



NIAID

# Bird Flu and the Threat of Pandemic Influenza

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# Influenza in humans

- **Symptoms of influenza infection:**

- fever
- cough
- headache
- muscle aches
- sneezing
- runny nose
- nausea

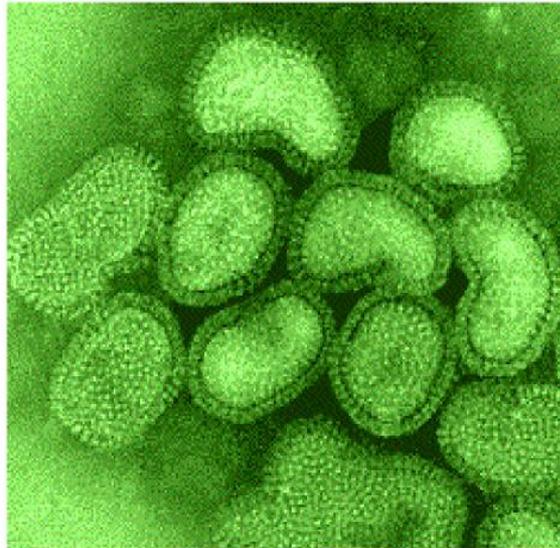
**Complications: pneumonia, secondary bacterial infections**



# Influenza is Caused by a Virus

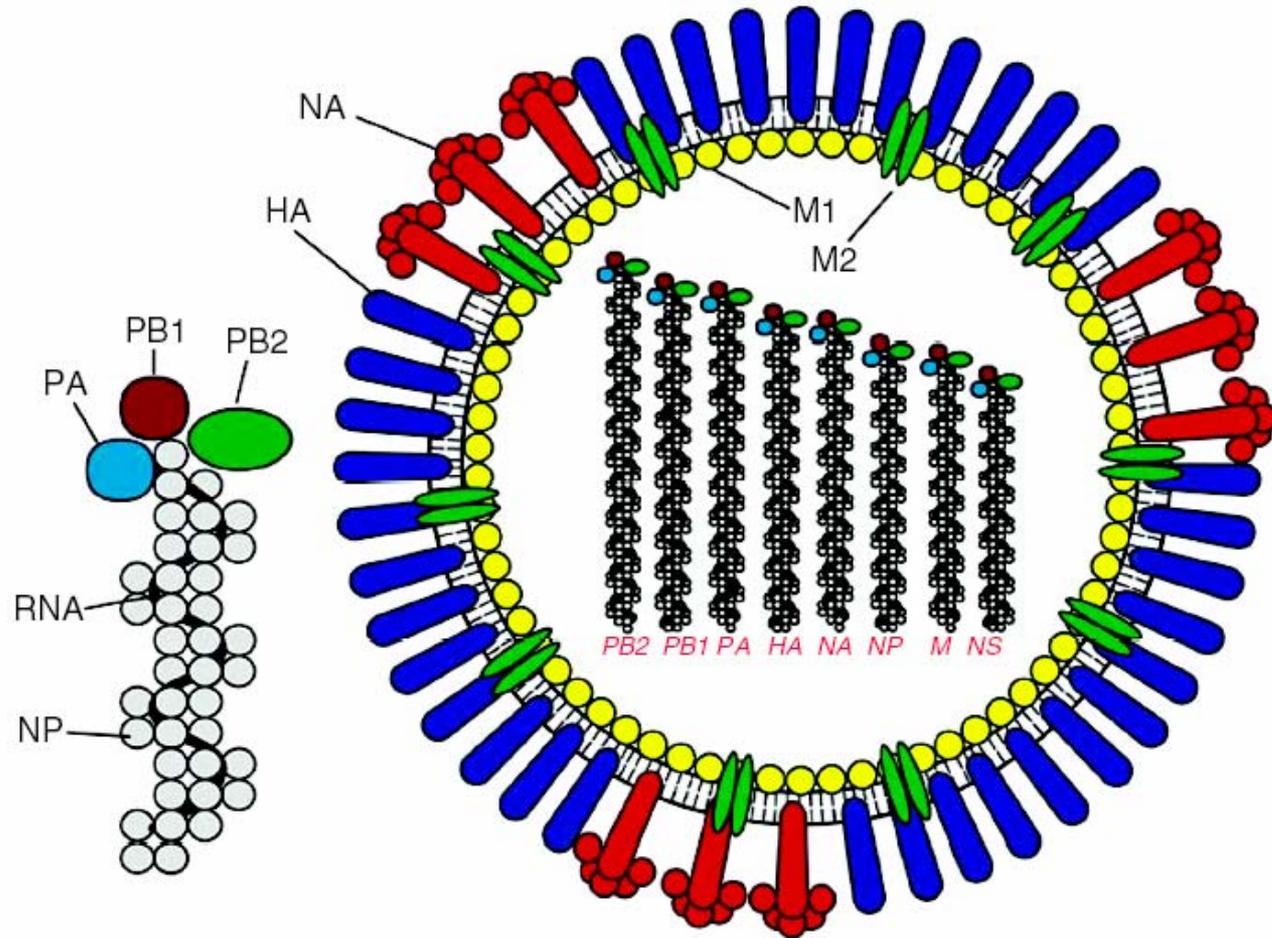
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- A virus is a small (20 to 300 nm), infectious agent that replicates only within the cells of living hosts



