



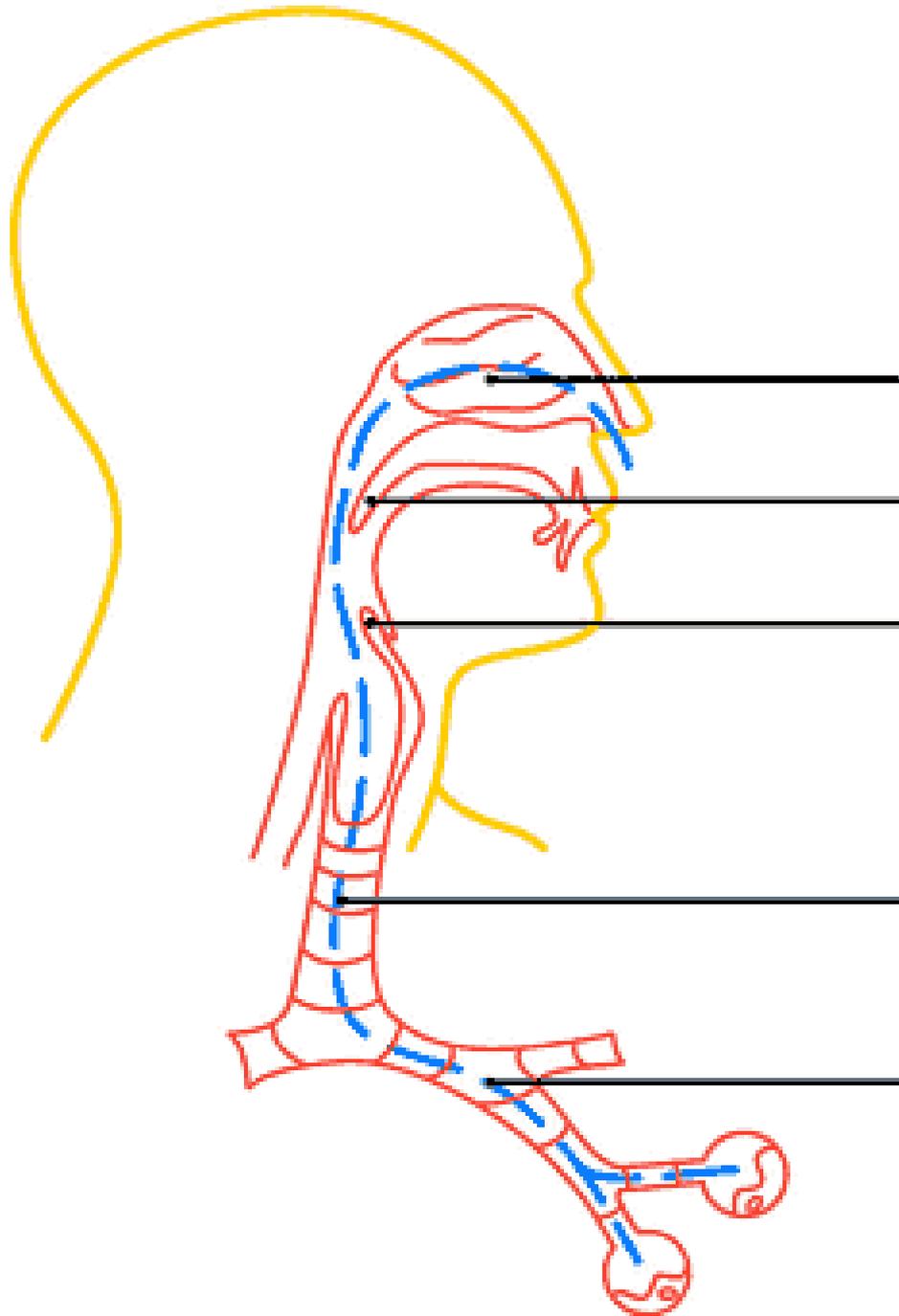
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CATARRHAL-RESPIRATORY SYNDROME IN CLINIC OF INFECTIOUS DISEASES

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CATARRHAL-RESPIRATORY SYNDROME

- inflammation of mucous membrane of respiratory tract with the hyper production of secret and activating of local protective reactions



Symptoms:
conjunctivitis
rhinitis,
pharyngitis,
tonsillitis,
laryngitis,
epiglottitis,
tracheitis,
bronchitis,
bronchiolitis,
pneumonia

Phases of catarrhal inflammation:

- **alteration** - necrosis of epithelium layers;
- **transsudation** – leakage of plasma with formation of serosal or serohemorrhagic exudate;
- **leukocyte infiltration** – suppurative transformation of exudate;
- **increase of mucin secretion** with appearance of viscid mucus;
- **regeneration of epithelial cells** and integrity of epithelial layer under the mucus cover

ACUTE RESPIRATORY INFECTIONS

group of polyetiologic infectious diseases, which characterized by likeness of clinical displays with the predominant affection of respiratory tract mucous membranes on a background of infectious toxicosis

ACTUALITY

- **70%** of infectious diseases (90% - in epidemic periods) and **83%** of total economic loss fall to share of Acute Respiratory Infections and Influenza.
- According to WHO data every habitant of a planet is annually suffer from Acute Respiratory Infections.

ETIOLOGY

VIRAL

- Influenza virus
- Parainfluenza virus
- Adenovirus
- Respiratory-syncytial virus
- Rhinovirus
- Reovirus
- Coronaviruses
- Enteroviruses

BACTERIAL

- Pneumococcus
- Staphylococcus
- Streptococcus
- Meningococcus
- Legionella
- Hemophilus influenzae B
- Chlamydia
- Mycoplasma

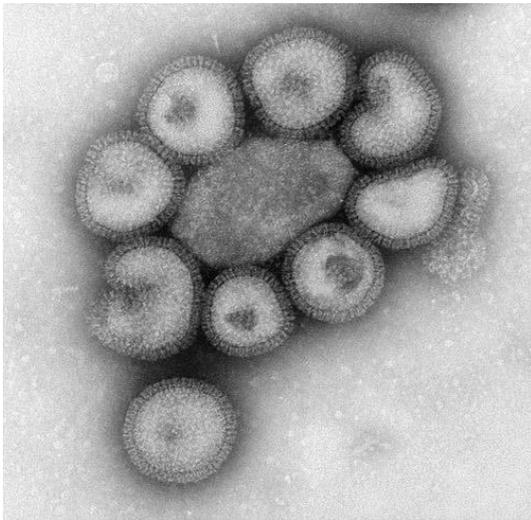
	conjunctivitis	rhinitis	pharyngitis	laryngitis	tracheitis	bronchitis	pneumonia
influenza	+	++	++	+	+++	+	+
adenoviral	+++	++	+++	+	+	+	
RS-viral		+	+			+++	+++
rinoviral		+++	+	+	+		
mycoplasmosis clamidiosis							+++
parainfluenza		+	+	+++			++
enteroviral		+	+/-	+/-			+/-

INFLUENZA (Grippe)

is an acute highly contagious and often epidemic viral disease caused by viruses of the family *Orthomyxoviridae* and characterized by abrupt onset, short course with symptoms of general intoxication and inflammation of the respiratory tract

ETIOLOGY

- The influenza viruses are **RNA** viruses of the family **Orthomyxoviridae**.
- The virus particle is **80-120 nanometers** in diameter and usually roughly spherical, although filamentous forms can occur.



Influenzavirus A

- Genus has one species ***influenza A virus***.
- Wild aquatic birds are the primary natural reservoir.
- Are found in many different animals, including **ducks, chickens, pigs, whales, horses, and seals**.
- The type A viruses are the most virulent human pathogens among the three influenza types and cause the most severe disease.

- The influenza A virus can be subdivided into different subtypes based on antibody responses to spike-like protein components on the surface of the virus - **haemagglutinin (H)** and **neuraminidase (N)**.
- There are **16 H** and **9 N** subtypes known in birds.
- The structure of these proteins differs from strain to strain due to rapid genetic mutation in the viral genome.

