

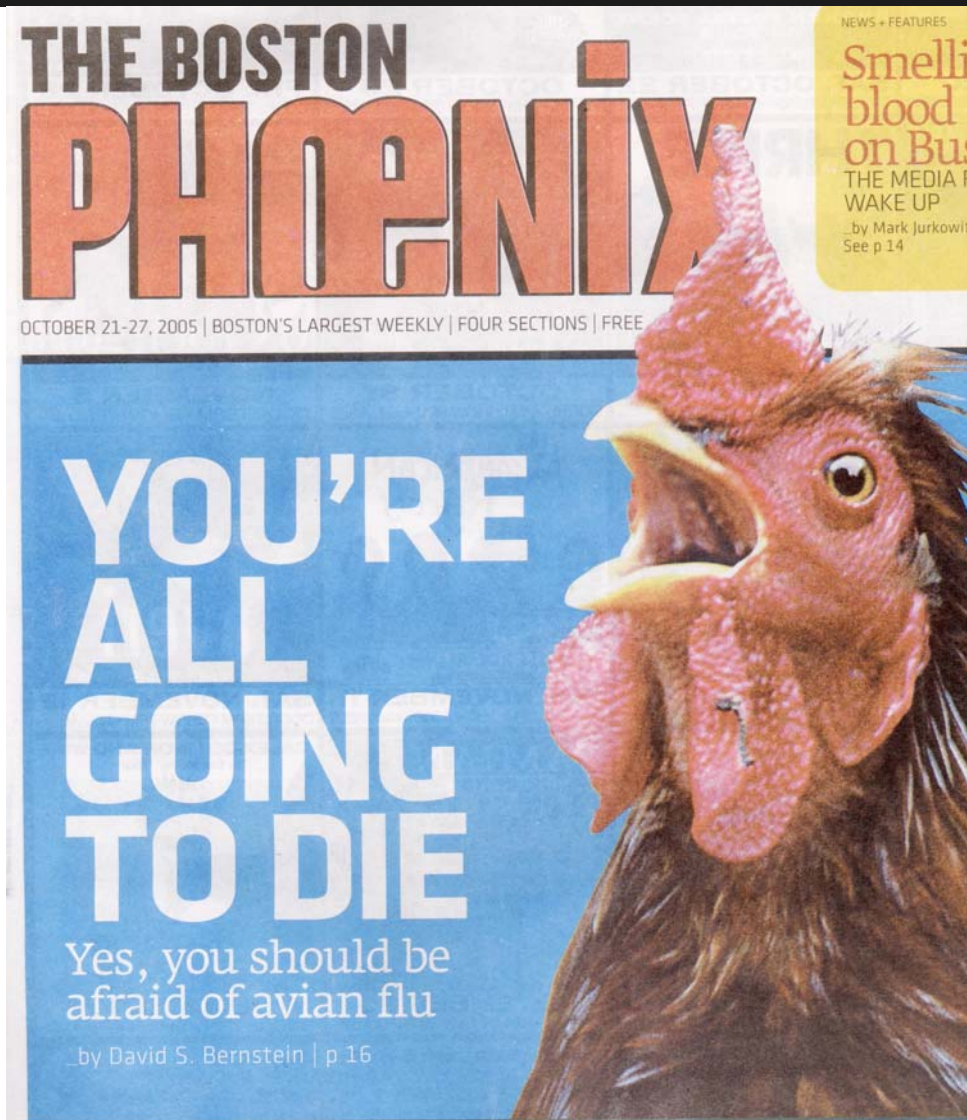


Influenza Biology and the Avian Flu

Allen Dodson

November 10th, 2005

The Phoenix says....