Electron micrograph of  
influenza virus

# Influenza A virus



# Distribution of Hemagglutinins in Nature

H1				
H2				
H3				
H4				
H5				
H6				
H7				
H8				
H9				
H10				
H11				
H12				
H13				
H14				
H15				

# Distribution of Neuraminidases in Nature

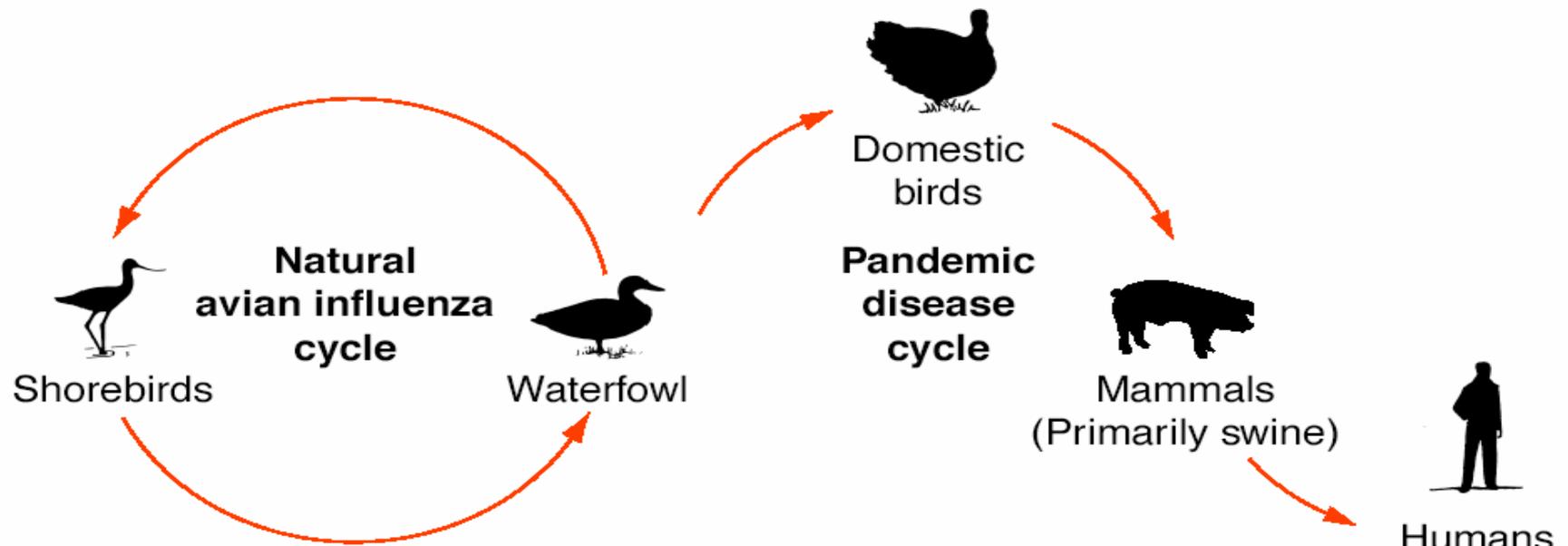
N1					
N2					
N3					
N4					
N5					
N6					
N7					
N8					
N9					

# The Influenza Problem

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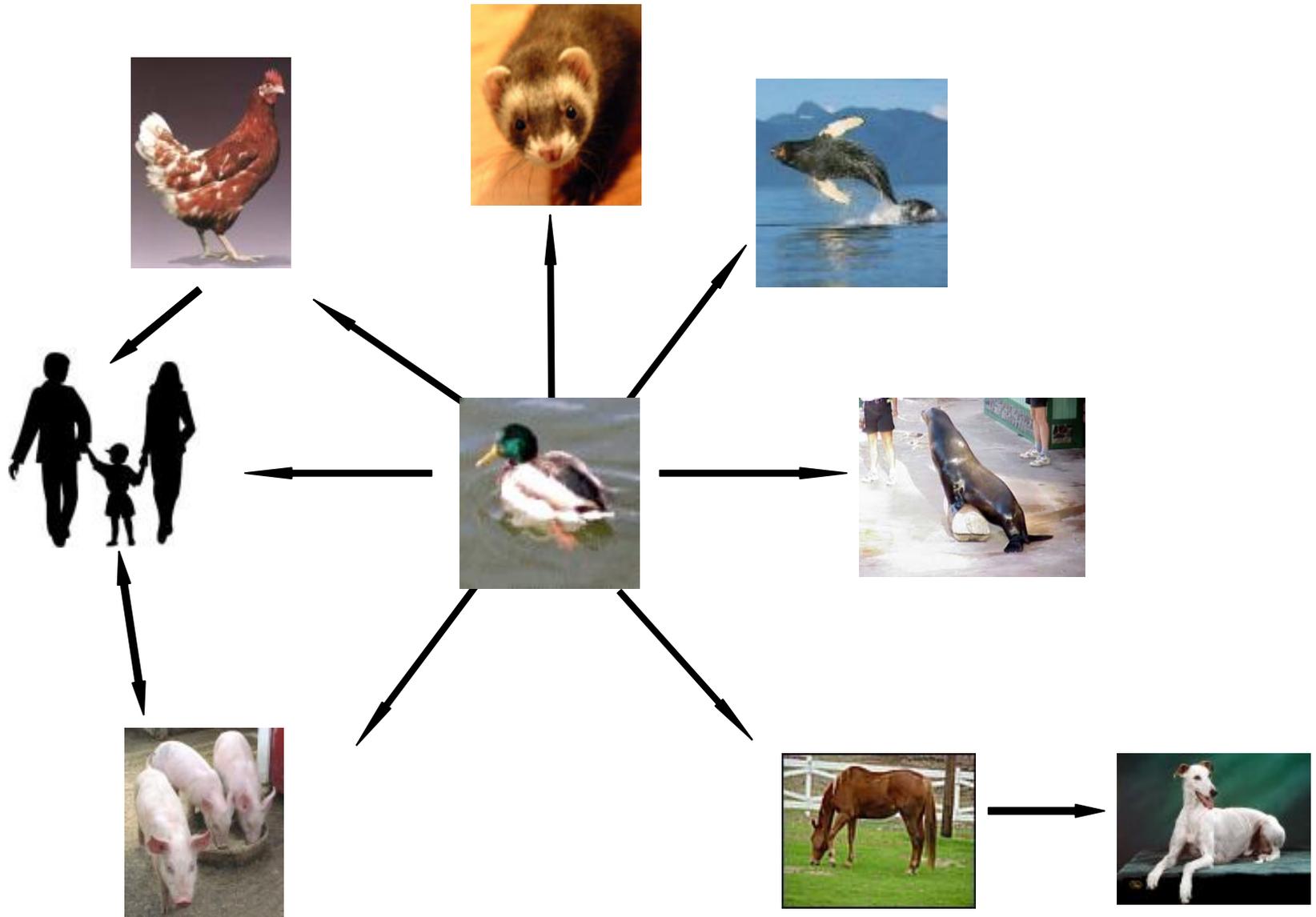
- **Seasonal Influenza:** Yearly influenza epidemics are a major cause of morbidity (illness) and mortality (death)
- **Pandemic Influenza:** Pandemics emerge sporadically and can range from mild (1968) to catastrophic (1918)
  - Compared to seasonal influenza, young people are more likely to die
- **Moving Target:** With current vaccine technology, yearly vaccinations are needed because the virus evolves from year to year.