Subtypes that have been confirmed in humans

H1N1 - H1N2

H2N2

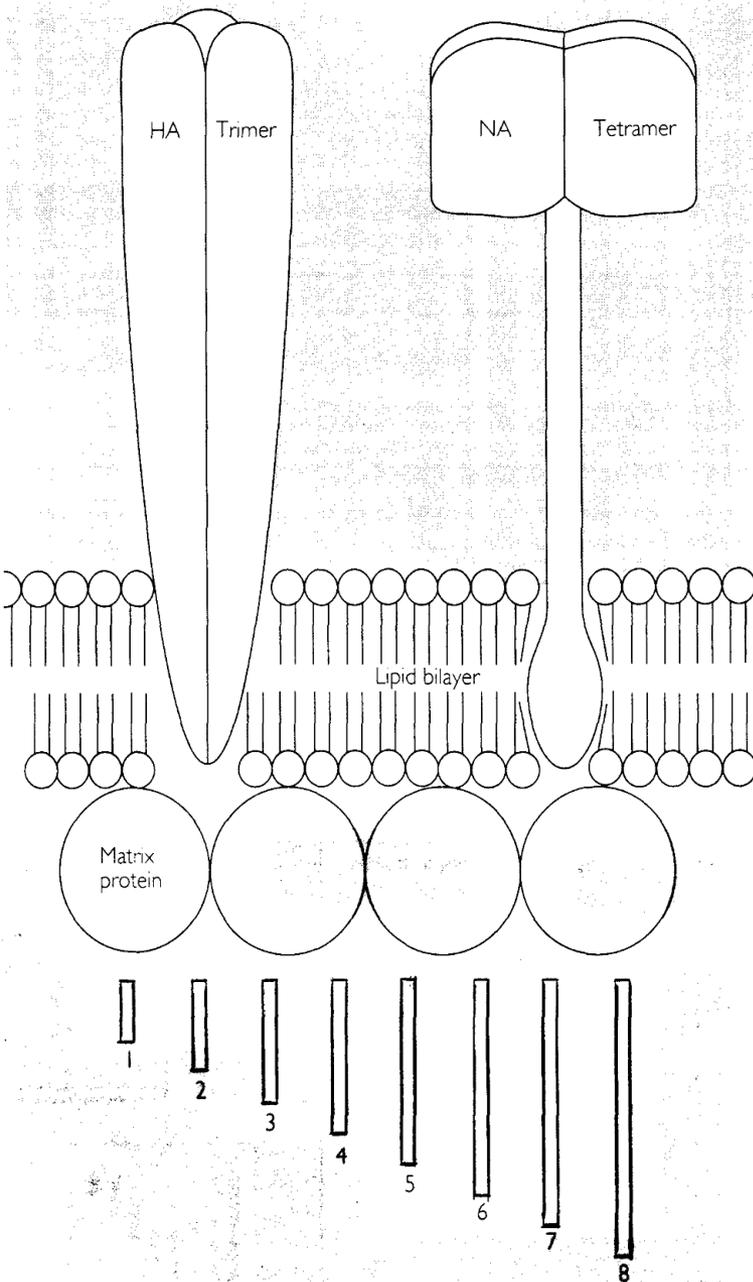
H3N2

H5N1 - H5N2

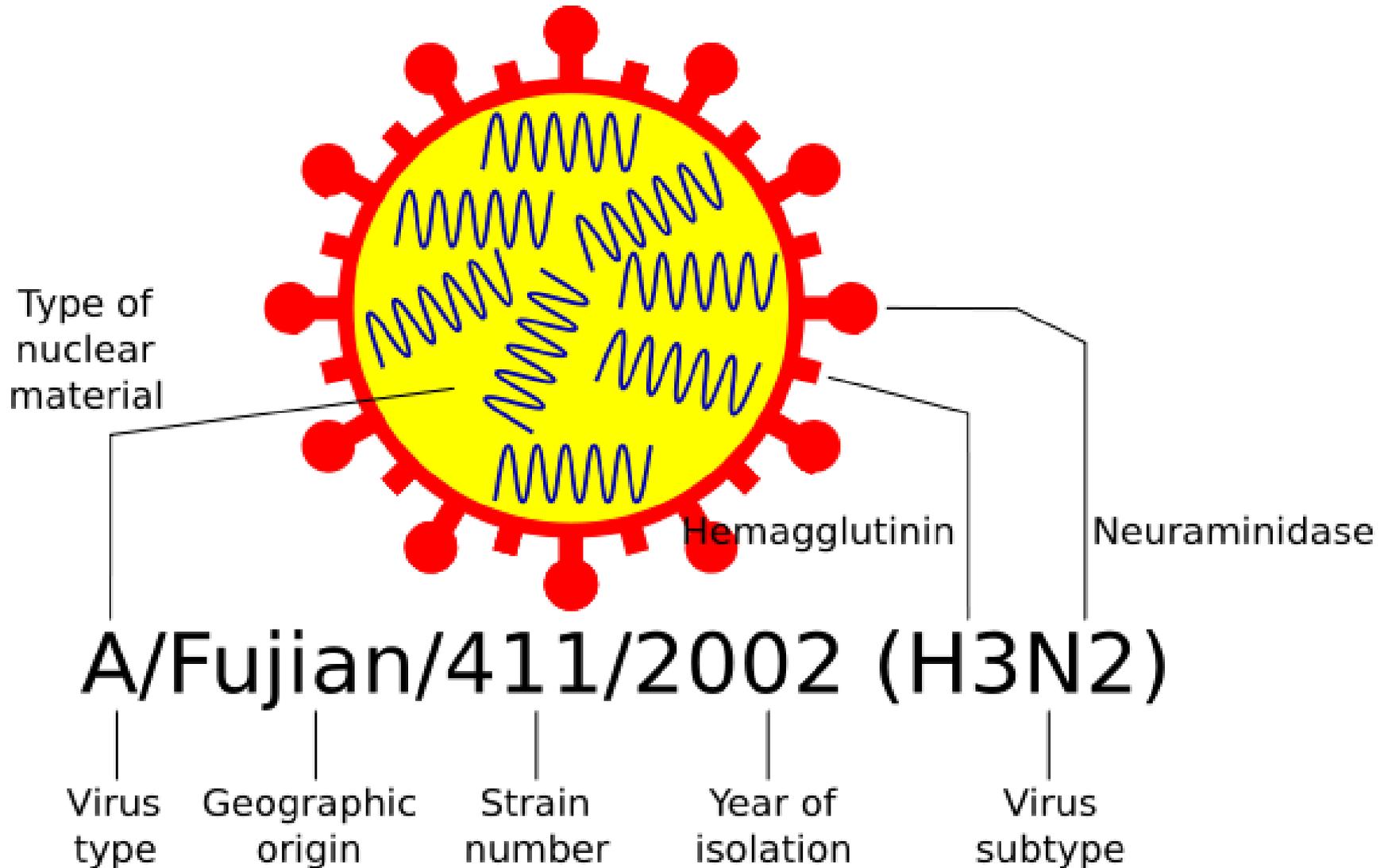
H7N2 - H7N3 - H7N7

H9N2

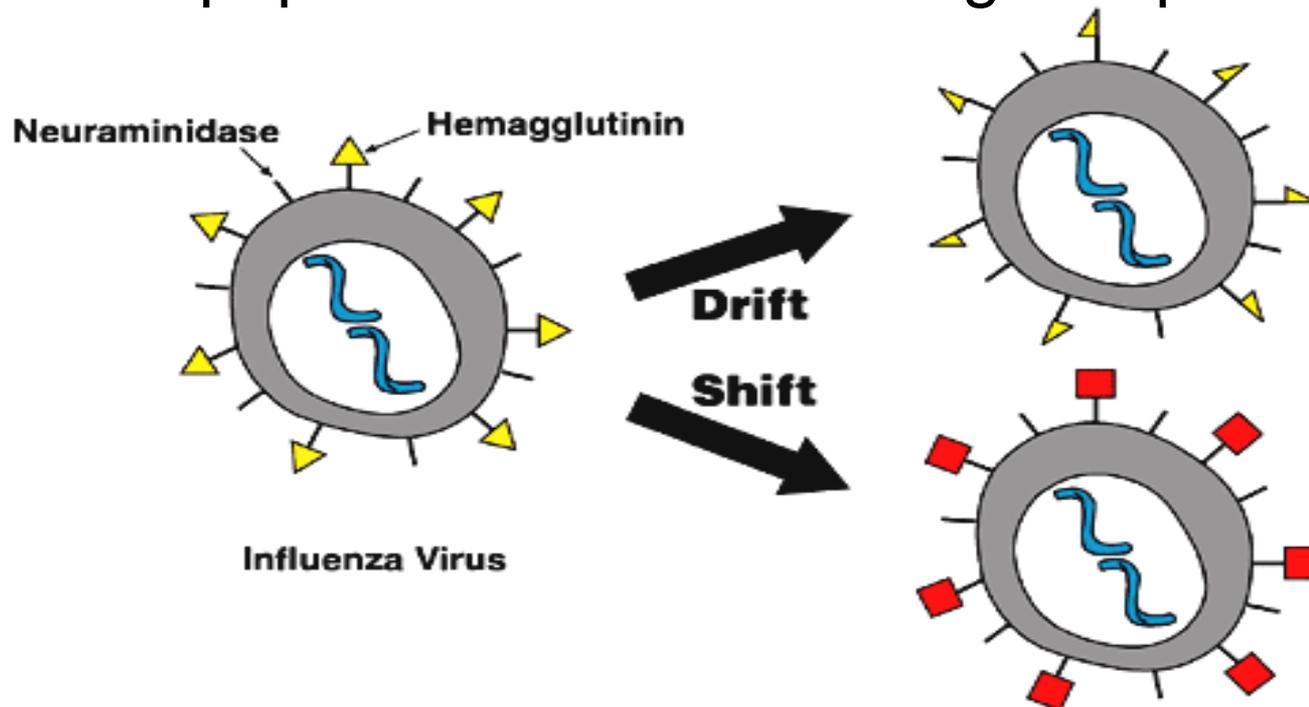
H10N7

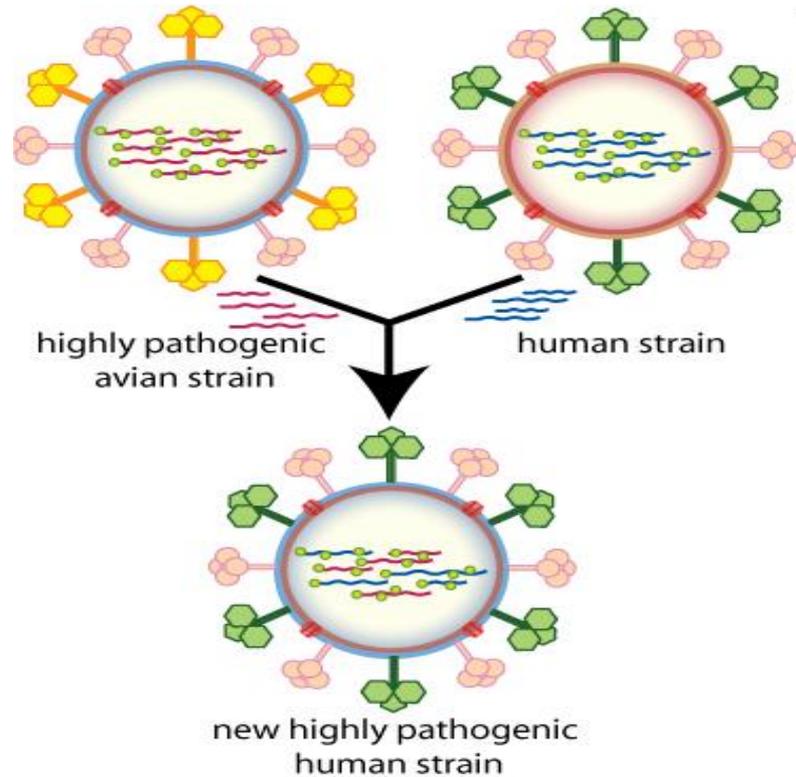


Influenza virus nomenclature



- **New influenza viruses are constantly being produced by mutation or by reassortment.**
- Mutations (**antigenic drift**) can cause small changes in H and N, creating an increasing variety