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Pandemic Influenza: Background and Challenges

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Pandemic Influenza Overview

Virus basics

Influenza A specifics

Connection between avian and human influenza

Epidemiology of influenza A

Potential impact of a pandemic

Challenges and dilemmas we will need to address

Influenza viruses: The ABCs

Influenza types A or B viruses cause epidemics of disease almost every winter.

- In the United States, these winter influenza epidemics can cause illness in 10% to 20% of people and are associated with an average of 36,000 deaths and 114,000 hospitalizations per year.

Influenza type C infections cause a mild respiratory illness and are not thought to cause epidemics.

What is a virus?

A virus is a bag of genes that sticks to and empties its contents into a living cell so it can take over the cell to make copies of itself.

The genes are made of RNA or DNA and contain the instructions for making proteins.

The envelope of a virus contains and protects the viral genes when virus is outside of a cell and infects new host cell.

Surface proteins in envelope allow the virus to attach to and enter host cells.

Our immune system learns to recognize specific surface proteins to trigger our immune responses.

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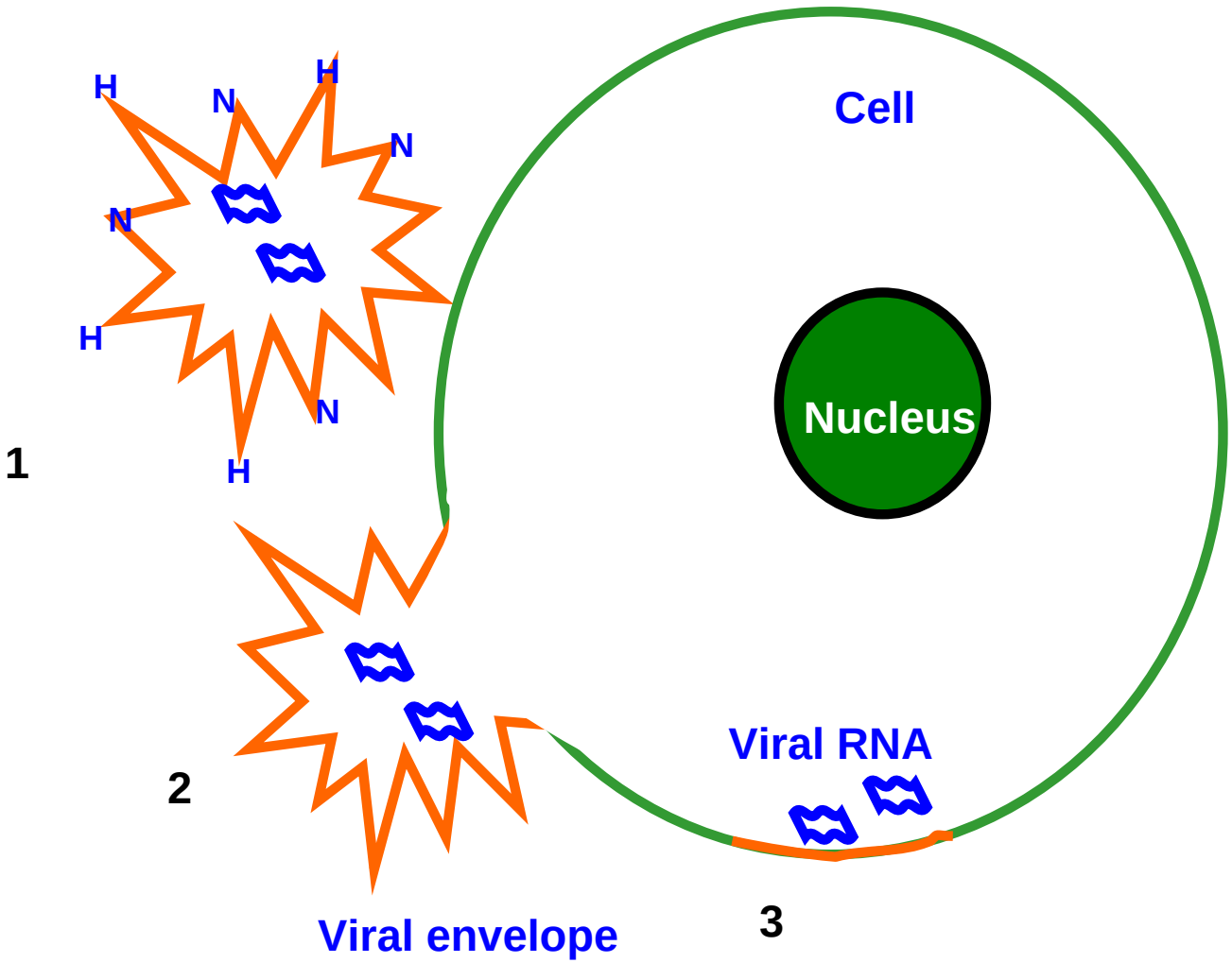