# Cycle of Influenza A viruses

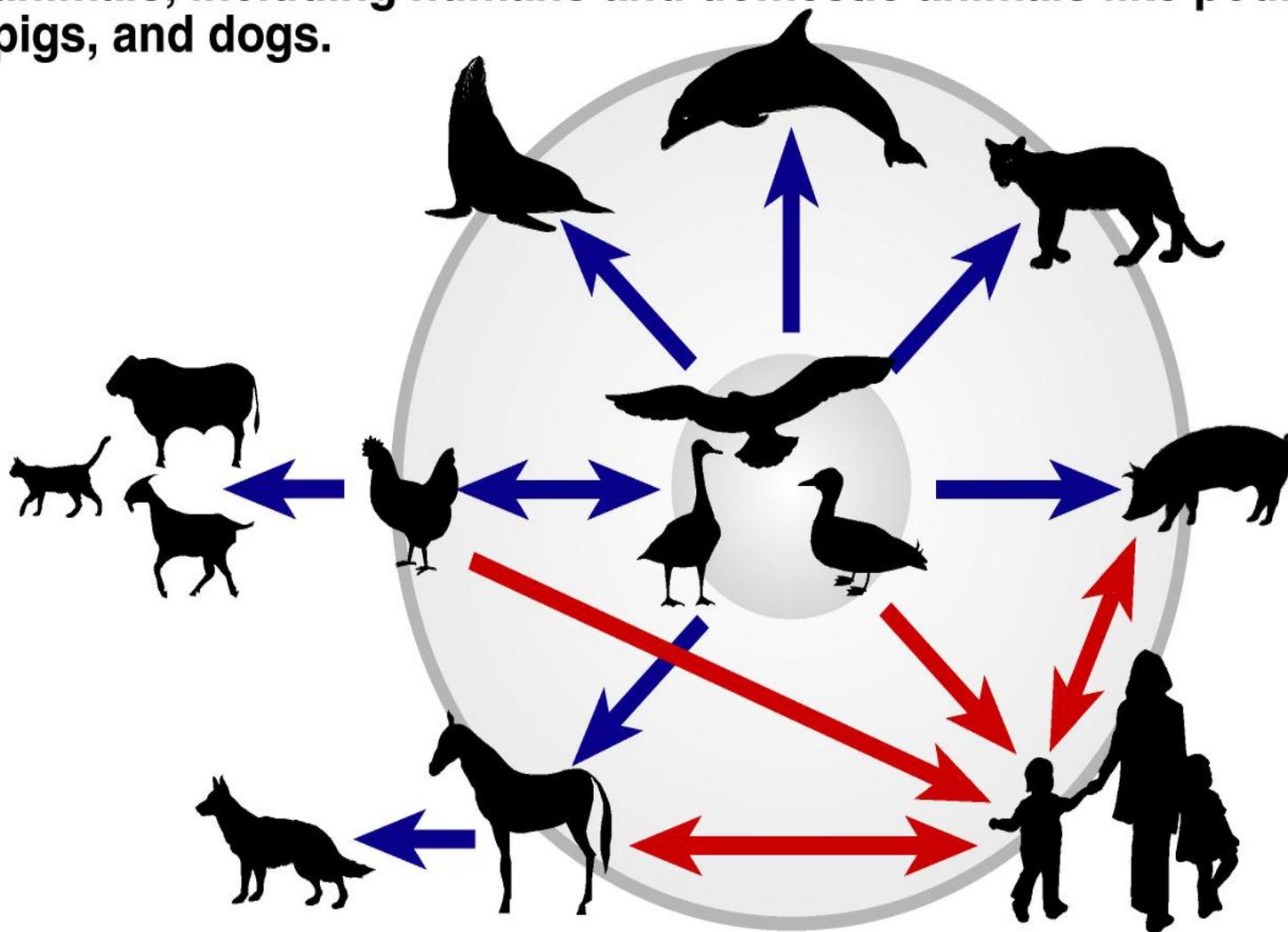


Source: Excerpt from 'Field Manual of Wildlife Diseases' (<http://www.pandemicflu.gov>)

# Flu viruses: not just for the birds.....



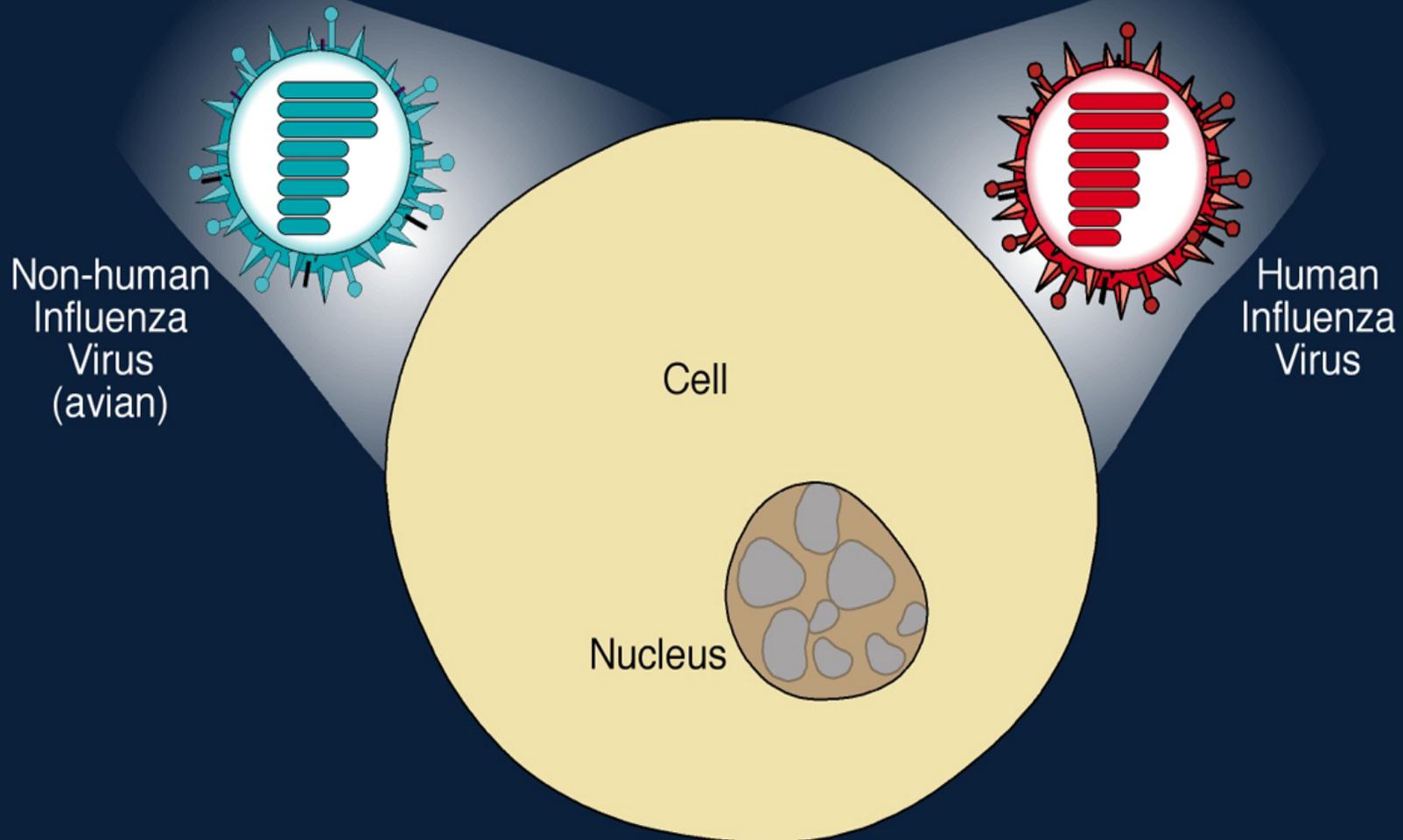
**Broad Host Range:** Influenza viruses cause disease in many different animals, including humans and domestic animals like poultry, horses, pigs, and dogs.



**Zoonotic Disease:** Influenza infection can occasionally transmit from animals to humans, which can lead to the emergence of a pandemic virus.