Influenza and Avian Influenza

- Influenza is an infectious disease caused by Influenza virus
- Estimated to infect ~20% of US population annually
- 40,000 US deaths annually, primarily due to pneumonia

Avian Flu

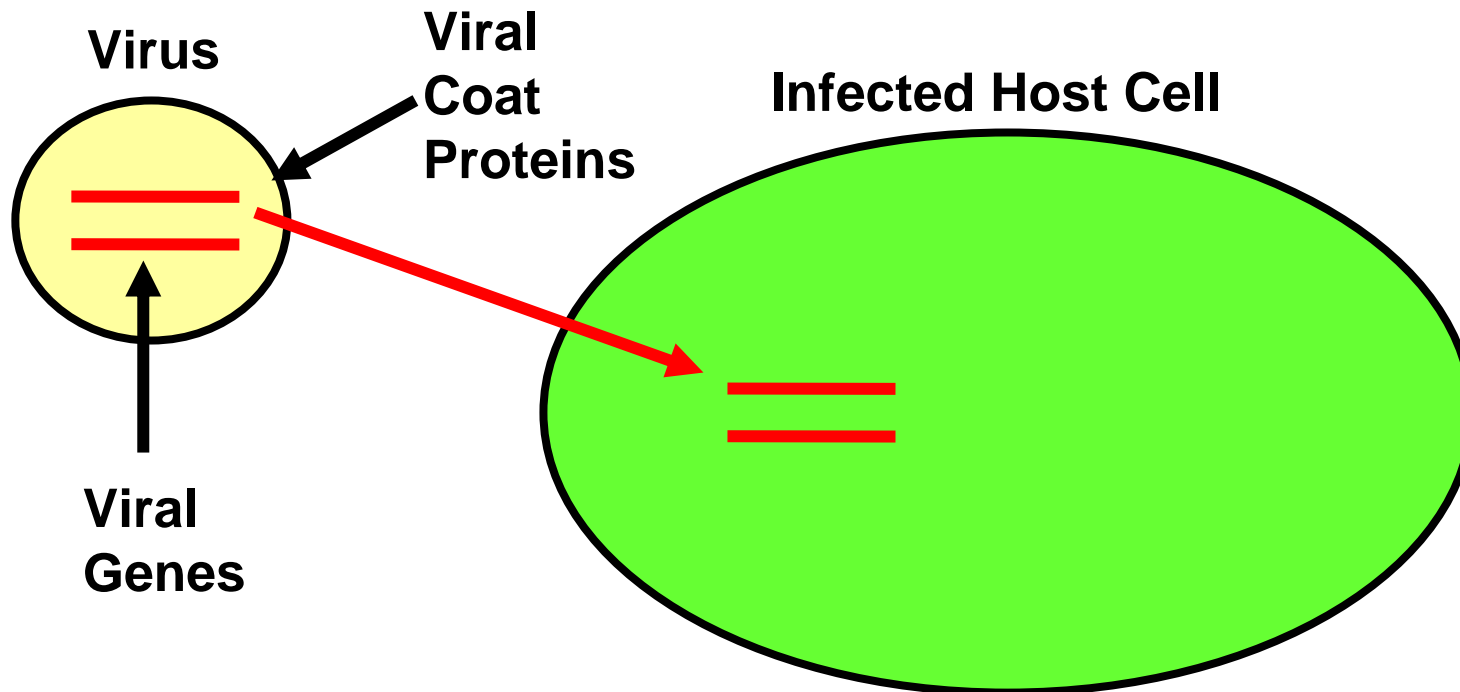
- Infects and kills poultry, wild birds
- Outbreak of human cases from birds in Hong Kong, 1997
- Current epidemic since 2003
- 125 cases, 64 deaths in Cambodia, Thailand, Indonesia, and Vietnam (Source: WHO, 11/9/05)
- Infected wild birds found in Europe

Talk Outline

- Overview of Viruses and Influenza
 - How do viruses replicate?
 - What is influenza?
 - How do new flu threats arise?
- 1918: A worst case scenario for flu pandemics
- Current treatments
- Future outlook