of strains over time until one of the variants eventually achieves higher fitness, becomes dominant, and rapidly sweeps through the human population - often causing an epidemic.





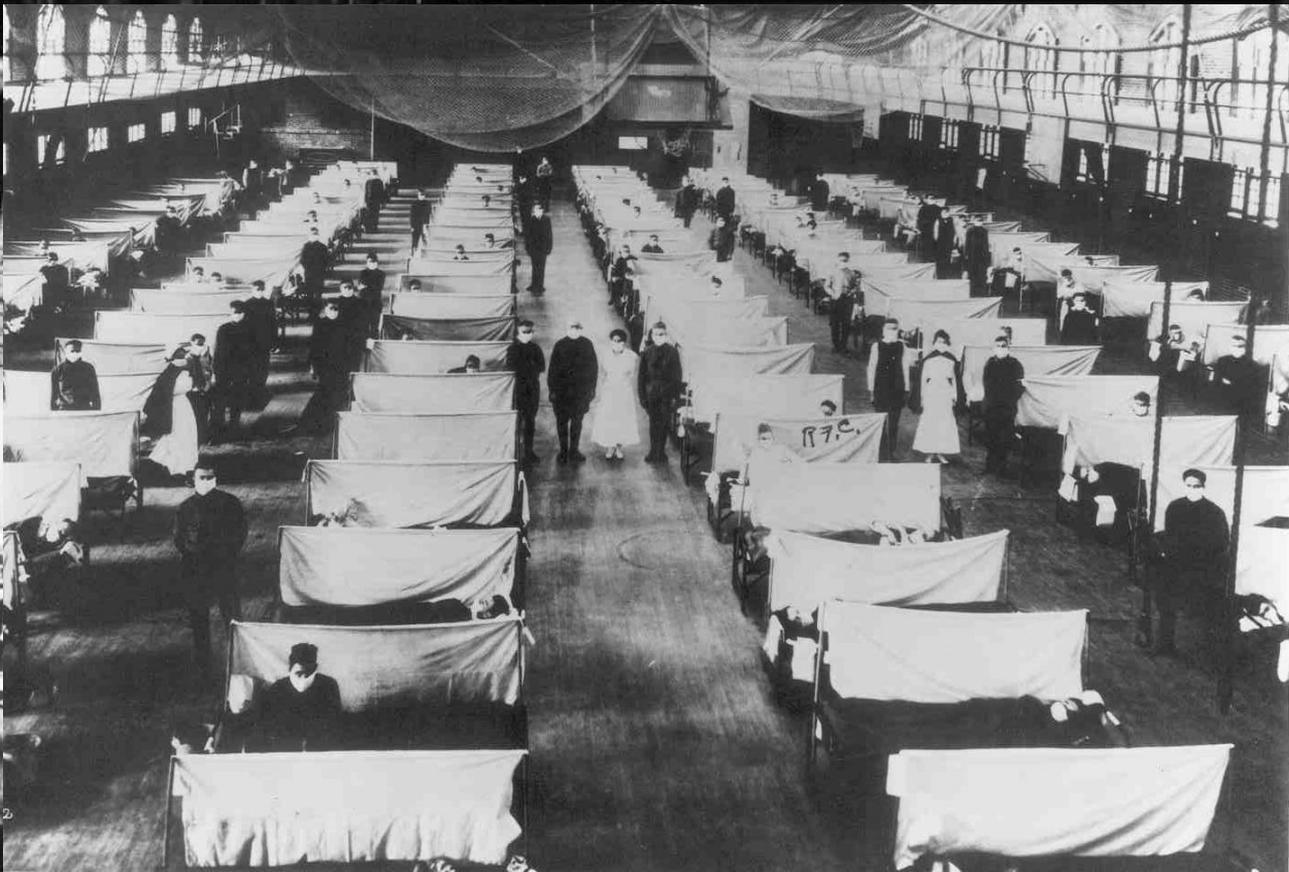
- When influenza viruses reassort (**antigenic shift**), they may acquire new antigens.
- If a human influenza **virus** is produced **with entirely novel antigens**, everybody will be susceptible, and the novel influenza will spread uncontrollably, **causing a pandemic**.