Attachment, fusion, and entry of influenza virus to cell

Influenza virus

Influenza type A viruses are divided into subtypes based on two proteins on the surface of the virus. These proteins are called hemagglutinin (H) and neuraminidase (N).

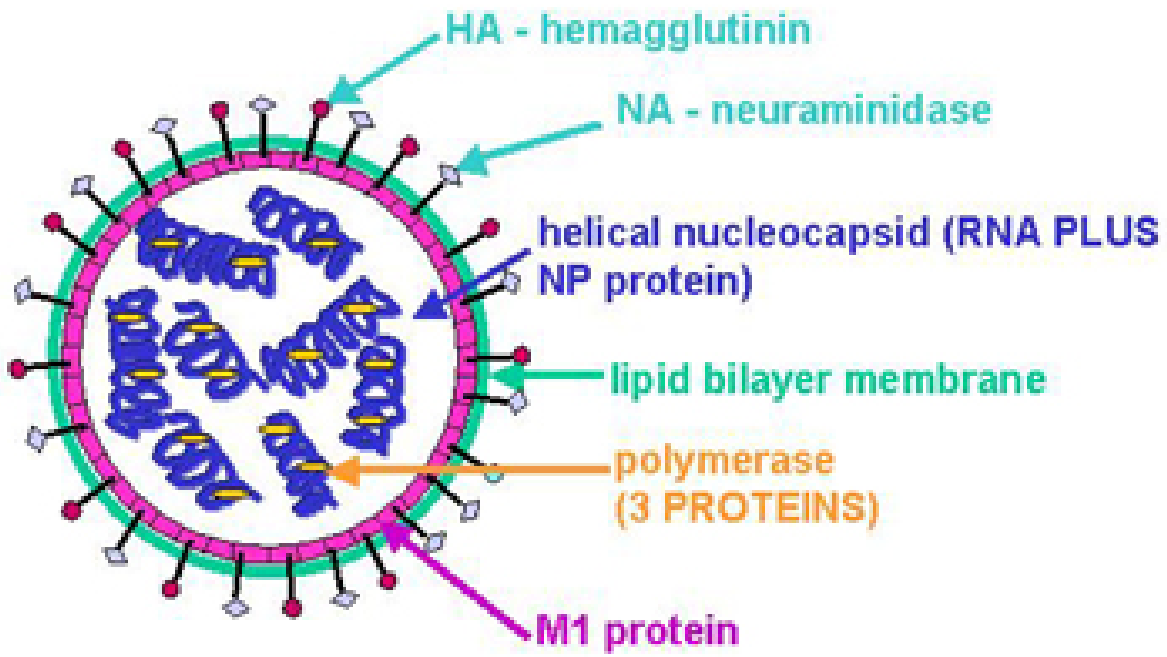
The current subtypes of influenza A viruses found in people are A/H1N1 and A/H3N2.

Influenza B virus is not divided into subtypes.

Influenza A/H1N1, A/H3N2, and influenza B strains are included in each year's influenza vaccine.

Influenza viruses mutate constantly and should not be thought of as identical viruses, even within a subtype, but as a swarm of closely related different viruses.

Influenza Virus Structure



type A, B, C : NP, M protein
sub-types: HA or NA protein

Influenza virus mutation

The differences between viruses affect how transmissible they are, how sick they can make infected individuals, and how resistant they are to antiviral medications.

The mutations also determine how well our immune systems recognize and inactivate the virus.

This constant mutation (***genetic drift***) is why the vaccine must be changed annually, even though every year it contains an A/H1N1, A/H3N2, and B virus.

Influenza in animals

Influenza A viruses are found in many different animals, including ducks, chickens, pigs, whales, horses, and seals.

Influenza B viruses circulate widely only among humans.

Influenza A in Birds

There are 15 different hemagglutinin (H) subtypes and 9 different neuraminidase (N) subtypes, all of which have been found among influenza A viruses in wild birds.