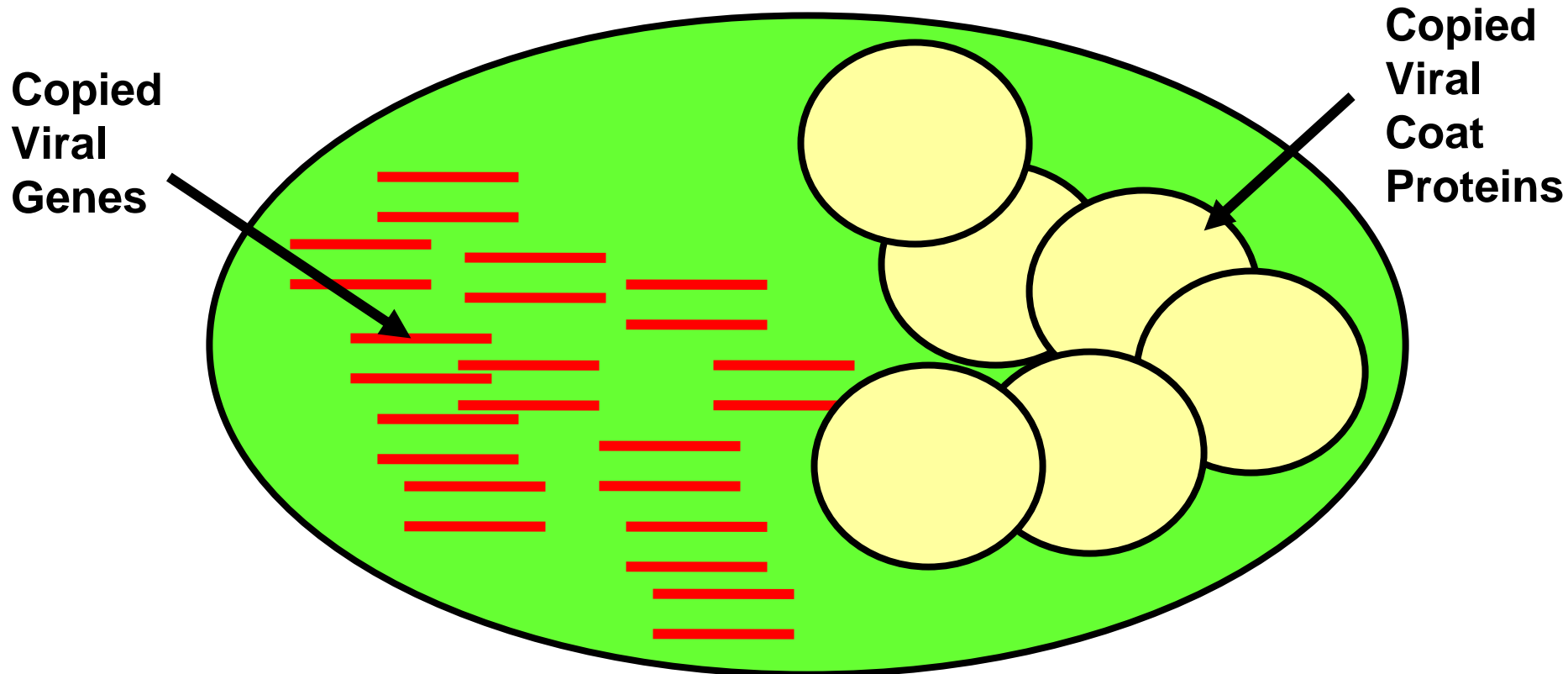
Generic Viral Life Cycle

- Get viral genes into host cell
- Use host cell to copy viral genes, proteins
- Assemble new virus to escape and infect new cells



