

# Influenza viruses

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# What is influenza?

- Influenza is an acute infectious respiratory disease caused by RNA viruses of the family orthomyxoviridae (the influenza viruses).
- The influenza virus, known to cause recurrent epidemics and global pandemics.
- Highly infectious and can spread rapidly from person to person.
- Some strains cause more severe illness than others.
- Virus first isolated in 1933

## **Infectious agent:**

Influenza viruses are RNA viruses of orthomyxoviridae family.

**Influenza Virus Types A, B & C** according to antigenic properties of 2 internal structure proteins: nucleo protein & matrix protein.

## Type A:

**Subtypes:** Influenza A viruses are divided into subtypes based on two proteins on the surface of the virus:

**Haemagglutinin H (H1, H2, H3)**

**Neuraminidase N (N1, N2)**

For example, “H5N1 virus” designates an influenza A subtype that has an HA 5 protein and an NA 1 protein

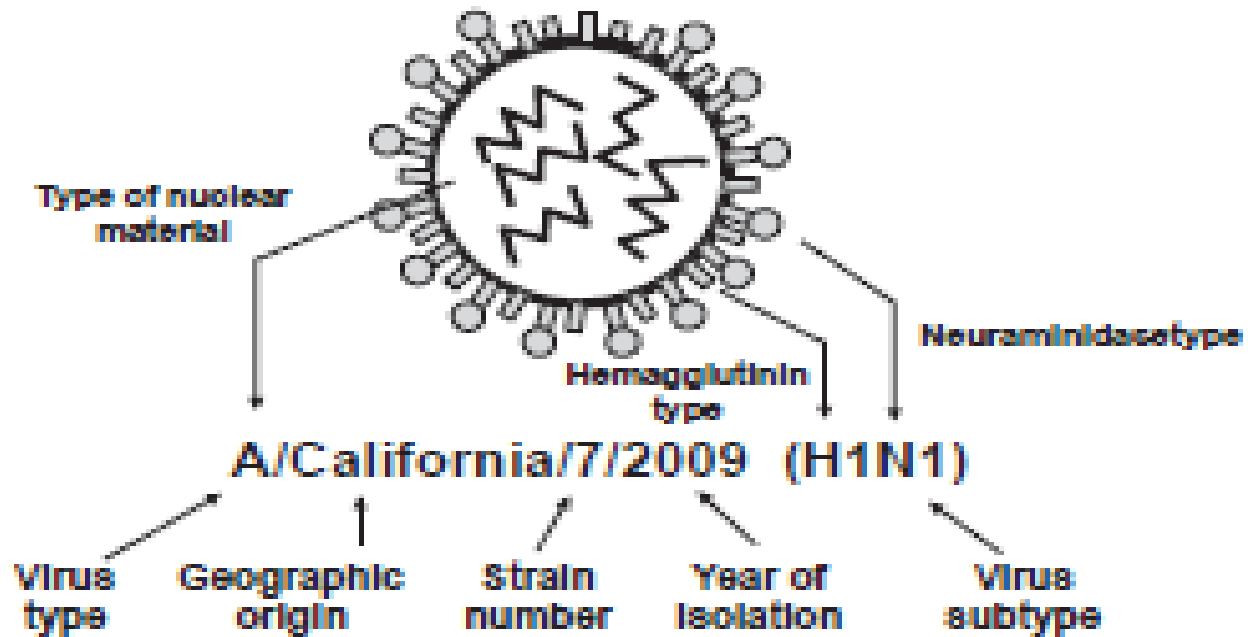
## Type A:

Influenza A include 3 subtypes {**H1N1, H2N2, H3N2**}. That are described by geographical site of isolation, culture no. & year of isolation .

Example:

Type / site origin / no. / year isolation / subtype  
**A / Johannesburg / 33 / 94 / (H3N2)**

# Influenza Virus



## Type A:

- Usually associated with widespread epidemics (seasonal flu) & pandemics (pandemic flu).
- Causes moderate to severe illness
- Affects all age groups.
- The virus infects humans and other animals.
- Influenza A viruses are perpetuated in nature by wild birds, predominantly waterfowl.
- Most of these viruses are not pathogenic to their natural hosts and do not change or evolve.

