Evolution of human pandemic viruses

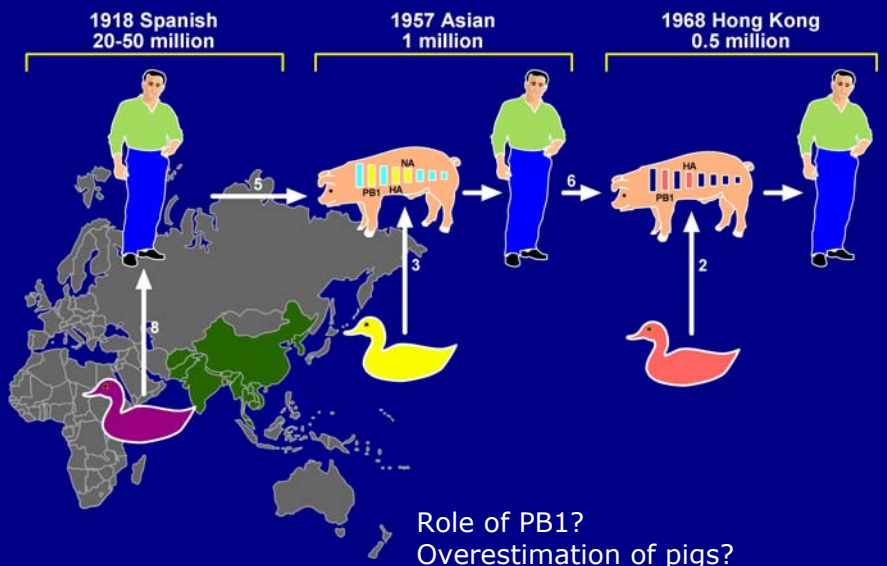
Requirements for pandemic

1) Virus must contain HA antigen to which the human population is immunologically naïve
   -*everything except H1, H3, $H2_{50}$*

2) Ability to replicate in humans
   -*H2, H5, H7, H9, H10, rest?*

3) Ability to efficiently transmit between humans
   -*H2, rest?*

Reassortment events in pandemic viruses

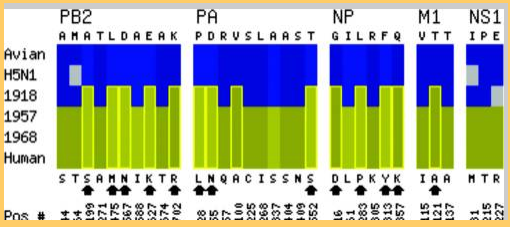


Role of PB1?
Overestimation of pigs?
Underestimation of domestic poultry?

St. Jude Children's Research Hospital

Mutations in pandemic strains

- We don't have precursors therefore don't really know
- Most data inferred by changes from avian consensus
- Changes in HA receptor linked to replication and transmission in humans. Occurs early after or soon before zoonotic transmission.[1]
- Changes in NA activity of human adapted N2 viruses (still primarily 2-3, but increased 2-6 via I275V)[2]



[1] Matrosovich 2000; [2]Kobasa 1999; [3]Finkelstein 2007

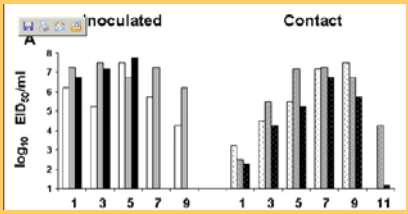
HA receptor changes

H3N2
- human strains Q226L and G228S
- Q226L most important for receptor specificity change (↓2-3,↑2-6)

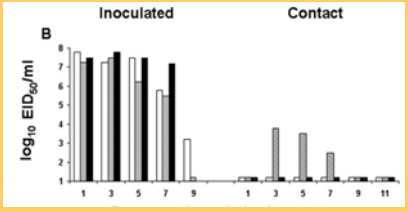
H2N2
- some earliest strains maintained avian consensus
- some had single Q226L change (↓2-3,↑2-6)
- later strains ↑2-6 affinity thru G228S

HA receptor changes

H1N1
- positions E190D and G225D linked with receptor switch.[1,2]
- A/SC/1/18 had dual change (↑2-6, ↑2-3)
- A/NY/1/18 had E190D change (↑2-6, =2-3)



A/SC/1/18



A/NY/1/18

[1]Glaser 2005, [2]Stevens 2006, [3]Tumpey 2007

Properties of early pandemic strains

- Generally increase in ability to grow in humans comes at loss of ability to grow in avian species (linked to HA and NA changes)

- Must remember most early pandemic strains have been passaged to some degree

H3N2

	Swine	Ferret	Duck	Chicken	Quail	other
HK/68	+++	+++			+/-	cats
Aichi/68	+++		– (organ culture)	– (organ culture)		
Udorn/72			– (HA mediated)			
Memphis/110/76			++ (tracheal)			
Texas/1/77			+ (tracheal)			

Transmission?

Webster 1978, Hinshaw 1981, Ohta 1981, Kida 1994, Naeve 1983, Perez 2003

H2N2

	Swine	Ferret	Duck	Chicken	Quail	other
Okuda/57		++				
Japan/305/57			–			
Moscow/65		+++				

Transmission?

Campbell 1979, Basarab 1969,

H1N1

	Swine	Ferret	Duck	Chicken	Quail	other
NJ/8/76	+++					
USSR/77					–	
1918		+++				

Transmission?

Hinshaw 1981, Perez 2003,

Summary

- H1, H2, and H3 are the only viruses we know of that have met all three criteria for pandemic viruses.
- We have some idea of what adaptive mutations in HA, NA, and PB2 do. Others we have no clue.
- *General* rule is once human adapted a virus loses its ability to grow in avians.

Ponderings

- Is there any way to model human infection/transmission potential? Which model?
- Impact of non-HA gene immunity on modulating pandemic severity is poorly understood. Does lack of poultry worker H5N1 infection imply good cross protection against poorly adapted strains?
- Would reverse adapting human strains give us any clues as to pathways to human adaptation?
- We may lose our chance to follow human adaptation unless all animal influenza's are followed.