PANDEMIC INFLUENZA

- Every 10 to 30 years, a pandemic occurs, which infects a large proportion of the world's population.
- **1918 – 1919 “*Spanish influenza*” H1N1**
 - caused death of more than 50 million people
- **1957 – 1958 “*Asian influenza*” H2N2**
 - 1 to 1.5 million die
- **1968 – 1969 “*Hong Kong influenza*” H3N2**
 - 0.75 to 1 million die
- **1977 – 1978 “*Russian influenza*” H1N1**
- These new strains result from the spread of an existing virus to humans from other animal species.

“SPANISH INFLUENZA”

- It is estimated that **25-35%** of the world were infected, **2.5-5%** of the world's population was killed (**2-20%** of infected, in usual epidemic mortality rate of 0.1%).
- **Mostly killed young adults** (15-35 years), with 99% of pandemic influenza deaths occurring in people under 65, and more than 50% in young adults 20 to 40 years old (influenza is normally most deadly to children under age 2 and the very old over age 70).
 - Deaths from ARDS, secondary bacterial pneumonia
 - Deaths within 48 hours of illness



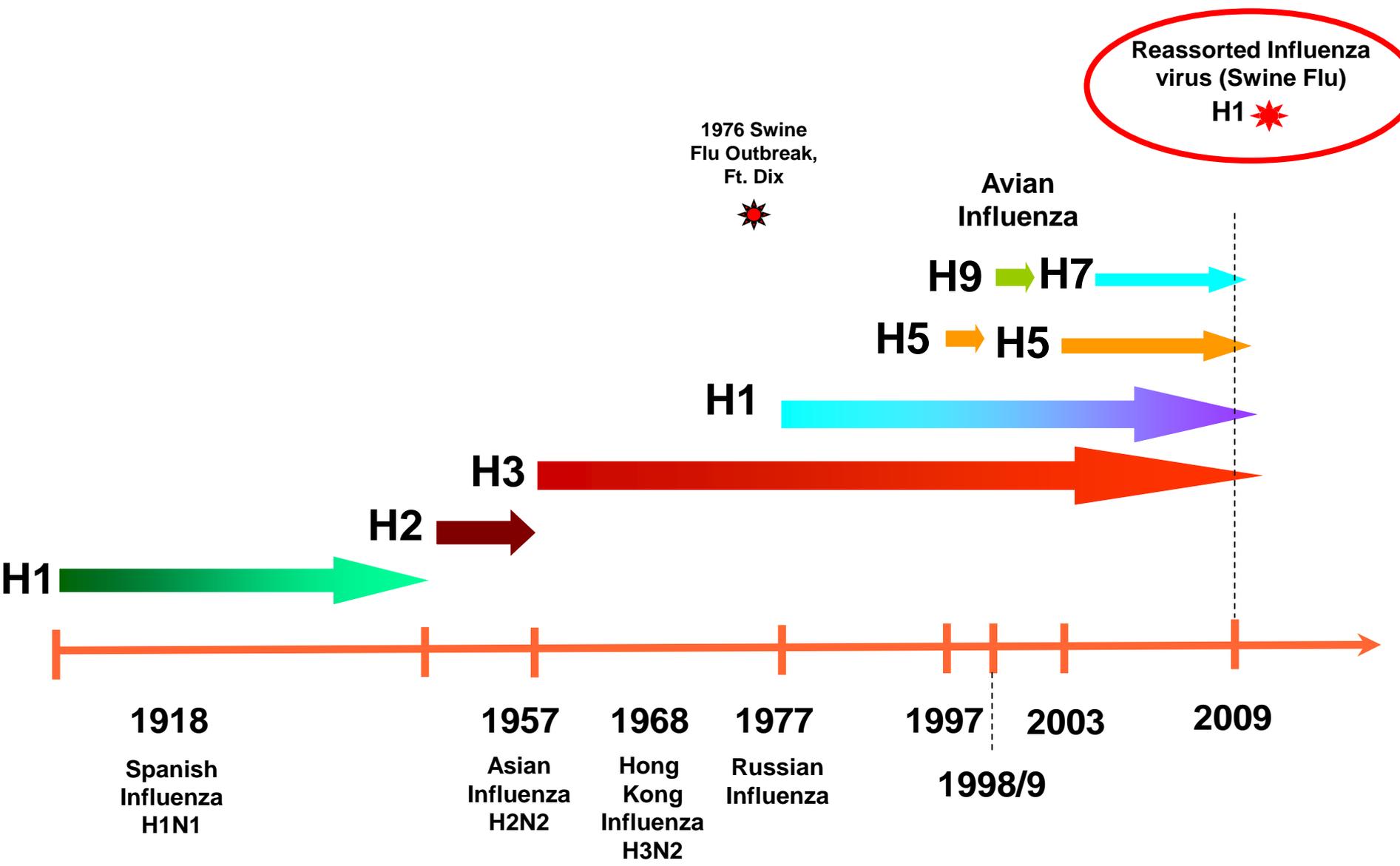
AVIAN INFLUENZA

- **1997** limited outbreaks of a new influenza subtype A (**H5N1**) directly transmitted from birds to humans have occurred in Hong Kong.
- From 20 September 2011 to 21 February 2012, 21 confirmed human cases of A(H5N1), 15 of which were fatal, were reported from Cambodia, China, Egypt, Indonesia, and Viet Nam.
- Since December 2003, a **total of 585 cases with 346 deaths** have been confirmed in 15 countries. **Mortality – 60%.**
- To date there has been no evidence of sustained human-to-human transmission.