# Type B:

- **Infrequently associated with regional or widespread epidemics (seasonal flu).**
- Generally causes milder disease than type A .
- Primarily affects children.
- It affects only humans.



## Type C:

- Rarely reported as a cause of human illness, probably because most cases are subclinical.
- It has not been associated with epidemic disease.

# Antigenic Changes

Hemagglutinin and neuraminidase periodically change, apparently due to sequential evolution within immune or partially immune populations.

## Influenza Antigenic Changes :

### 1-Antigenic Drift

- minor change, same subtype , new strain
- caused by **point mutations** in gene
- may result in epidemic

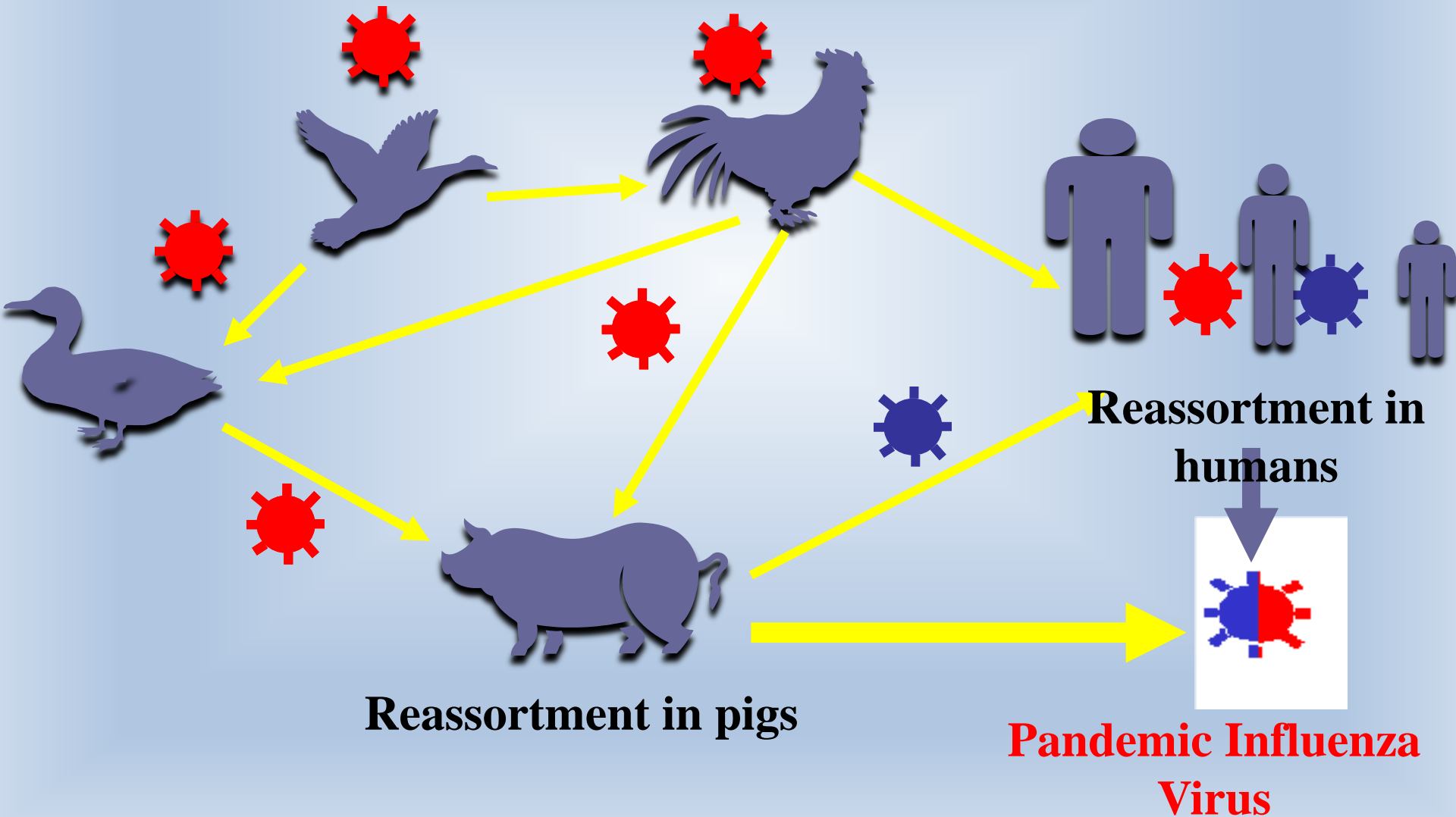
### 2-Antigenic Shift

- major change, new subtype (NOVEL)
- caused by **exchange of gene segments**
- may result in pandemic

