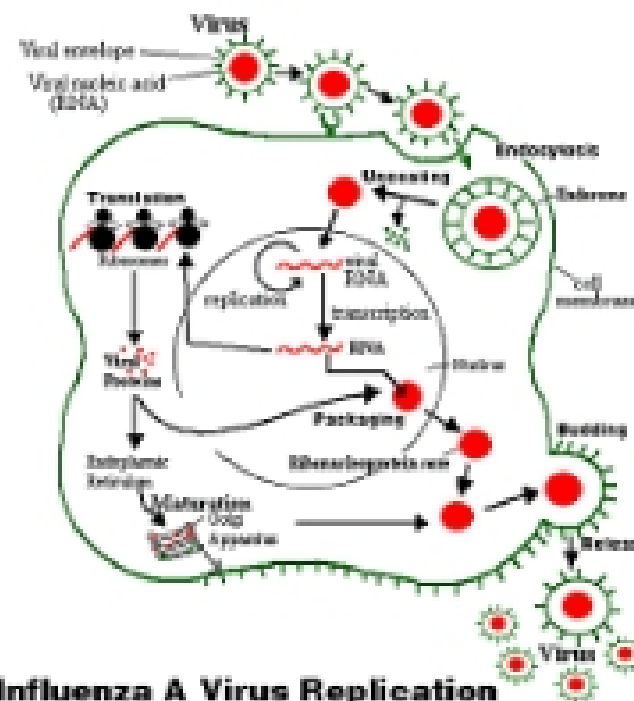
Endemic in water birds (ducks,
gulls, shorebirds)

Invasion mediated by HA
protein (hemagglutinin)
binding to sialic acid

Birds mostly α 2,3 linkage to
galactose, humans mostly α 2,6
linkage

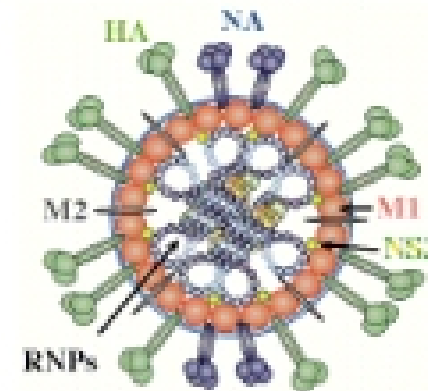
Neuraminidase cleaves sialic
acid links; required for viral
shedding (target of Tamiflu)

Virus also encodes an RNA-
dependent RNA polymerase

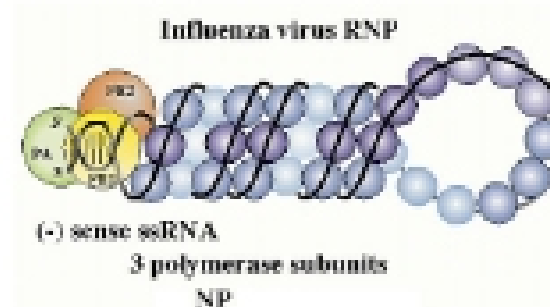


Genome has 8 RNA segments

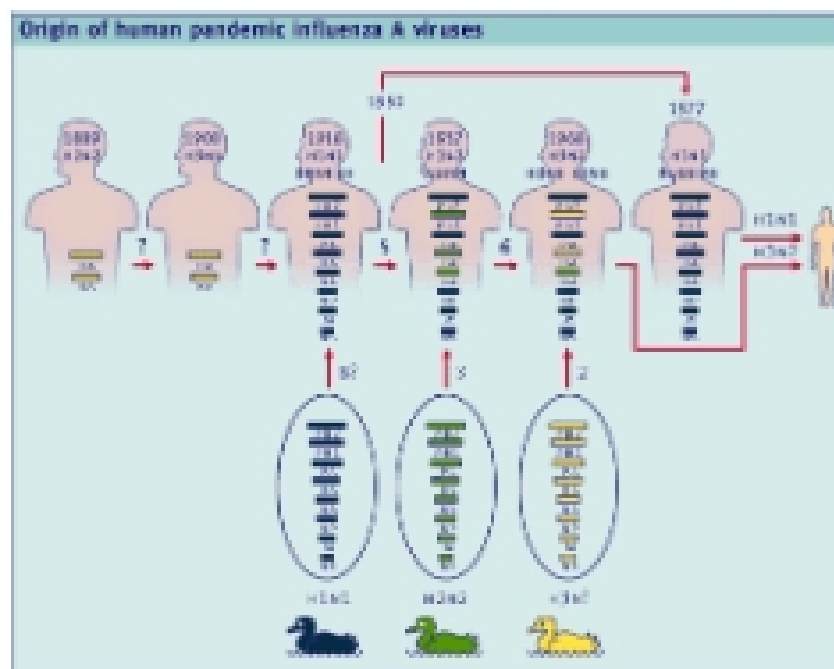
RNA segment	Nucleotides	Protein	Amino acids	Molecules per virion
1	4741	polymerase PB1	759	30-60
2	4341	polymerase PB2	727	30-60
3	2429	polymerase PA	720	30-60
4	4778	hemagglutinin HA	588	500
5	4945	nucleoprotein NP	498	1000
6	3483	neuraminidase NA	454	100
7	3827	matrix protein M1 matrix protein M2	254 97	3000 20-60
8	890	non-structural protein NS1 non-structural protein NS2	290 100	- 130-200



Each viral RNA segment is packaged by the nucleoprotein NP with a polymerase heterotrimer (PA, PB1, PB2) ready to go



Segments reassort when distinct viruses infect the same cell



Major antigenic determinants are HA (hemagglutinin) and NA (neuraminidase)
 16 HA types and 9 NA types found in waterfowl
 Antigenic SHIFT is due to a new HA or NA type
 Antigenic DRIFT is due to point mutations in HA and NA
 PANDEMICS arise when human populations are immunologically naïve for a new type