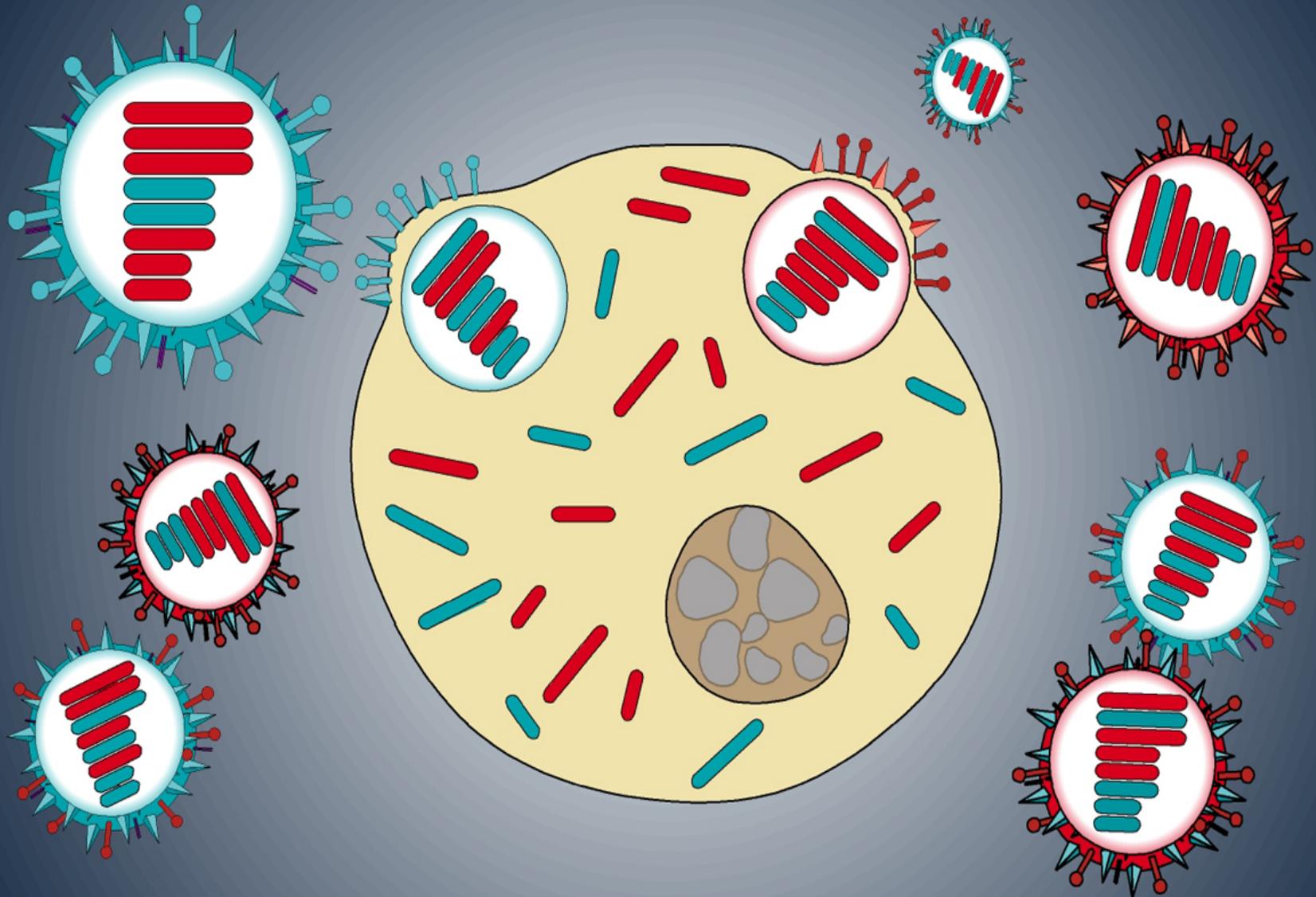
# Generation of New Pandemic Virus by Gene Exchange: Antigenic Shift

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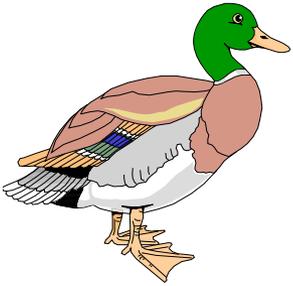


# Replication Followed by Reassortment

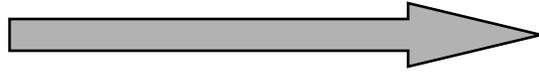
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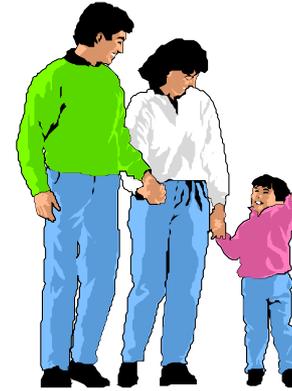
**Birds**



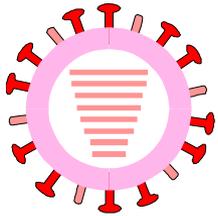
**A) Direct infection**



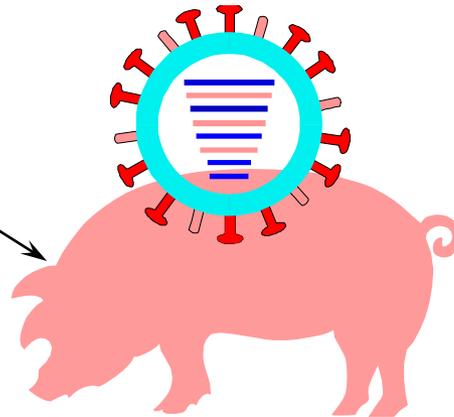
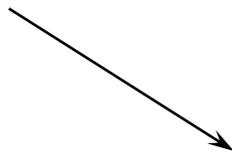
**Humans**



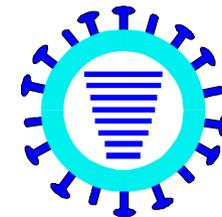
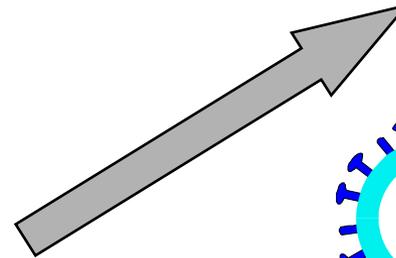
**B) Passage in an intermediate host without reassortment**