- Antigenic drift occurs in both Influenza **A and B viruses**. Influenza B viruses undergo antigenic drift less rapidly than influenza A viruses
- These point mutations occur unpredictably and result in **new virus strains**.
- ie: a person infected with a particular influenza virus strain develops antibody against that strain. As newer virus strains appear, the antibodies against the older strains might not recognize the "newer" virus, and infection with a new strain can occur.
- Antigenic drift explains why a person can be infected by Influenza A viruses several times and also why **Influenza vaccine need to be updated every year.**

- Antigenic shift refers to an **abrupt, major change** to produce a **novel influenza A virus subtype in humans** that was not currently circulating among people. Antigenic shift can occur either through **direct animal to human transmission** or through **mixing of human influenza A and animal influenza A virus genes** to create a new human influenza A subtype virus through a process **called genetic re-assortment**. Antigenic shift results in a new human influenza A subtype.
- Antigenic shift is noted only with type A influenza virus.

# Viral Re-assortment



# Epidemiology

## Occurrence

Influenza occurs throughout the world.

## Reservoir

- Humans are the only known reservoir of influenza types B and C.
- Influenza A viruses may infect both humans and animals.
- There is no chronic carrier state.

# History of influenza:

- 412 BC - first mentioned by Hippocrates
- 1580 - first pandemic described
- 1580-1900 - 28 pandemics
- **Pandemic influenza in the 20th Century**
- 1918 “Spanish Flu” (H1N1) 20-40 million deaths
- 1957 “Asian Flu” (H2N2) 1 million deaths.
- 1968 “Hong Kong Flu”(H3N2) 1 million deaths.

# Epidemiology

## Transmission

- Influenza is primarily transmitted from person to person via large droplets (**particles more than 5 microns in diameter**) that are generated when infected persons cough or sneeze.
- Transmission may also occur through direct contact or indirect contact with respiratory secretions such as when touching surfaces contaminated with influenza virus and then touching the eyes, nose or mouth.



## **Temporal Pattern**

- Influenza activity peaks from December to March in temperate climates, but may occur earlier or later.
- Influenza occurs throughout the year in tropical areas.

## **Communicability**

- Adults can transmit influenza from the day before symptom onset to approximately 5 days after symptoms begin.
- Children can transmit influenza to others for 10 or more days.

- A large number of cases are either **missed** or are **unreported** because of their mildness.
- Morbidity rate varies from **15%** to **25%** of the population exposed to risk in case of large communities.
- The rate may be as high as **40%** in case of closed populations.
- Once an epidemic starts, its peak is reached in **three** to **four** weeks before declining.

## Incubation period:

- The **incubation period** for influenza is usually 2 days, but can vary from 1 to 4 days.
- **Clinical Features**
- Influenza illness can vary from asymptomatic infection to severe.
- In general, only about 50% of infected persons will develop the classic clinical symptoms of influenza.

“Classic” influenza disease is characterized by the abrupt onset of fever, myalgia, sore throat, nonproductive cough, and headache.

Myalgias mainly affect the back muscles.

Additional symptoms may include rhinorrhea (runny nose), headache, substernal chest burning and ocular symptoms (e.g., eye pain and sensitivity to light).

**Systemic symptoms and fever usually last from 2 to 3 days, rarely more than 5 days.**

# Influenza Complications

- 1-Pneumonia secondary bacterial or primary influenza viral.
- 2-Reye syndrome
- 3-Myocarditis
- 4-Death is reported less than 1 per 1,000 cases

Severe illness and death during annual influenza epidemics (seasonal influenza) occur primarily among elderly (80-90% of deaths occur in persons over 65 yrs) and those debilitated by chronic illnesses.