Wild birds are the primary natural reservoir for all subtypes of influenza A viruses and are thought to be the source of influenza A viruses in all other animals.

Most influenza viruses cause no symptoms or mild infection in birds; however, the range of symptoms in birds varies greatly depending on the strain of virus.

Infection with certain avian influenza A viruses (for example, some strains of H5 and H7 viruses) can cause widespread disease and death among some species of wild and especially domestic birds such as chickens and turkeys.

Avian Influenza A in Humans

People can become infected with avian influenza.

Avian influenza either does not pass from human to human, or does so rarely with very close contact.

Human disease from avian influenza can range from mild to severe or fatal.

Avian Influenza Infections in Humans, 1997-2005

Table. Avian Influenza Infections in Humans, 1997–2005

Strain	Location	Date	Findings in Patients
H5N1	Hong Kong	1997	18 flu cases; 6 deaths
H9N2	China	1999	Two nonfatal flu cases in children
H7N2	Virginia	2002	1 asymptomatic case
H7N7	The Netherlands	2003	78 cases of conjunctivitis and 7 flu cases; 1 death
H5N1	Hong Kong and China	2003	2 flu cases; 1 death
H5N1	Thailand, Vietnam, Cambodia	2003–June 2005	88 flu cases; 50 deaths
H9N2	Hong Kong	2003	1 nonfatal flu case
H7N2	New York	2003	1 nonfatal flu case
H7N3	Canada	2004	Conjunctivitis

Bartlett, J. G. et. al. Ann Intern Med 2005;143:460-462

How Avian Flu becomes Human Flu

Although people can become infected with avian influenza, it does not spread easily between humans.

With re-assortments or mutations of viral genes, an avian influenza can become transmissible between humans and become a new human influenza.

This ***genetic shift*** results in spread of an influenza virus new to human populations, causing a pandemic (worldwide epidemic).

Re-assortment

Pigs are an important link between avian and human influenza.

Pigs can be infected with and spread both avian and human influenza A.

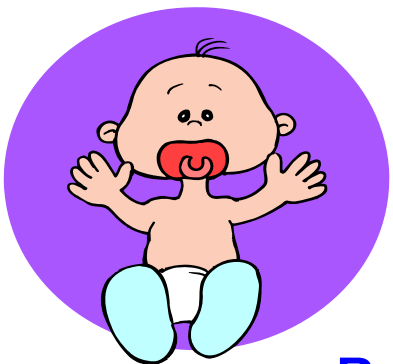
If a pig is infected at the same time with both human and avian influenza, the viral genes may re-assort, and a new combination transmissible between people can result.

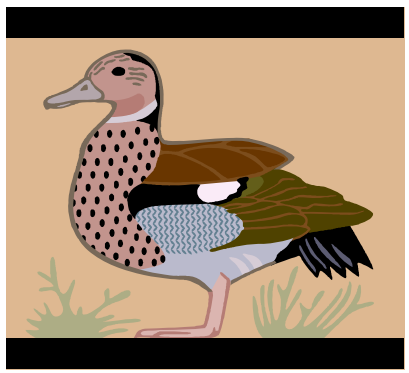
Human

H2N2

Avian

H5N1

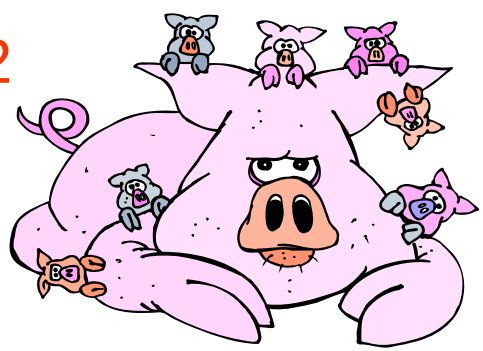




Re-assorted virus

H5N2

H2N2



H5N1

Mutation

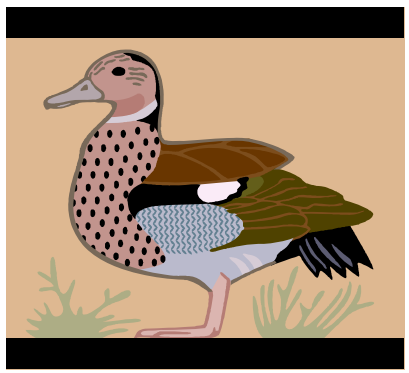
An avian influenza A virus can mutate and develop the ability to infect and spread between humans.

