



## Influenza An Ever Evolving Disease

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### The History of Influenza

- An old disease – many centuries
- Ever evolving and ever will be
- Changes and adapts more than most

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### The History of Influenza

- Influenza-like diseases as early as 412 BC
- Better records describe disease in 1173
- Most intense to date was the pandemic of 1918-19 (Spanish flu) 500,000 deaths in the US, 20 million deaths worldwide

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### The History of Influenza

- Other pandemics have occurred in 1957-58 (Asian flu) 70,000 deaths in the US
- 1968-69 (Hong-Kong flu) 34,000 deaths in the US
- Why these pandemics?
- Two factors make this virus so dangerous
  - Genetic make-up of the virus
  - Animals are mixing vessels for the virus

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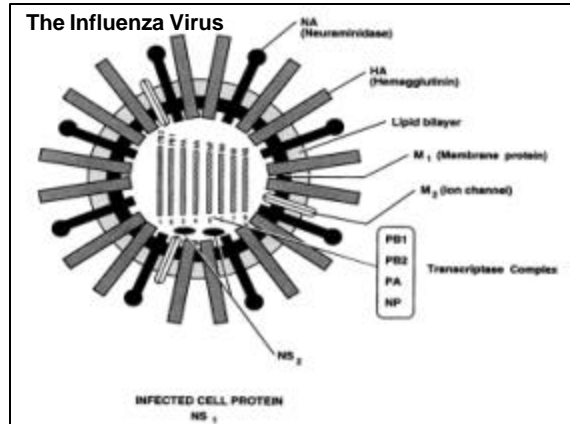
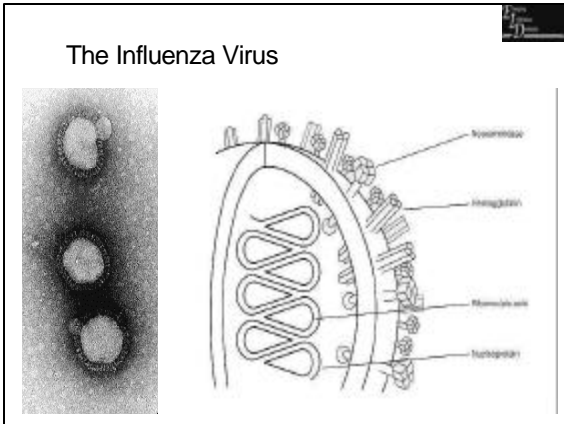
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### Influenza – the Virus

- Orthomyxovirus
- Enveloped, RNA genome
- 8 segments of NA
- Surface glycoproteins – 15 hemagglutinin (H) and the 9 neuraminidase (N) eg. H1N1

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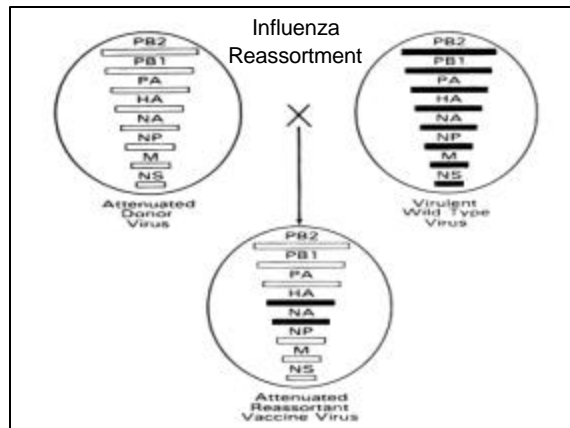
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### Shift

- Shift is due to an abrupt change in the H or N proteins
- Occurs due the reassortment of viral genes
- Can occur when a cell is infected with two strains of virus
- Can occur in animals

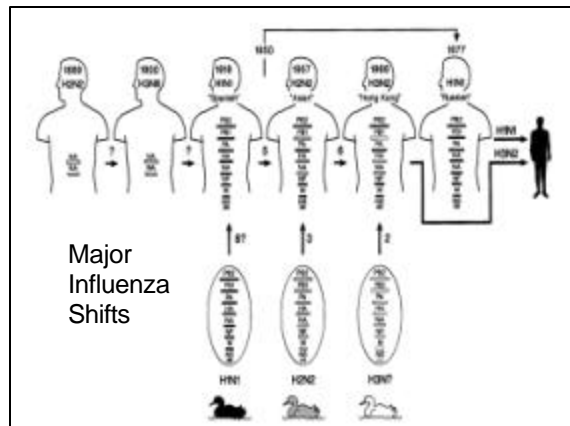
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### Shift