# Laboratory confirmation

- is made by recovery of virus from throat washings or by demonstration of significant rise of influenza antibodies in the serum in acute and convalescent stages of the disease or by direct identification of the virus in nasopharyngeal cells

# What causes a pandemic?

- Pandemics occur when a new avian influenza strain acquires the ability to infect people and to spread easily from person to person.

## **This can occur in two ways:**

- A. Re-assortment (an exchange of seasonal and avian influenza genes in a person or pig infected with both strains).
- B. Mutation (an avian strain becomes more transmissible through adaptive mutation of the virus during human avian influenza infection).



# CHARACTERISTICS OF INFLUENZA PANDEMICS

1. Occurrence outside the usual season.
2. Extremely rapid transmission with concurrent outbreaks throughout the globe.
3. High attack rates in all age groups with high mortality rates even in young adults.

# HOST FACTORS

## Age and gender:

- The influenza virus maximally attacks those in the age group 5 to 15 years
- But no age group or gender is spared.
- Rates of infection are highest among children,
- But death and serious illness are common amongst persons aged 65 years, children below two years and persons of any age with associated medical conditions that place them at increased risk for complications from influenza.

# CONTROL OF INFLUENZA

- **Influenza vaccination** is the key strategy for the prevention of influenza during the inter pandemic periods and a pillar of pandemic preparedness.
- **Antiviral drugs** can only be used as an adjunct.

# Influenza Vaccines

1-Inactivated subunit (IIV) intramuscular or intra-dermal (available in Iraq).

2-Live attenuated vaccine (LAIV) (intranasal).

# Route and dose:

- **Inactivated influenza** vaccines (**killed**) derived from A and B viruses that circulated during previous season, 70-90% protection.
- are given via the intramuscular route in the deltoid muscle, except in infants where the recommended site is the anterolateral aspect of the thigh.
- **A single dose** of inactivated vaccine annually is appropriate.
- **Recently: live attenuated trivalent vaccine A**  
Given intranasal, promising results.
- **Seroprotection** is usually obtained within two to three weeks and the **post-vaccination immunity** lasts for about 6 to 12 months.

# WHO RECOMMENDS THE FOLLOWING PRIORITY CASES FOR VACCINATION

1. Elderly individuals suffering from chronic conditions such as Pulmonary or Cardiovascular disease, metabolic illness including diabetes mellitus and renal dysfunction,
2. Various types of immunosuppression including persons with AIDS and transplant recipients.
3. Health care persons in regular and frequent contact with high risk persons.
4. Household contacts of high-risk persons including elderly and the disabled.
5. Pregnant women who will be in their second or third trimester by the start of the influenza season.
6. When adequate vaccine supplies are available, vaccination of general public may be considered.

# Prevention and control strategies:

- People with respiratory infection symptoms should practice the following respiratory protection . All symptomatic people should:
  - 1. Avoid close contact (less than 1 meter) with other people.**
  - 2. Cover their nose and mouth when coughing or sneezing.**
  - 3. Use disposable tissues to contain respiratory secretions.**
  - 4. Immediately dispose off used tissues.**

# Cough etiquette

Respiratory etiquette

- Cover nose / mouth when coughing or sneezing
- Hand washing.





# Pandemic flu 2009 “H1N1” (Swine flu Or Pig flu)

## Introduction :

- It is a highly contagious respiratory disease in pigs.
- Caused by swine influenza A virus (H1N1).
- Transmission of virus from pigs to human is not common.
- People with regular contact to infected pigs increase risk of infection then after human to human transmission could occur.

## History :

- Swine influenza was first proposed to be a disease related to human influenza during 1918.
- 1976 U.S. out break in New-jersey, more than 200 cases with 1 death (soldier).
- The vaccine program was started on October 1, 1976, (GBS of 3 cases but not proved).
- Another out breaks in 1988, 1998 (US).

## 2009 out break in Human :

- **June 11, 2009 WHO declared onset of influenza pandemic.**
- **Globally: CFR 0.02 %.**
- **The most common cause of death is respiratory failure.**

**Reservoir** : swine.

**Mode of transmission:**

- The 2009 H1N1 virus is contagious and is spreading from human to human, like seasonal flu directly by cough, sneeze . Or indirectly by touching infected surface or object and then touching there mouth or nose.
- 2009 H1N1 not spread by food (pork), assumed properly handled and cooked.