The 1918 A/H1N1 pandemic virus is thought to have mutated directly from an avian A/H1N1 without going through re-assortment with human influenza A virus in a pig.

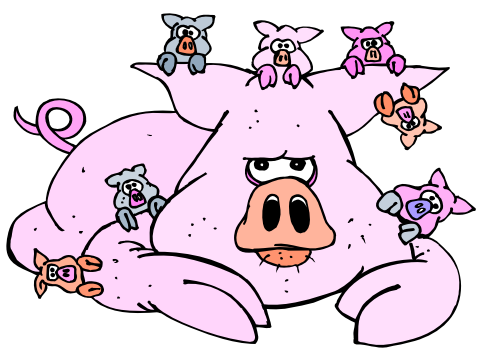
The current A/H5N1 avian influenza has the potential to do this as well.

Human H5N1
(mutated Avian H5N1)

Avian H5N1



Direct mutation without re-assortment



20th century influenza pandemics

1918 - A/H1N1 "Spanish flu"

500,000 deaths in US, 40-50 million worldwide

1957 - A/H2N2 "Asian flu"

70,000 deaths in the US

1968 - A/H3N2 "Hong Kong flu"

34,000 deaths in the US

[Compare to seasonal flu, averaging 36,000 deaths per year.]

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Pandemic Influenza

Outbreak of Avian Influenza A (H5N1) in Asia

"We at WHO [the World Health Organization] believe that the world is now in the gravest possible danger of a pandemic…"

Dr. Shigeru Omi, the WHO's Western Pacific Regional Director, 23 February 2005

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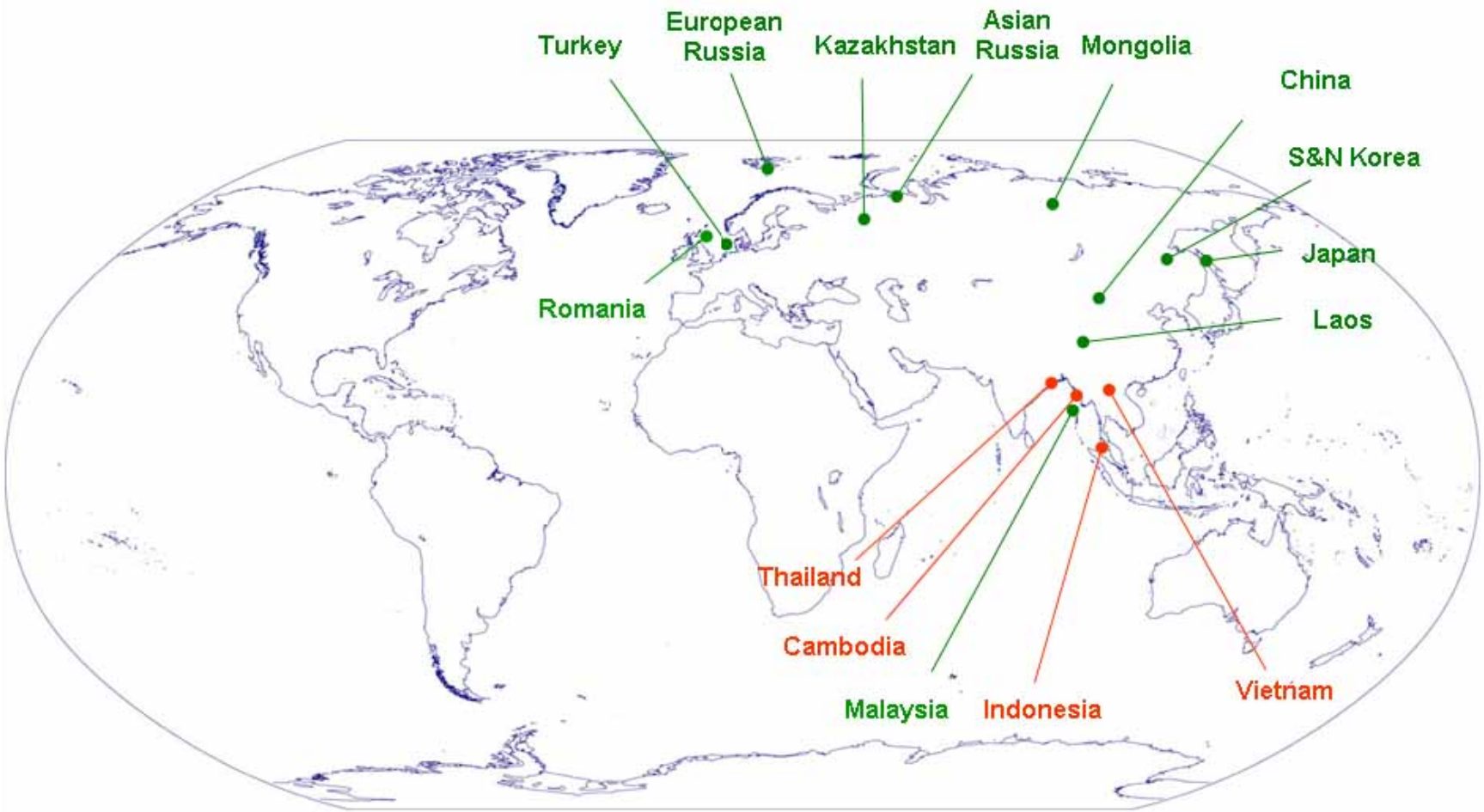
Countries reporting confirmed animal and/or human A/H5N1 infections in Dec 2003 – Oct 2005*