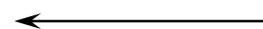
**Avian influenza A virus**



**C) Reassortment in an intermediate host**

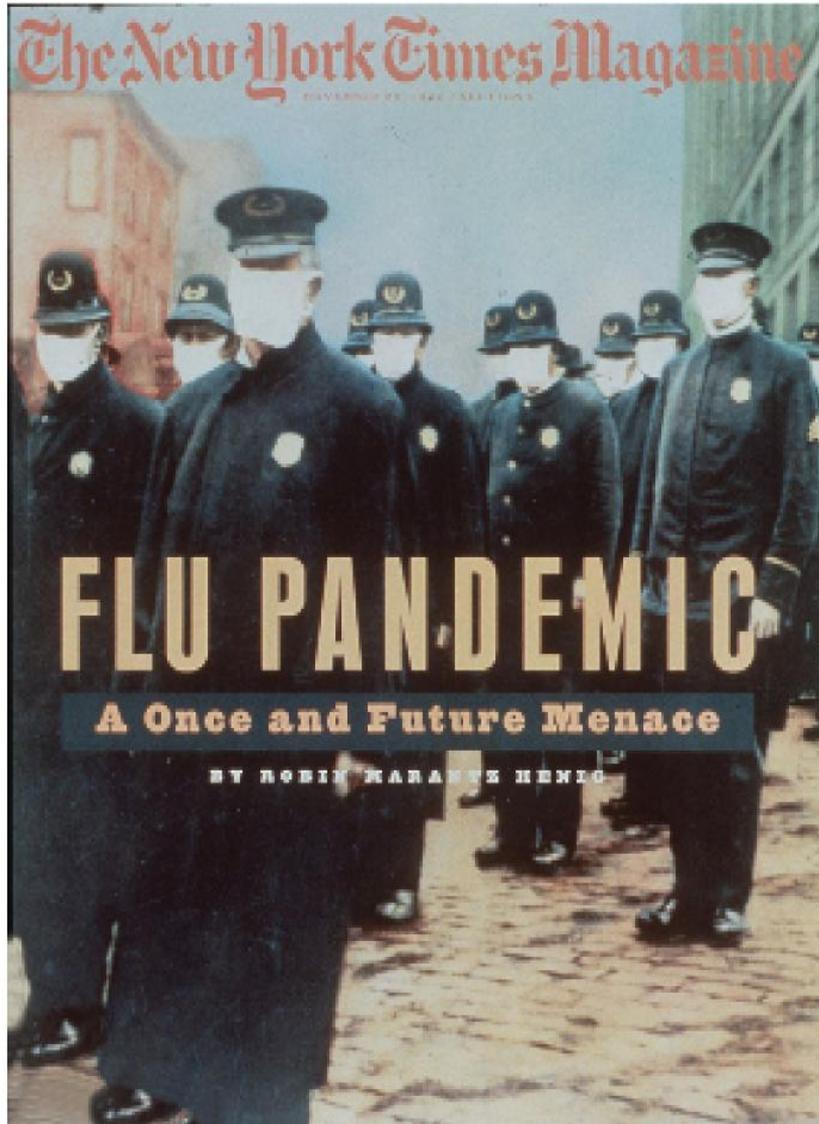


**Human influenza A virus**



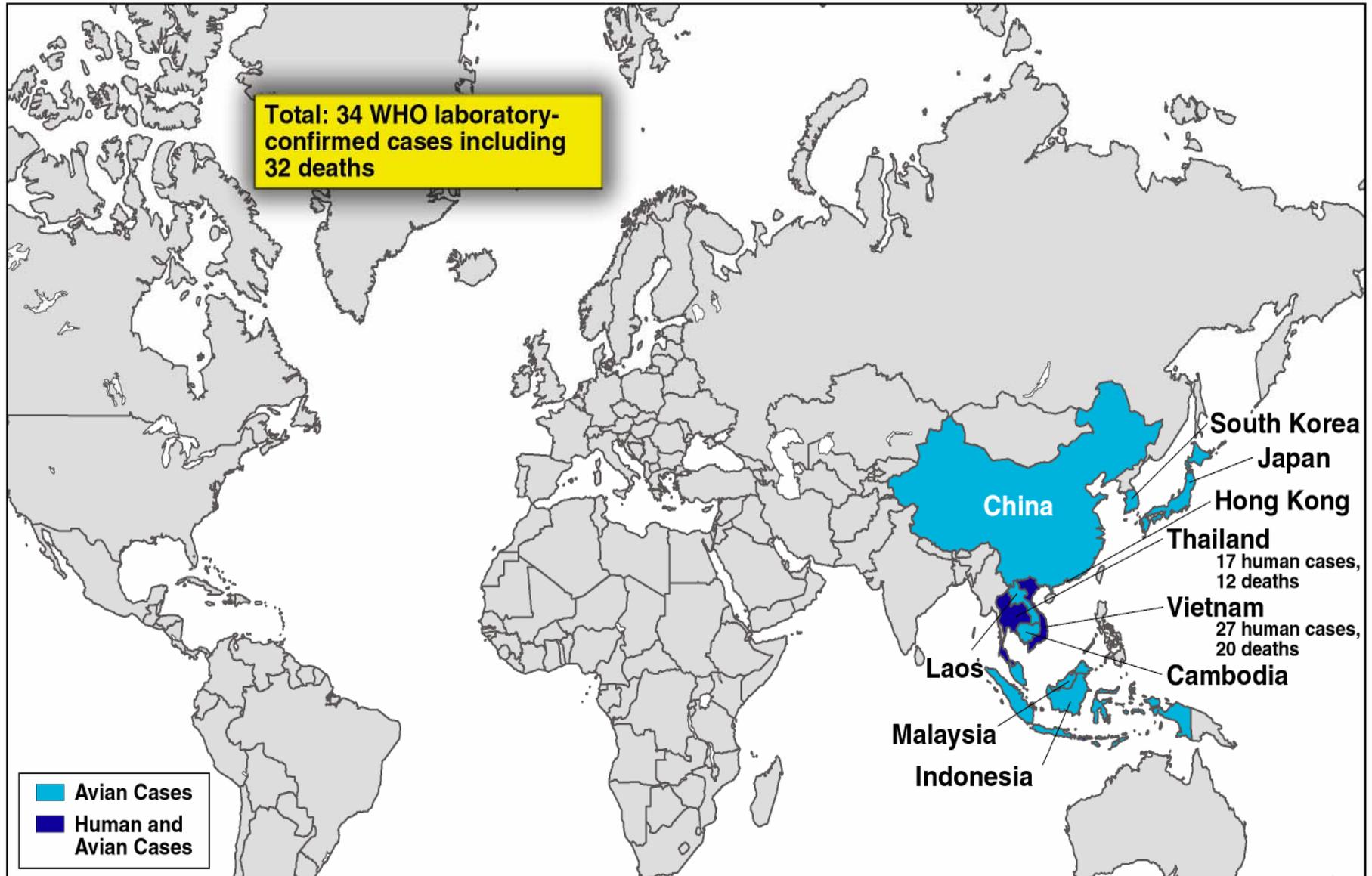
# The Influenza Pandemic of 1918-1919

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- 500 million people infected worldwide
- 20-40 million deaths worldwide; ~50 percent in people aged 20-40
- >500,000 deaths in United States