# Prevention

## **Has three component:**

1. Prevention in swine by vaccination.
2. Prevention of pig to human transmission: mainly in farmers & vet. encouraged to use face mask and gloves.
3. Prevention of human to human transmission.

**Vaccination:** single dose of swine flu vaccine are available for human.

**Chemoprophylaxis:** oseltamivir, zanamivir.



## Treatment :

- 1- Majority of people make a full recovery without requiring medical attention or antiviral drugs.
- 2- Supportive care, relief pain, maintaining fluid balance and treatment of secondary infection.
- 3- **Specific treatment:**
  - Oseltamivir cap.
  - Or Zanamivir inhaled orally.

# Avian influenza (bird flu)



An unusually lethal virus with a history of jumping species.

## Avian influenza in birds

Avian influenza is an infection caused by avian (bird) influenza (flu) viruses. These influenza viruses occur naturally among birds.



## ***Human infection with avian influenza viruses***

There are 16 known HA subtypes and 9 known NA subtypes of influenza A viruses.

Many different combinations of HA and NA proteins are possible. Each combination represents a different subtype. All known subtypes of influenza A viruses can be found in birds.

# Avian Influenza A Virus Infections in Humans

- Although avian influenza A viruses usually do not infect humans, rare cases of human infection with avian influenza A viruses have been reported .
- Most human infections with avian influenza A viruses have occurred following direct or close contact with infected birds.
- Illness in humans has ranged from mild to severe.

- The spread of avian influenza A viruses from one ill person to another has been reported very rarely.
- However, because avian influenza A viruses have the potential to change and gain the ability to spread easily between people, monitoring for human infection and person-to-person transmission is extremely important for public health.

- Infected birds shed avian influenza virus in their saliva, mucous and feces. Human infections with bird flu viruses can happen when enough virus gets into a person's eyes, nose or mouth, or is inhaled.

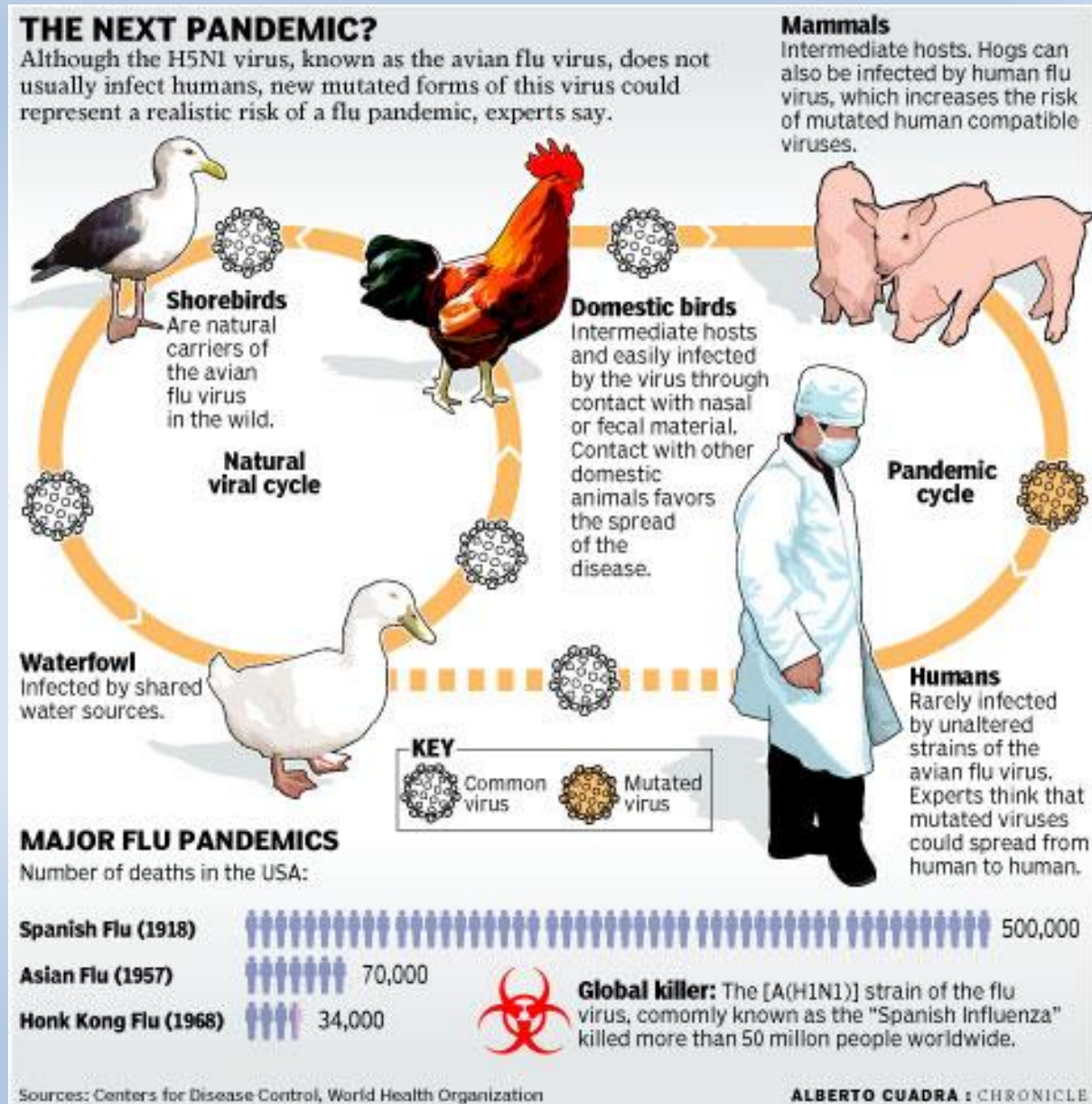
Infection with avian influenza viruses in domestic poultry causes two main forms of disease that are distinguished by low and high extremes of virulence