** WHO & FAO as of 10/15/2005*

Cumulative Number of Confirmed Human Cases of Avian Influenza A/(H5N1) Reported to WHO 09 November 2005

Date of onset	Indonesia		Viet Nam		Thailand		Cambodia		Total	
	cases	deaths	cases	deaths	cases	deaths	cases	deaths	cases	deaths
26.12.03 - 10.03.04	0	0	23	16	12	8	0	0	35	24
19.07.04 - 08.10.04	0	0	4	4	5	4	0	0	9	8
16.12.04 - to date	9	5	65	22	3	1	4	4	81	32
Total	9	5	92	42	20	13	4	4	125	64

Total number of cases includes number of deaths.
WHO reports only laboratory-confirmed cases.

Seasonal flu compared to human cases of avian flu H5N1

Seasonal flu: primarily upper airway infection, may be complicated by secondary bacterial infection. Severe cases usually elderly or other high risk.

Human avian H5N1: usually a primary viral pneumonia, may also infect intestines or brain. Young, healthy adults and children commonly affected.

Impact of 1918 Pandemic

1918 - A/**H1N1** "Spanish flu"

500,000 deaths in US

40-50 million deaths worldwide

US population about 100 million in 1918

Death rate from pandemic influenza about 0.5%

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Impact of potential pandemic in Whatcom County

Whatcom County population is about 180,000

If a third become ill with influenza and the death rate is 0.2%, then 120 deaths from influenza.

If half become ill and the death rate is 0.5%, then 450 deaths from influenza.

Compare to 1300 deaths from all causes in Whatcom County in 2004.

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What can we do to prevent pandemic influenza?

Global effort, requires rapid identification of avian influenza outbreaks and human cases of avian influenza.

Culling of infected domestic birds.

Identify early human to human transmission, treat cases, isolate and quarantine to prevent spread if localized.

If it spreads, isolation and quarantine will not be effective tools.

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What can we do once a pandemic starts?

Overall goal is to slow the spread so that fewest people are ill at the same time, to maintain essential services.

- Infection Control
- Antiviral Medications
- Vaccine

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Infection Control

- Cough etiquette
- Handwashing
- Masks
- Social distancing

Vaccine

Needs to be for specific pandemic virus strain, not the same as the current avian influenza.

H5N1 avian influenza vaccine will not fully protect, but may provide primer dose of vaccine during the months it takes to develop specific vaccine after pandemic strain is identified.

Need to develop cell culture technique to speed production. Current egg-based vaccine production is slow and vulnerable to avian influenza.

Antivirals

- Neuraminidase inhibitors like Tamiflu®and Relenza® are currently in short supply
- Amantadine and rimantadine are not effective for H5N1
- Resistance may develop
- Must be given early to be effective (not effective after 48 hours)
- May require higher than normal doses to be effective.

Challenges of pandemic influenza

- Limited or no supplies of vaccine or antiviral medicines
- Caring for the sick and maintaining our communities as best we can, whether or not vaccine or antivirals are available
- Going beyond “business as usual” in anticipating and responding to a pandemic