SWINE FLU

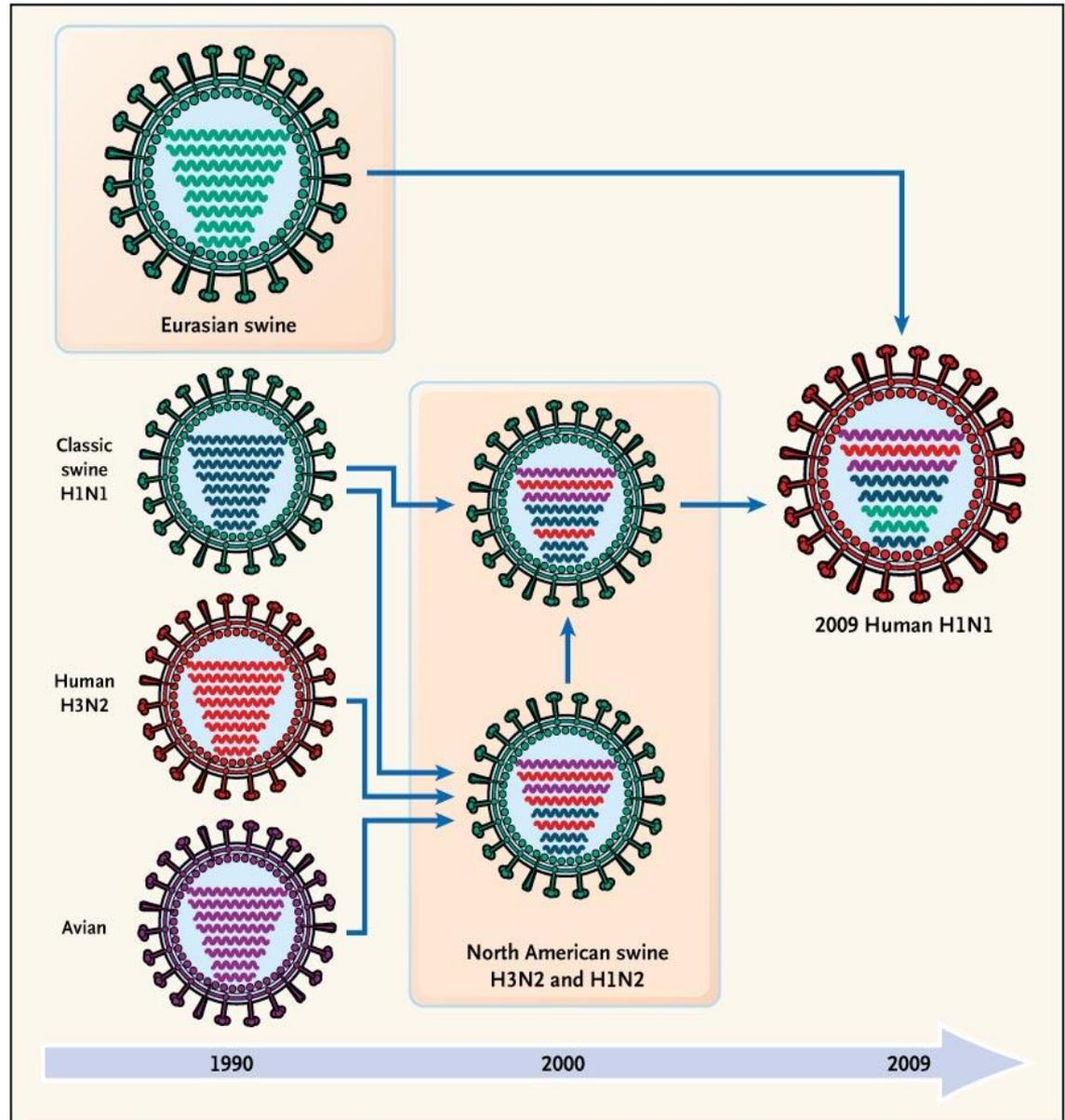
- New subtype of A/H1N1 not previously detected in swine or humans **A/California/04/2009 (H1N1)** was identified in April 2009. Primarily was a respiratory disease of pigs affecting human beings.
- In 2012 Influenza A(H1N1)pdm09 viruses circulated at very low levels in general.
- Regional activity was reported in some countries of Asia, Oceania and the Americas.
- Widespread activity was reported in Mexico.



A/California/04/2009 (H1N1)

The virus contains gene segments from 4 different influenza viruses:

- North American swine
- North American avian
- North American human
- Eurasian swine



Influenzavirus B

- Genus has one species, ***influenza B virus***.
- Influenza B almost exclusively infects humans and **is less common** than influenza A. The only other animal known to be susceptible to influenza B infection is the seal.
- This type of influenza mutates at a rate 2-3 times lower than type A and consequently is less genetically diverse, with **only one influenza B serotype**. As a result of this lack of antigenic diversity, a degree of immunity to influenza B is usually acquired at an early age.
- However, influenza B mutates enough that lasting immunity is not possible. This reduced rate of antigenic change, combined with its limited host range (inhibiting cross species antigenic shift), ensures that pandemics of influenza B do not occur.

Influenzavirus C

- Genus has one species, **influenza C virus**, which infects humans and pigs.
- Influenza C is less common than the other types and usually seems to cause mild disease in children.

- Viruses can remain infectious for about one week at human body temperature, over 30 days at 0°C, and for much longer periods at very low temperatures.
- **Hard non-porous surfaces 24-48 hours**
 - Plastic, stainless steel
 - Recoverable for > 24 hours
 - Transferable to hands up to 24 hours
 - **Porous surfaces 8-12 hours**
 - Cloth, paper & tissue
 - Recoverable for 8-12 hours
 - Transferable to hands 15 minutes
- **Water- 4 days at 22°C (30 days at 0°C)**
- **Viable on hands <5 minutes only at high viral titers**
 - **Potential for indirect contact transmission**
- Most influenza strains can be inactivated easily by disinfectants and detergents.

EPIDEMIOLOGY

- **Airborne:** person-to-person transmission of influenza virus occurs through the air **by droplets and small particles** excreted from the respiratory tract when infected individuals cough or sneeze.
- **Direct contact:**
 - Pigs/Bird to human
 - Contaminated environment (by fomites) to human
 - Non-sustained limited human-human (by hands contaminated with respiratory secretions and body fluids - diarrheal stool)
- The influenza virus enters the body through the nose, throat or conjunctiva.

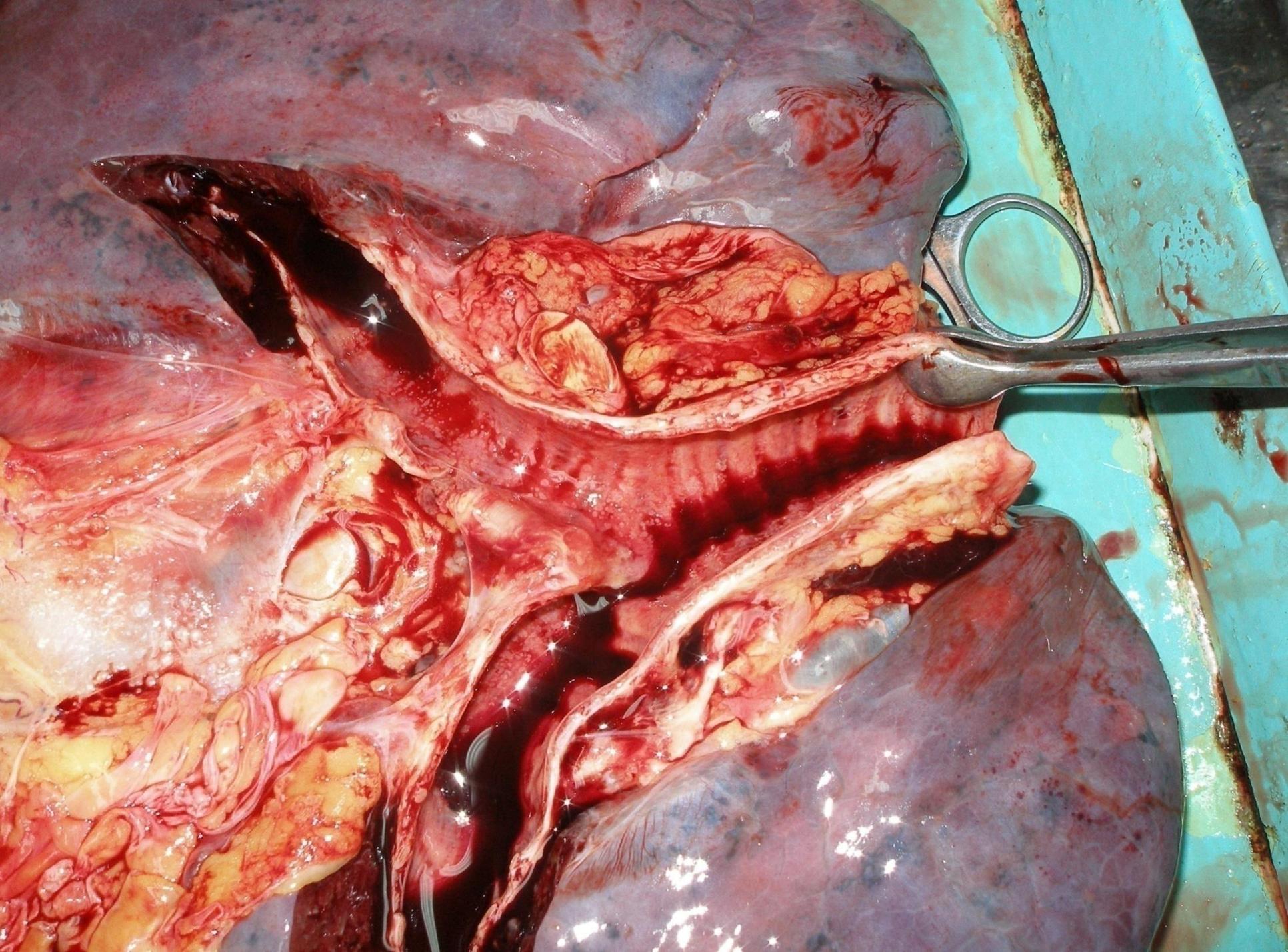
- Adults spread influenza to others during a period from **1 day before symptom onset to up to 7-10 days afterwards**. Children may have more prolonged viral shedding.
- A contributing factor is that **aerosol transmission of the virus is highest in cold environments** (less than 5°C) with low humidity, as a consequence, seasonal epidemics in the Northern and Southern Hemispheres occur almost exclusively during the winter months.