- 1918 – H1N1 (Spanish flu)
- 1957 – H2N2 (Asian flu)
- 1968 – H3N2 (Hong Kong flu)
- 1977 – H1N1 (Russian flu)

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## Drift

- Small changes in the surface proteins H and N proteins
- Due to error rate of RNA polymerase
- Generates quasispecies
- Selection of strain(s) that encounter the least resistance

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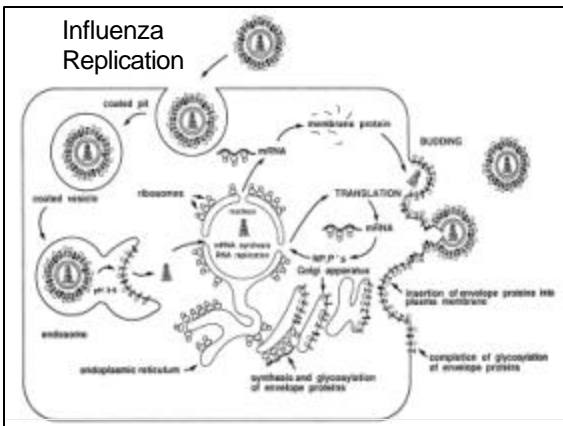
## Mechanisms of Virulence

- Primary mechanism is cleavage of HA
- HA needs to be cleaved into two to enter the host cell
- Cleavage sites with multiple basic aa are readily cleaved by common enzymes in all cells
- Cleavage sites with few basic aa are cleaved only in resp or int tracts

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## Influenza Replication



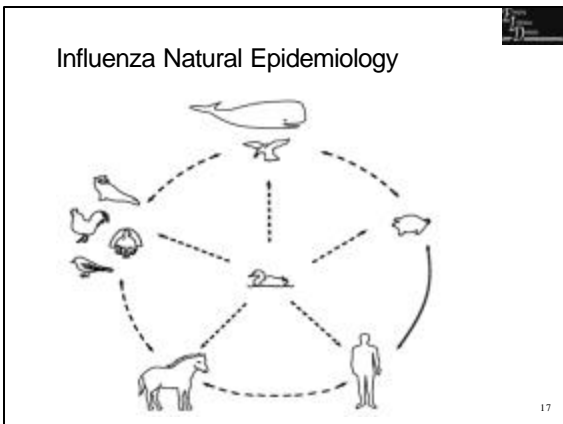
## Influenza Epidemiology

- All mammalian viruses derive from the avian influenza reservoir
- Avian influenza viruses are at an adaptive optimum
- Interspecies transmission of flu is common and continued
- Occurs in areas where susceptible species are found in close proximity

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## Influenza Natural Epidemiology



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## Disease Emergence

Examples of disease emergence:

1. Shift of virus genomes – pandemics of human disease
2. Change from low virulence to high virulence avian influenza
3. Virulent infection of new host species

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## Low Virulence to High

In 1983, a low virulence H5N2 avian virus became virulent in Pennsylvania

- Single aa change

In 1993, a low virulence H5N2 avian virus became virulent in Mexico

- Acquisition of more basic aa

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## Crossing the Species Barrier

- Historically only H1, H2 or H3 strains infect humans
- In 1997 an H5N1 avian influenza virus was isolated from people in China
- A total of 18 cases were reported – 6 of which were fatal
- Virus was shown to be totally avian, but evolving rapidly

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## Stopping the Epidemic



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## Crossing the Species Barrier

- Historically only H1 or H3 strains infect pigs
- In 1998 an H9N2 avian influenza virus was isolated from pigs in China
- In 1999 the same virus was isolated from people in China with mild flu symptoms

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## Summary

- Influenza, more than any other virus can evolve rapidly and will
- Need increased awareness and monitoring with rapid response
- There will be another epidemic – just not known when or where

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## Where to Get More Information

- Veterinary Microbiology Vol. 74, 2000
- [www.cdc.gov/ncidod/flu/fluah5n1.htm](http://www.cdc.gov/ncidod/flu/fluah5n1.htm)
- [www.nobl.com/justpigs/articles/mar98/maripswineflu.htm](http://www.nobl.com/justpigs/articles/mar98/maripswineflu.htm)
- [www.time.com/time/magazine/1998/dom/980223/cover1.html](http://www.time.com/time/magazine/1998/dom/980223/cover1.html)

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Questions or comments?

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