**“low pathogenic”**

**“highly pathogenic”** forms.

## Antigenic shift:

This mechanism produces a new subtype of influenza A v. through reassortment of the genetic material.



Despite the infection of tens of millions of poultry over large geographical areas for more than last 3-5 years, The total number of confirmed human cases of H5N1 reported till

**November 13, 2015 has reached 844 worldwide, 449 deaths (CFR = 59%).**

Most of them in Asia and the Middle East, and nearly all those who caught the virus were infected by handling or eating infected poultry.

***Cumulative number of confirmed human cases of Avian Influenza A(H5N1) :  
(2003 – 2015).***

Country	Total	
	cases	deaths
Azerbaijan	8	5
Cambodia	56	37
China	52	31
Djibouti	1	0
Egypt	346	116
Indonesia	199	167
Iraq (2006)	3	2
Lao People's Democratic Republic	2	2
Myanmar	1	0
Nigeria	1	1
Pakistan	3	1
Thailand	25	17
Turkey	12	4
Vietnam	127	64
<b>Total</b>	<b>844</b>	<b>449</b>

Source: [WHO](#)

**CFR = 59%**





# Warning signals of a pandemic

- Clusters of patients
  - Closely related in time & place
  - The detection of cases in health workers caring for H5N1 patients
- Indicates human to human transmission

Reservoir: Wild water fowl.

## Treatment and vaccination for H5N1 virus in humans:

- The H5N1 virus is resistant to amantadine and rimantadine.
- Two other antiviral medications: **Oseltamivir** (commercially known as **Tamiflu**) and **zanamivir** (commercially known as **Relenza**).

### *C. Epidemic Measures*

The current way to prevent the disease in animal population during epidemics is to destroy infected animals.

- a. Health education to avoid contact with sick or dead birds.
- b. Avoid poultry farms and bird markets.
- c. Avoid contact with any surface or substance appear to be contaminated with poultry feces or secretions.
- d. Frequent hand washing, and use alcohol based hand gels.
- e. Thorough cooking of all foods as poultry egg and meat.
- f. Persons with flu like symptoms, should visit doctor and stay away from contact with other people until prove that no H5N1 infection.

**THANK  
YOU**