- **Influenza A** epidemics begin abruptly, peak over a 2- to 3-week period, generally last for 2 to 3 months, and often subside almost as rapidly as they began.
- **A major determinant** of the extent and severity of an outbreak **is the level of immunity** in the population at risk.
- With the emergence of an **antigenically novel influenza virus** to which little or no antibody is present in a community, **extensive outbreaks may occur**.
- When the **absence of antibody is worldwide**, epidemic disease may spread around the globe, **resulting in a pandemic**. Such pandemic waves can continue for several years, until immunity in the population reaches a high level.

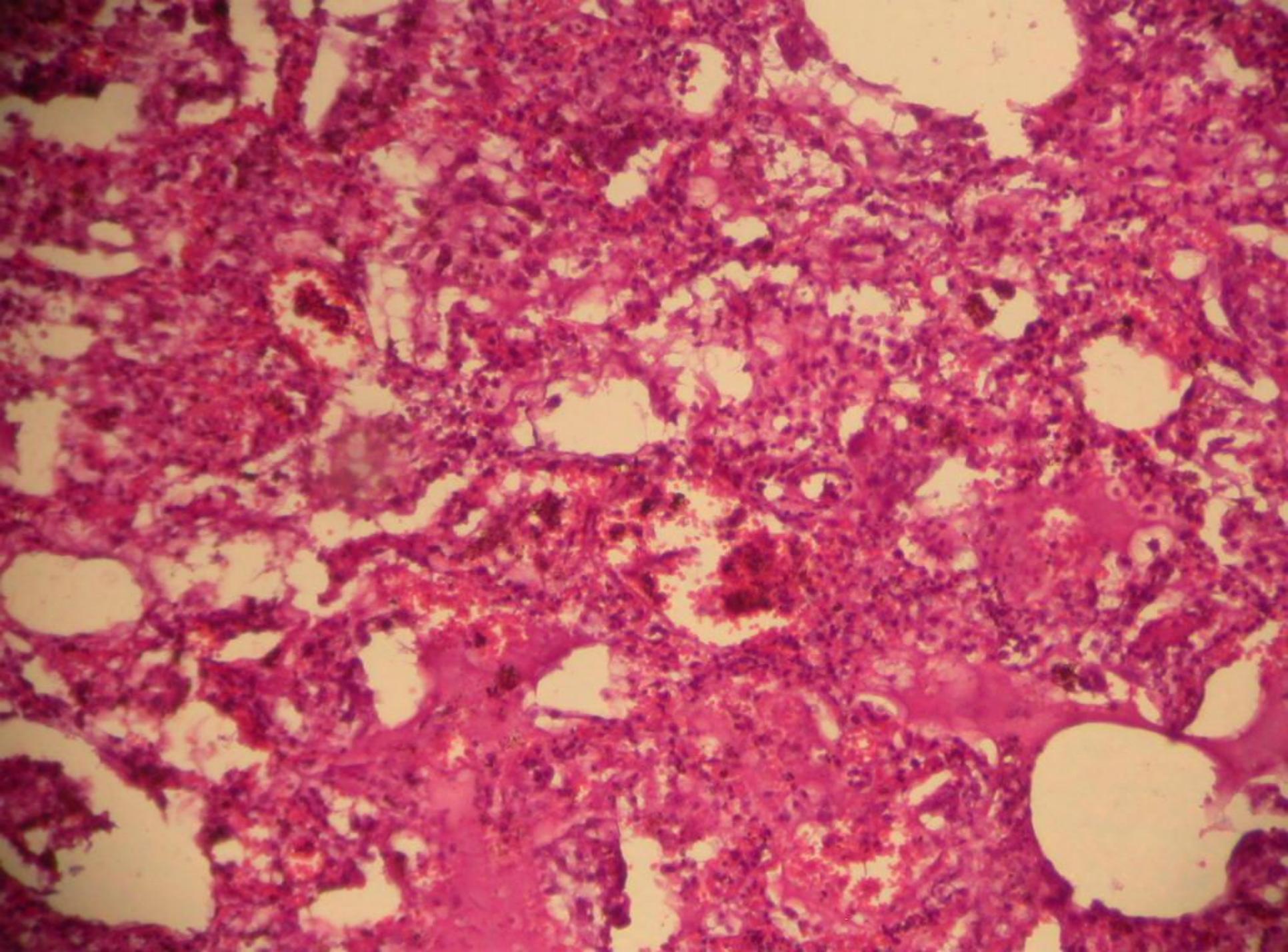
- **Influenza B** virus causes **outbreaks** that are generally **less extensive** and are associated with **less severe disease** than those caused by influenza A virus. Influenza B outbreaks are seen most frequently **in schools and military camps**, although outbreaks **in institutions** in which elderly individuals reside also have been noted on occasion.
- **Influenza C** virus has been only infrequently associated with human disease, although the wide prevalence of serum antibody to this virus indicates that **asymptomatic infection may be common**.