# Cumulative H5N1 Cases, October 2004



# Cumulative H5N1 Cases, October 2005











# Direct Infection of Humans with Avian Influenza Viruses

Year	Country	Subtype	Cases	Deaths
1959	US	H7N7	1	0
1978-79	US	H7N7	?	0
1996	England	H7N7	1	0
1997	Hong Kong	H5N1	18	6
1999	China	H9N2	5	0
1999, 2003	Hong Kong	H9N2	3	0
2002-03	US	H7N2	2	0
2003	Hong Kong	H5N1	5	2
2003	Netherlands	H7N7	89	1
2004	Canada	H7N3	2	0
2004	Egypt	H10N7	2	0
2003-2007	12 countries	H5N1	366	232

# How do people get infected ?

Human cases so far only in areas where there are outbreaks in poultry



COURTESY (CBC)

# What is a pandemic ?

An epidemic, spread over a wide geographic area, that affects a large proportion of the population

(from the Greek words

Pan - all

Demos - people)

# Characteristics of Pandemic Influenza

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- **Infection in humans with a new influenza virus.**
- **Susceptibility (lack of immunity) to this novel virus, in a large proportion of the population.**
- **Ability of the virus to cause disease and spread from person-to-person.**

# Phases of a Pandemic: Where We Are Now

<b>Inter-pandemic phase</b>  New virus in animals, no human cases	Low risk of human cases	1
	Higher risk of human cases	2
<b>Pandemic alert</b>  New virus causes human cases	No or very limited human-to-human transmission	3
	Evidence of increased human-to-human transmission	4
	Evidence of a significant human-to-human transmission	5
<b>Pandemic</b>	Efficient and sustained human-to-human transmission	6

# How Is Influenza Spread?

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- **Coughing or sneezing (through air)**
- **Unclean hands**
- **Contact with contaminated objects**



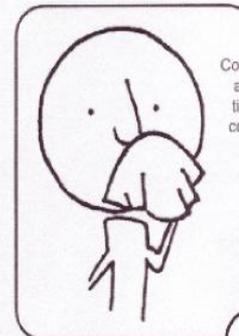
Source: Andrew Davidhazy, Professor,  
School of Photo Arts and Sciences,  
Rochester Institute of Technology

**High Speed Photograph of a Sneeze**

Practicing good  
“Respiratory  
Etiquette” can  
help reduce  
influenza  
transmission...

Stop the spread of germs that make you and others sick!

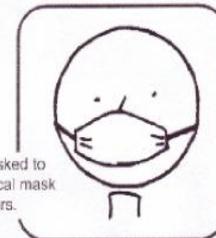
# Cover your Cough



Cover your mouth and nose with a tissue when you cough or sneeze or cough or sneeze into your upper sleeve, not your hands.



Put your used tissue in the waste basket.



You may be asked to put on a surgical mask to protect others.

# Clean your Hands

after coughing or sneezing.



Wash hands with soap and warm water for 20 seconds or

clean with alcohol-based hand cleaner.



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202-638-1000

APIC  
Association for Professionals in Infection Control and Epidemiology, Inc.  
1000 Corporate Park Drive, Suite 100  
Atlanta, GA 30329  
404-525-8800

# What Tools Do We Have To Control Influenza?

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## Surveillance and detection:

- **Diagnostics**

## Mitigation

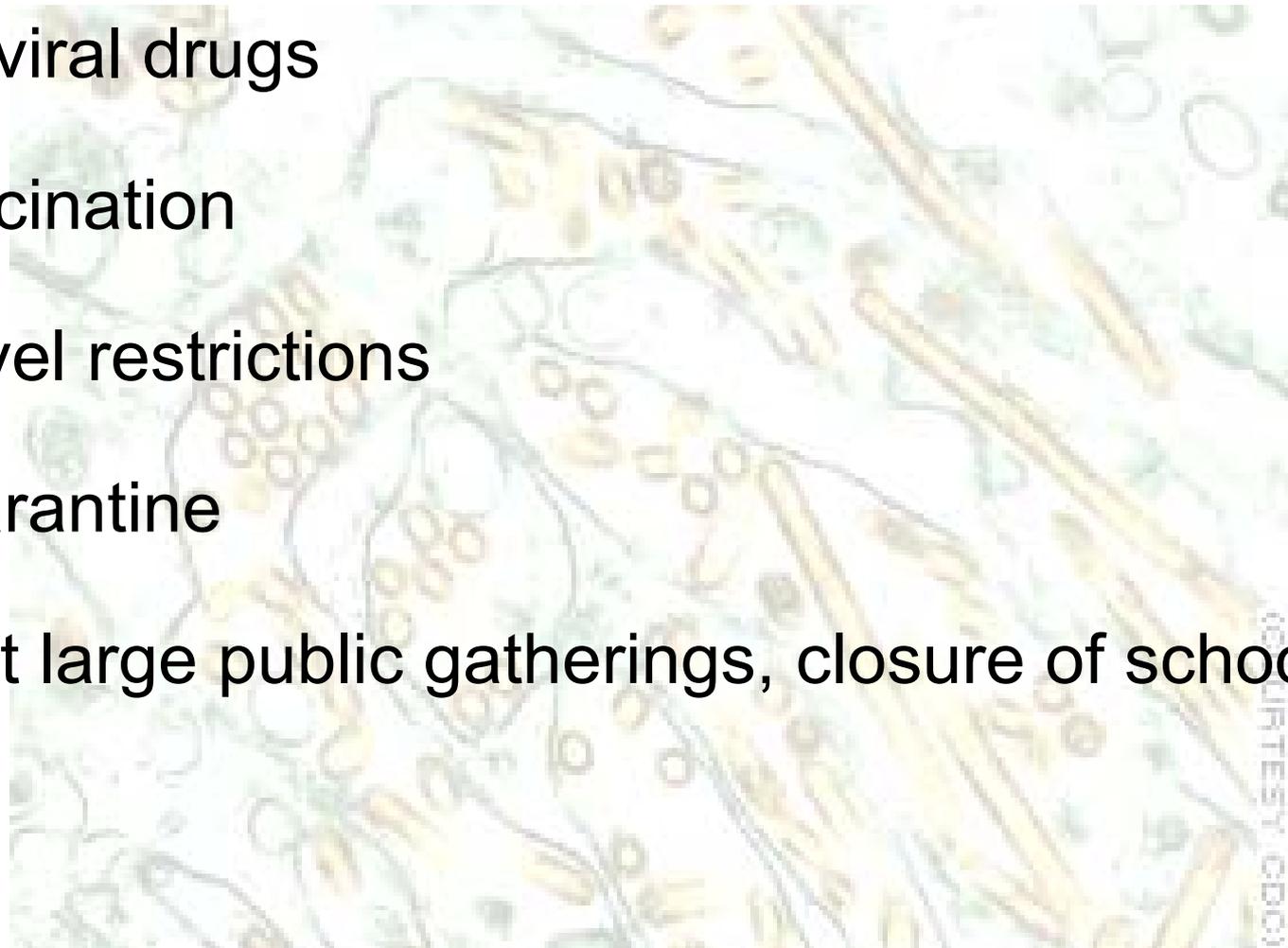
- **Medical interventions such as antiviral medications and vaccines**
- **Non-medical interventions such as social distancing, cough etiquette, hand hygiene**