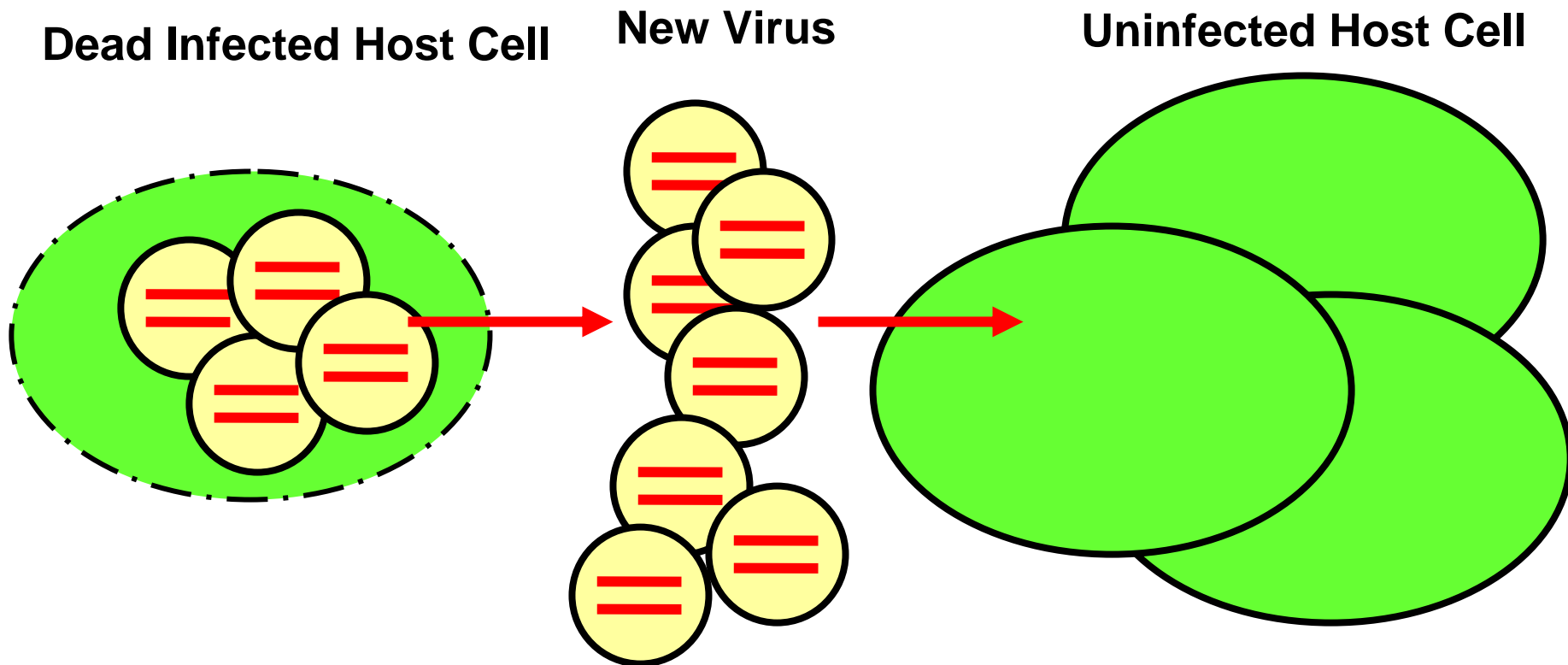
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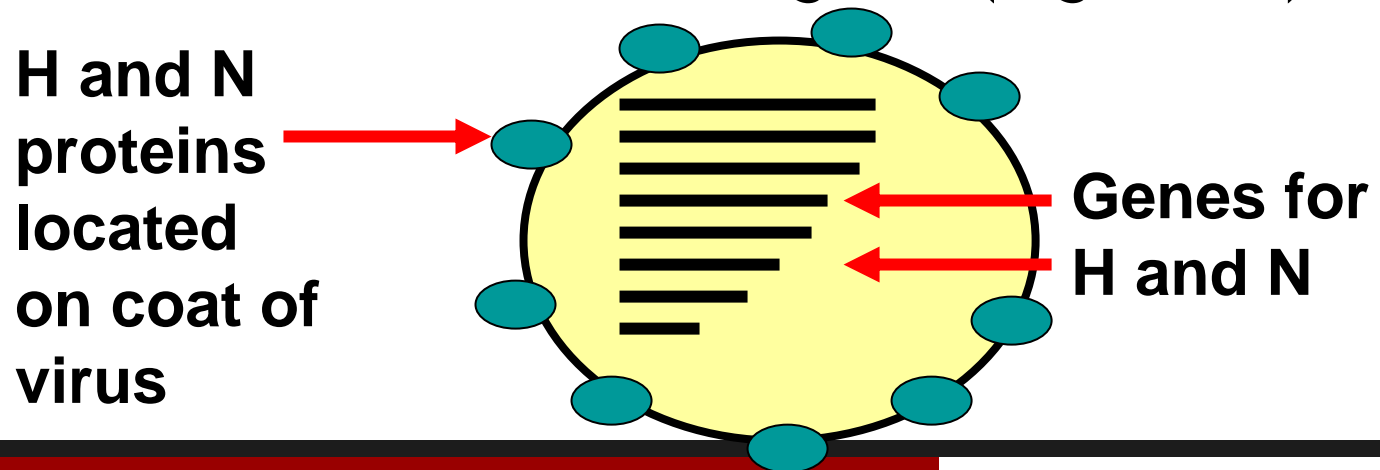