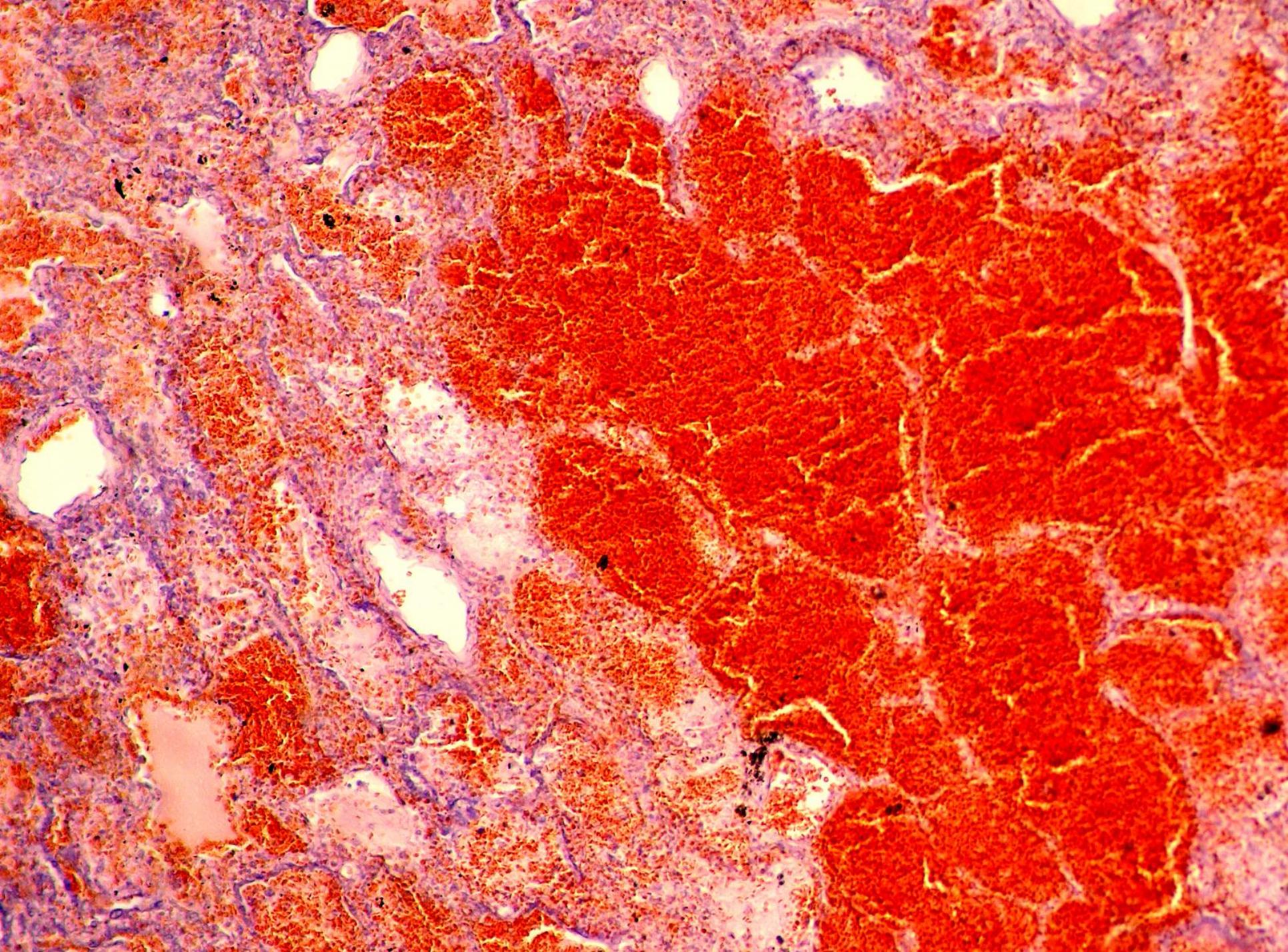
PATHOGENESIS

- **Invasion of virus in the epithelium of upper respiratory tract.**
- **Replication of virus.**
- **Virusemia.**
- **Toxic and toxic allergic reactions.**
- **Lesions of respiratory tract.**
- **Dyscirculatory vascular disorders.**
- **Bacterial complications.**
- **Immune reactions.**









Clinical classification

- **Typical influenza:**

- Intoxication syndrome
- Respiratory syndrome
- Hemorrhagic syndrome
- Neurological syndrome

- **Atypical influenza:**

- Afebrile
- Acatarrhal

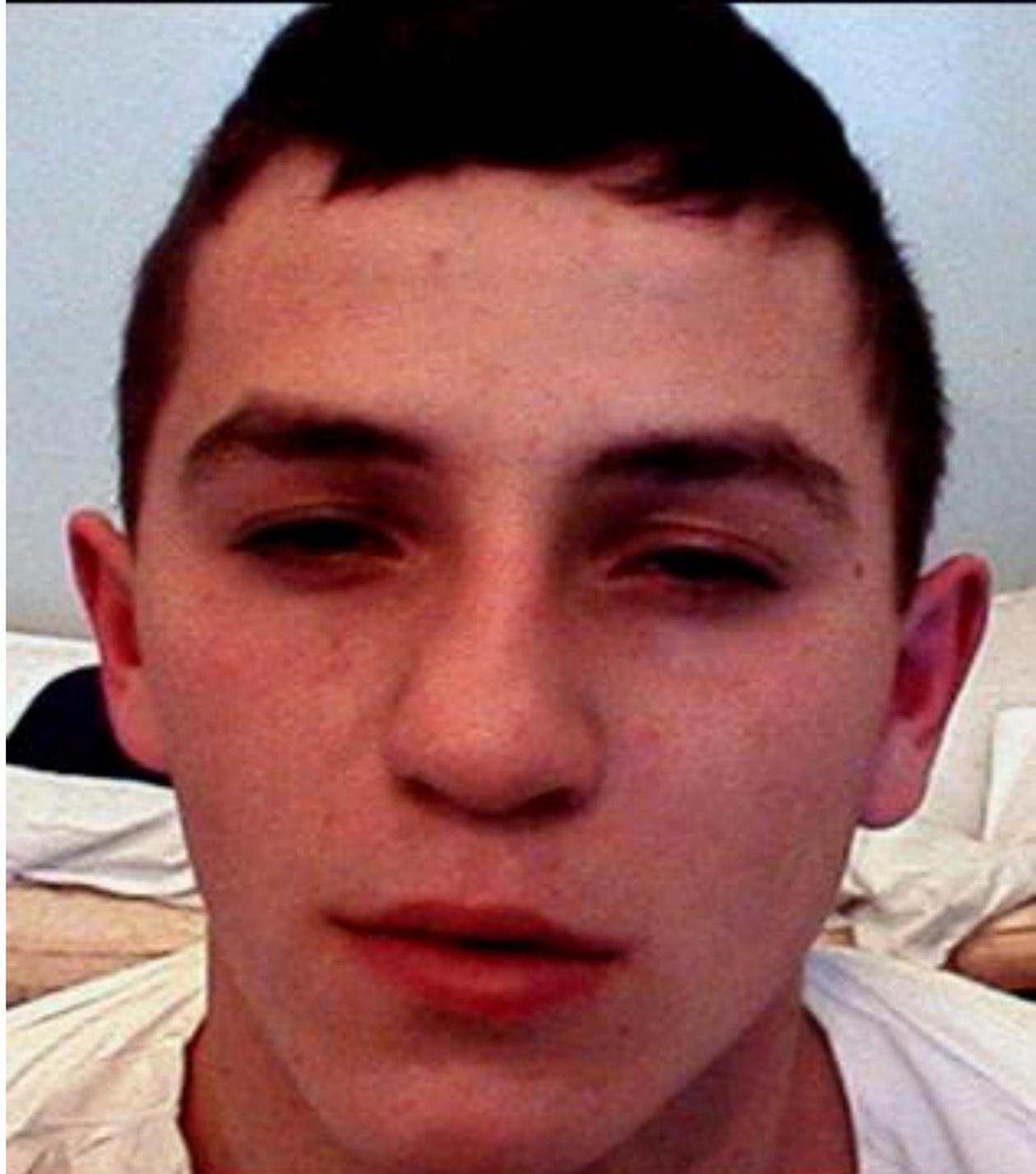
- **By severity:**

- Mild
- Moderate
- Severe
- Hypertoxic

Manifestations

- **Incubation period:** 1 - 2 days.
- **Abrupt onset:**
 - Extreme chills (true rigors are rare) and fever of 38 to 41°C
 - Malaise, fatigue
 - Myalgias (involve any part of the body but are most common in the legs and lumbosacral area), arthralgias
 - Headache (generalized or frontal)
 - Abdominal pain (in children with influenza B)
 - Coughing and sneezing
 - Sore throat

- Pain on motion of the eyes, photophobia, and burning of the eyes (Irritated watering).
- Reddened skin (especially face)
- Nasal congestion



- Respiratory complaints often become more prominent as systemic symptoms subside. **Cough** is often accompanied by **substernal discomfort**.
- Examination of the pharynx: **injection of the mucous membranes and postnasal discharge**.
- **Mild cervical lymphadenopathy** may be noted, particularly in younger individuals.
- The results of chest examination are largely negative in uncomplicated influenza, although **rhonchial, wheezes, and scattered rales** may be found under auscultation.
- Frank dyspnea, hyperpnea, cyanosis, diffuse rales, and signs of consolidation are indicative of **pulmonary complications**.
- In uncomplicated influenza, the acute illness generally resolves over a 2- to 5-day period, and most patients have largely recovered in 1 week. In a significant minority (particularly the elderly), however, symptoms of weakness or lassitude (**postinfluenzal asthenia**) may persist for several weeks.