# Methods to control infection in birds

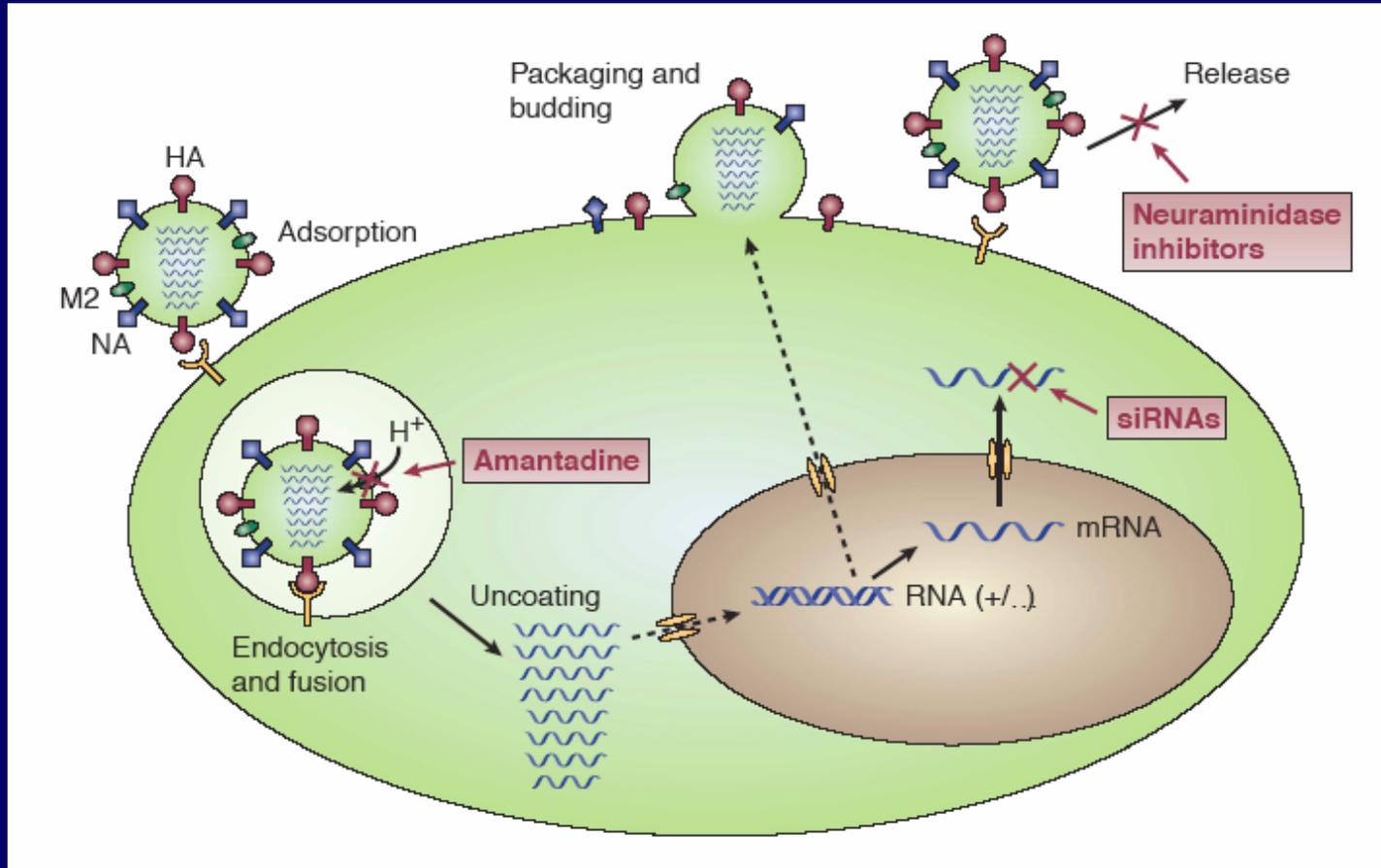
- Increased surveillance
- Increased biosecurity and minimizing exposure of poultry to wild birds
- Keep poultry & waterfowl separate in live bird markets
- Close live poultry markets; encourage people to buy ready prepared poultry
- 'Rest days' at live bird markets
- Culling of poultry
- Vaccination of poultry
- Import and trade restrictions

# Methods to control infection in humans

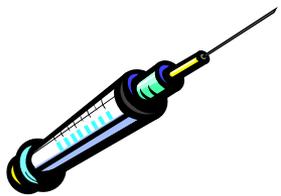
- Antiviral drugs
- Vaccination
- Travel restrictions
- Quarantine
- Limit large public gatherings, closure of schools



# Antiviral drugs for influenza



# Making influenza vaccines



6 + months



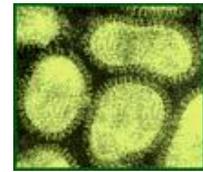
**Organization of egg supply**



**Selection of vaccine strains**



**Production of seed virus**



6 + months



**Testing**

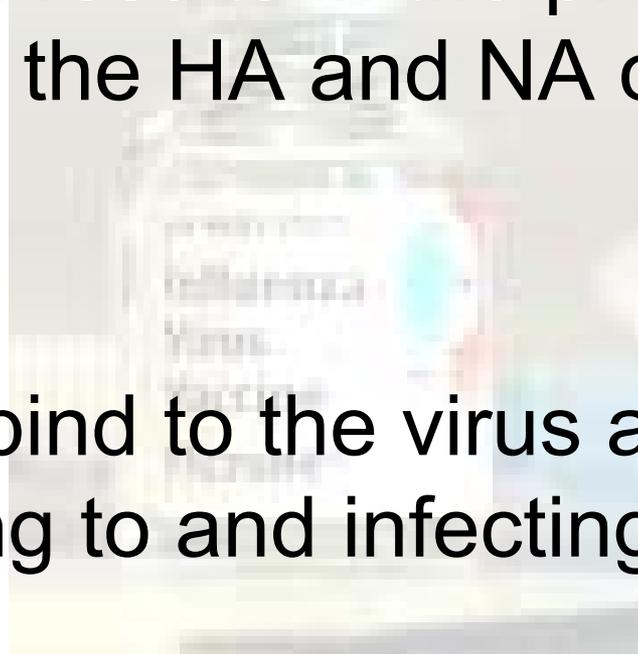


**Vaccine on the market**



# How do vaccines against flu work ?

- Vaccination results in the production of antibodies to the HA and NA of the virus
- Antibodies bind to the virus and prevent it from attaching to and infecting cells



# Vaccines against influenza

## Inactivated



- killed virus
- grown in eggs
- injected (flu shot)

## Live



Image courtesy of Aflonit

- live, weakened virus
- grown in eggs
- given intranasally
- for healthy individuals, aged 5-49 years

Identifying an influenza patient can be tricky because many pathogens cause influenza-like illness and pneumonia...