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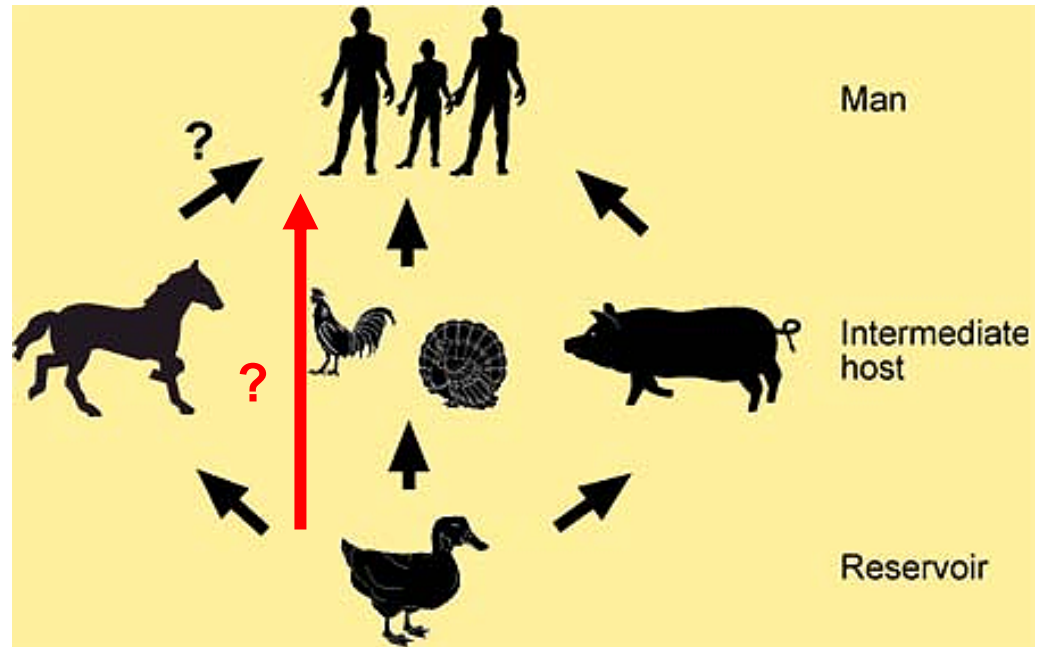
Anatomy of Influenza

- Influenza virus has a small genome:
 - Influenza: 13,500 bases
 - Humans, Mice: 3 Billion bases
- Influenza genome has 8 segments, like chromosomes
- Influenza encodes only 10 proteins (30,000? for humans)
- Two viral proteins determine how serious disease will be - Hemagglutinin (H) and Neuraminidase (N)
- Flu viruses are named for their H and N genes (e.g. H5N1)



Influenza Diversity

- Influenza can infect:
 - Birds
 - Pigs
 - Horses
 - People



- Viruses from other animals may not be as good at spreading in people, but can be more deadly
- Tremendous genetic diversity between types of influenza
- Genes can be traded through Reassortment

