Viral factors involved in reassortment and mutation

“what are the viral factors influencing how viruses get to be worrisome”

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1) Review of mutations and reassortment events leading to previous 3 human pandemic strains & H1 2009
The possible generation of pandemic strains through a series of reassortment events in mammals over a period of years before pandemic recognition suggests that appropriate surveillance strategies for detection of precursor viruses may abort future pandemics.

Smith PNAS 2009
2) What data on viral characteristics exist that might allow us to predict or reduce the risk of reassortment events

What controls reassortment

- Frequent in wild birds (*Macken J Gen Virol* 2006)
- HA/NA balance (*e.g.*, *Shtyrya Glycoconj J* 2009)
- Polymerase compatibility (*e.g.*, *Naffakh J Gen Virol* 2000)
- Much work done on H5/H3 compatibility (*e.g.*, [Chen PLoS Path 2008 and Li PNAS 2009](#))
- Host herd immunity
Successful versus unsuccessful

Virus Titer (TCID)

NC/98
TX/98

Small differences big effects
4) How might receptor distributions in different species impact reassortment?

Mixing vessel revisited

• Humans too (Van Riel Science 2006 and Shinya Nature 2006 but Nichols Nat Med 2007)
5) What is pandemic H1 gonna do?

- Triple reassortant (TRIG) compatible with H1, H3, H2
- Pandemic virus in swine, cats, turkeys
- Known double infections in humans
- H5N1/pH1N1?
- Is it time for H9?
Summary

- Reassortment complex
- We know some of the viral factors (but not for the most part at the mechanistic level)
- Impact of host poorly studied
- TRIG cassette of some concern