## Is It a Cold or the Flu?

Symptoms	Cold	Flu
Fever	Rare	Usual; high (100°F to 102°F; occasionally higher, especially in young children); lasts 3 to 4 days
Headache	Rare	Common
General Aches, Pains	Slight	Usual; often severe
Fatigue, Weakness	Sometimes	Usual; can last up to 2 to 3 weeks
Extreme Exhaustion	Never	Usual; at the beginning of the illness
Stuffy Nose	Common	Sometimes
Sneezing	Usual	Sometimes
Sore Throat	Common	Sometimes
Chest Discomfort, Cough	Mild to moderate; hacking cough	Common; can become severe
<b>Treatment</b>	Antihistamines Decongestant Nonsteroidal anti-inflammatory medicines	Antiviral medicines—see your doctor
<b>Prevention</b>	Wash your hands often Avoid close contact with anyone with a cold	Annual vaccination; antiviral medicines—see your doctor
<b>Complications</b>	Sinus congestion Middle ear infection Asthma	Bronchitis, pneumonia; can be life threatening

# **Selected Clinical Features of H5N1 Influenza in Humans**

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- **Incubation period (time from infection to symptom onset) ranges from 2-8 days (versus 2-3 days with seasonal flu).**
- **Symptoms include high fever and influenza-like symptoms (fever with respiratory symptoms such as cough, sore throat, and headache, body aches).**
- **Diarrhea, vomiting, abdominal pain, chest pain, and bleeding from the nose and gums also reported.**
- **Early involvement of lower respiratory tract.**
- **On occasion acute encephalitis and diarrhea observed without respiratory symptoms.**

# **What PPE Does a Clinician Wear When Treating a Potential H5N1 Influenza Patient?**

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- **Gloves**
- **Gown**
- **Shoe covers**
- **Protective eyewear**
- **Surgical mask**
- **Bouffant cap**

# **Influenza Diagnostics: What Do You Want To Know?**

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- **Is your patient sick with influenza or another infectious agent?**
- **If your patient is suspected to be infected with influenza, is it the pandemic virus?**

# What PPE Does a Virologist Wear When Working with H5N1 Influenza Virus?

## BioSafety Level 3-Enhanced (BSL 3+) PPE

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1. Put on Tyvek® Coveralls



2. Put on nitrile gloves and tape OVER coverall cuffs



3. Put on latex gloves



4. Attach breathing tube to Powered Air Purifying Respirator (PAPR)



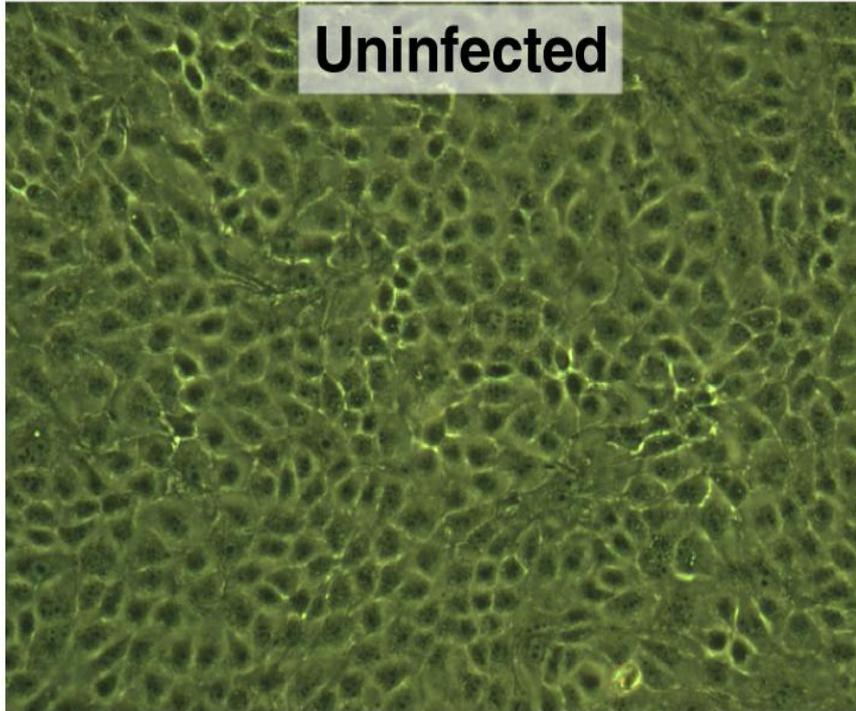
5. Turn PAPR on. Put on face shield and PAPR belt

# What Are Diagnostic Tests?

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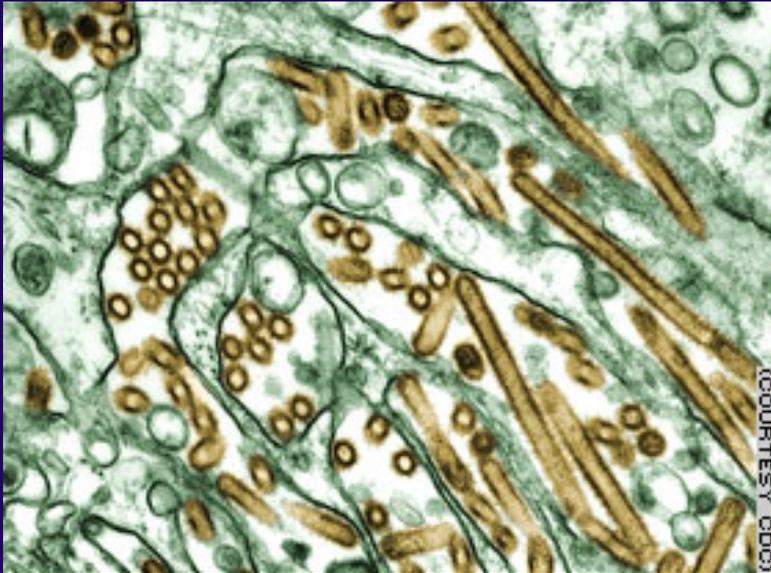
- **Diagnostic tests allow physicians to determine the cause of a patient's illness.**
- **In infectious diseases, the physician is trying to determine the specific infectious organism responsible for the illness. The physician uses this diagnostic information to make treatment decisions and infection control decisions.**
- **For patients with influenza it is important to make an accurate diagnosis so treatment can be started within the first 48 hours and infection control measures initiated.**

# How Do Cells Look When They Are Infected With Influenza Virus?



- Although influenza viruses cannot be seen with a light microscope, scientists can see the effect influenza viruses have on living cells.
- Influenza virus-infected cells die, are shed from the growth surface, become more rounded and reflect more light.

# Electron Micrographs of Influenza Virus



# Sources & Recommended Reading

- [www.who.int](http://www.who.int)
- 'Avian Influenza: Assessing the pandemic threat' (WHO, January 2005)
- [www.fao.org](http://www.fao.org)
- [www.oie.int](http://www.oie.int)
- [www.cdc.gov](http://www.cdc.gov)
- [www.pandemicflu.gov](http://www.pandemicflu.gov)
- 'The Great Influenza' by John Barry

# Reports on avian influenza