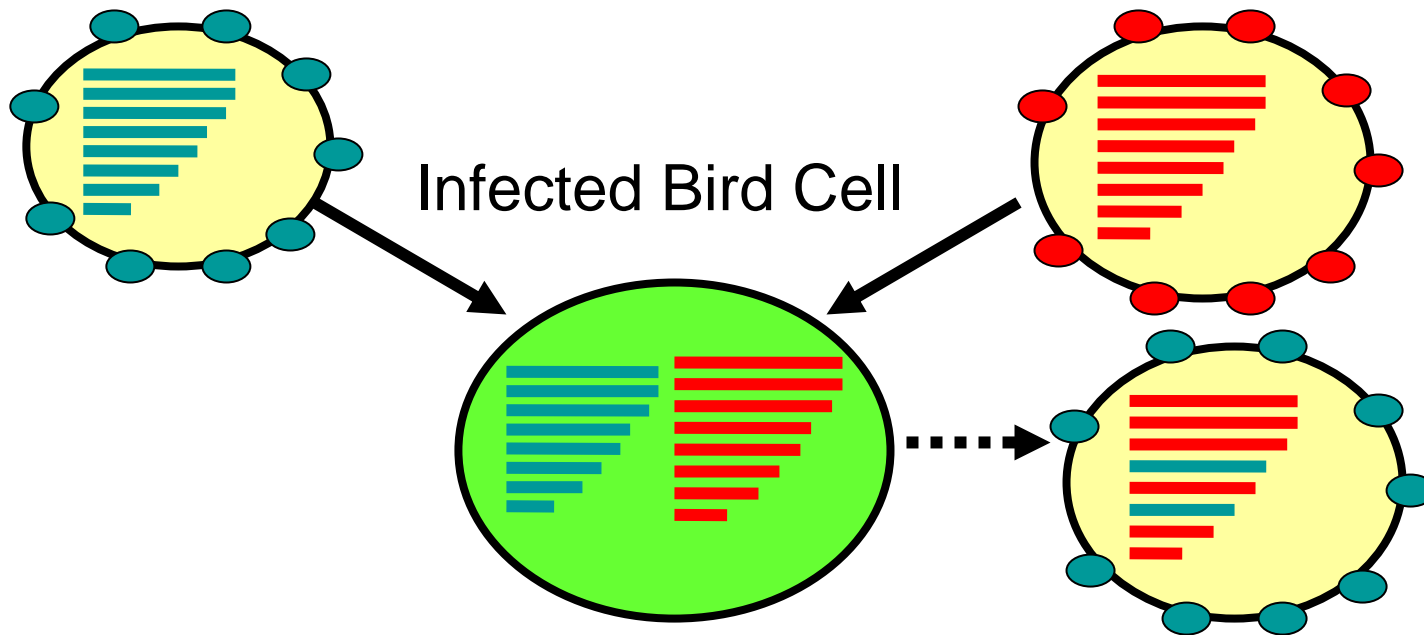
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Influenza Reassortment

Avian Virus: Exists today
Contains H5N1,
Cannot spread between People

Human Virus: Exists today
No H5N1,
CAN spread between People



Reassorted Virus: Does not yet exist.
Contains H5N1,
CAN spread between People

Why does reassortment matter?

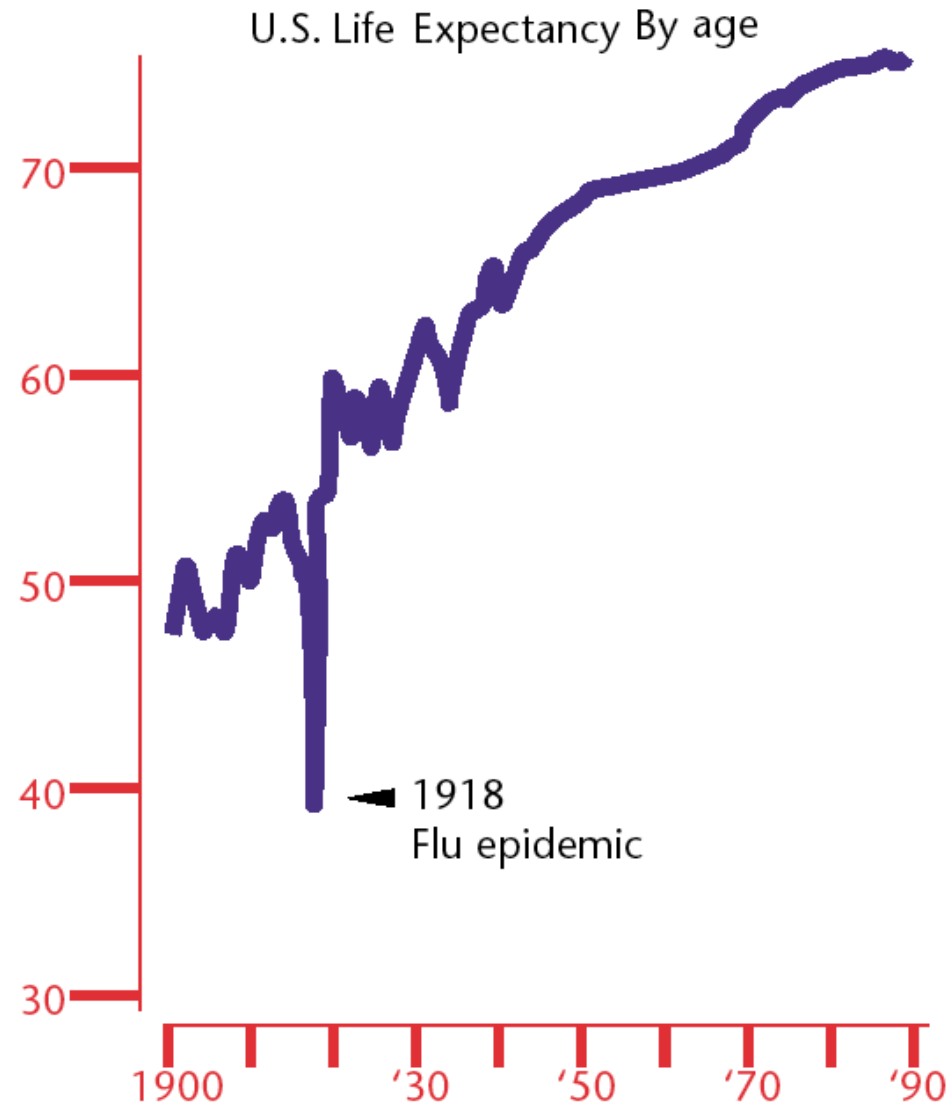
- Referenced by the media: Avian virus “mutating” to a form that can infect humans
- In addition to gradual evolution over time, influenza can change very rapidly by reassortment
- New types of influenza that people have no immunity to can gain the ability to spread rapidly
- What happens when influenza rapidly changes?

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A case of Avian Flu

- “Spanish” Flu pandemic led to 500,000 deaths in US
- 50+% of US Army deaths during WW I
- 20-50 million deaths worldwide
- What happened?



Palese et al. *Nature Med* (2002)

Why was the 1918 Virus So Deadly?

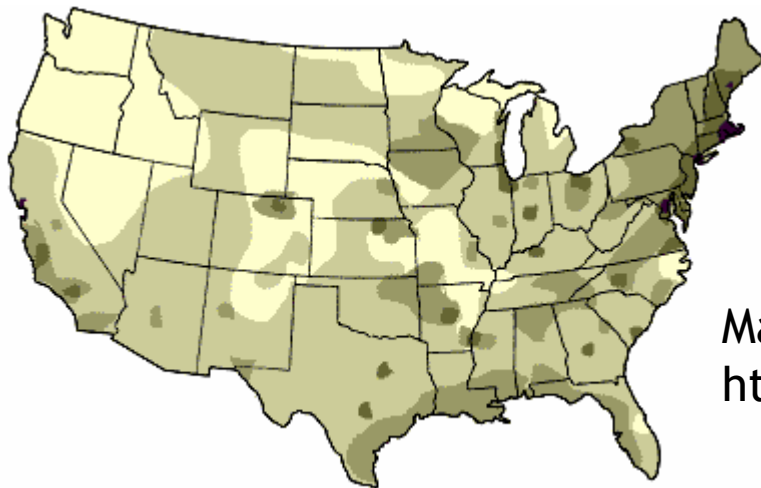
- New Avian influenza strain spread rapidly in people
- Most peoples' immune systems were unprepared for this new strain
- Wartime conditions facilitated spread, impeded containment (only neutral Spain admitted they had an outbreak)



Pictures from the National Museum of Health and Medicine
<http://nmhm.washingtondc.museum/>

What did 1918 teach us?

- New strains kill
- Rapid spread even easier today with more global transportation
- Epidemiologists need to track information on outbreaks and respond quickly
- The world needs to be prepared for treatment of large numbers of people, anywhere, at any time



Map of 1918 Pandemic in the US from:
<http://www.pbs.org/wgbh/amex/influenza/maps/>



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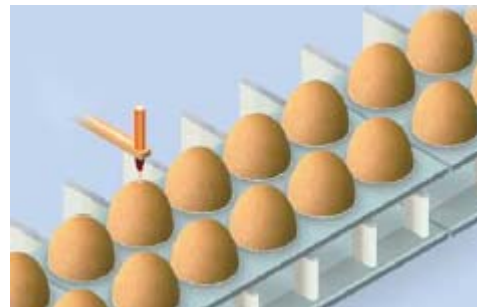
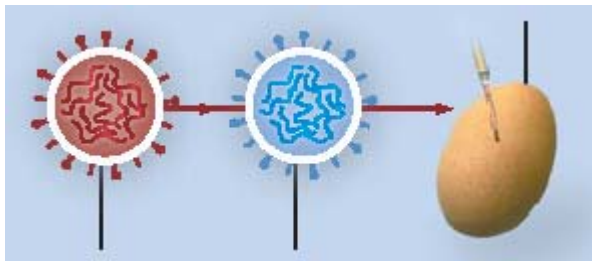
Fighting Influenza: Immune Response

- Your body's immune system naturally fights off most cases of influenza
- Two lines of defense
 - Rapid, non-specific response
 - Long term, specific response
- Avian influenza weakens your immune system by blocking a chemical called Interferon
 - Interferon is normally your first line of defense against viruses - it reacts before your immune system can determine what the exact threat is
 - By preventing this response, Avian viruses have longer to do damage before you can react

Influenza Vaccine Issues

- Takes 8-10 months to design, produce, and test a vaccine for a new strain
- Current vaccine does NOT protect against Avian flu
- Mass production is expensive and prone to contamination
- Recent trials suggest that Avian flu may require eight times more vaccine than typical for influenza

Design Vaccine Strain



Antiviral Drugs: Tamiflu

- The best known anti-Influenza drug is Tamiflu (Oseltamivir)
- Drug against Influenza Neuraminidase
- Currently derived from the Chinese Star Anise plant, other sources are possible
- Drug is expensive and in short supply
- Why? Companies think it's hard to profit from treating survivable infections



Roche plans to scale up production, make 300 million doses per year by 2007 (still too little!)

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What can we do?

Individuals:

- Wash your hands
- Exercise, good nutrition, sleep, and not smoking keep you healthy enough to avoid infection
- High risk people may qualify for a vaccine (against seasonal influenza, not avian influenza)
- Do NOT ask your doctor for antibiotics or hoarde Tamiflu

Public health officials:

- Detect outbreaks early
- Use drugs to protect first responders, prevent spread

Outlook

- Influenza virus is highly adaptable and almost certain to pose a threat to public health in the future.
- Treatment options are limited and insufficient to protect the entire world.
- More research is needed to find better treatments that are easier to manufacture.

Up Next: Maria will discuss the kinds of facilities needed for this and other kinds of research.