Criteria of severity

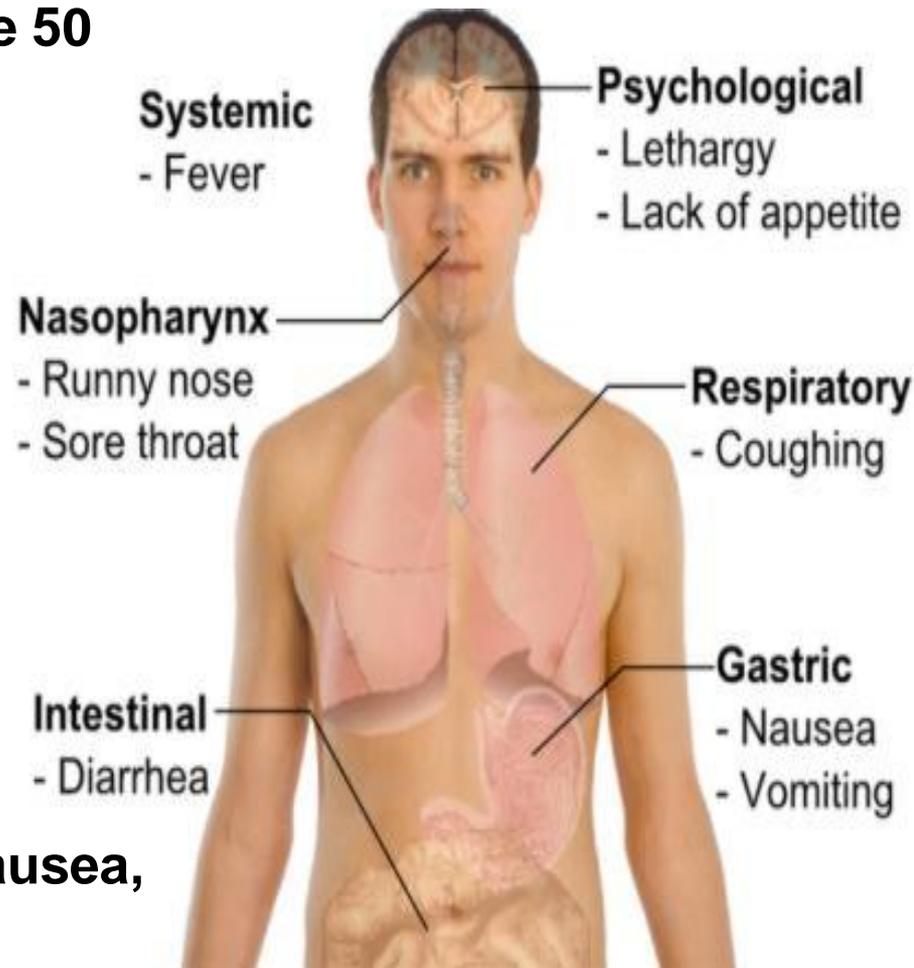
- **Mild** – 1-3-d increase of T°C up to 38°C, moderate headache, early appearance of catarrhal symptoms. The symptoms of general intoxication and tracheobronchitis are expressed poorly. PS < 90. BP 115-120 mmHg. RR < 24.
- **Moderate** – T°C – 38,1 - 40°C. Moderate expressed syndrome of general intoxication. Expressed intoxication and lesions of the respiratory system. Fever lasts 4-5 days. PS 90-120. BP < 110 mmHg. RR > 24. Dry painful cough, pain under breastbone.

- **Severe** – T°C of body more > 40°, protracted fever with the sharply expressed symptoms of intoxication (severe headache, adynamia, dizziness, insomnia or somnolence, delirium, hallucinations, anorexia, nausea, vomiting, cramps, loss of consciousness, meningeal signs, encephalitic syndrome). Often hemorrhagic displays. Skin is greyish-pale, acrocyanosis. PS > 120, weak, arrhythmical. BP < 90 mmHg. The shortness of breath is marked. RR > 28, painful cough, pain under breastbone. Different complications.

- **Hypertoxic** – fulminate developing symptoms of intoxication, toxic shock without the catarrhal symptoms. T°C of body does not serve as a criteria of severity. On the first plan are displays of vascular insufficiency, acute meningoencephalitis (cerebral edema), acute respiratory insufficiency (hemorrhagic pulmonary edema), acute cardiac insufficiency. Death through a few hours from the moment of appearance of the first signs of illness.

Symptoms of swine/avian flu

- Incubation period: 1 - 7 days
- Severe disease in adults under age 50
- Chills and fatigue
- Headache
- Body aches
- Anorexia
- Fever >39.5 C
- Moderate conjunctivitis
- Nasal secretions
- Sore throat
- Barking-like cough
- Laboured breathing
- Sometimes abdominal pains, nausea, vomiting, diarrhea
- Nephritis (often necrotizing) with kidney insufficiency



LABORATORY FINDINGS:

- Leucopenia, lymphopenia
- Mild to moderate thrombocytopenia
- Elevated aminotransferases
- Hypoalbuminemia

Complications

- Toxic shock
- Acute respiratory distress syndrome requiring mechanical ventilation
- Pneumonia progresses to respiratory failure
- Otitis and sinusitis
- Exacerbation of underlying chronic medical conditions
- Multi-organ failure
- Cardiac and renal dysfunction
- Gastrointestinal involvement
- Croup (in children)
- Reye's syndrome (in children)
- Sepsis-like syndrome
- Myocarditis and pericarditis (infrequently)
- Encephalitis, transverse myelitis, Guillain-Barre syndrome, meningitis, myositis, rhabdomyolysis, acute and post-infectious encephalopathy, febrile seizures and status epilepticus.



SP-CR

156375
10-JUL-1946
15-APR-1997
13 28 45.79

H-SP-CR

R



100

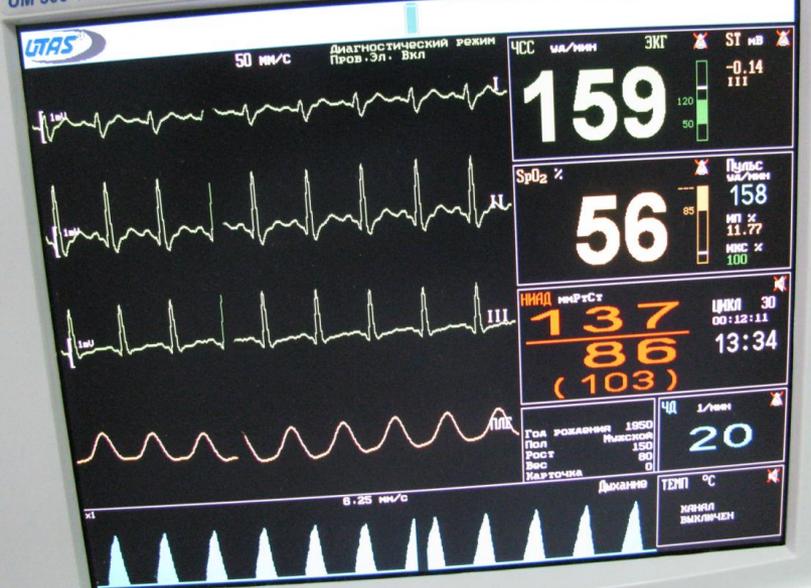
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1563/5
10-JUL-1946
15-APR-1997
13:29:54.31

SO-ARTOM PLUS 4
H-SP-CR

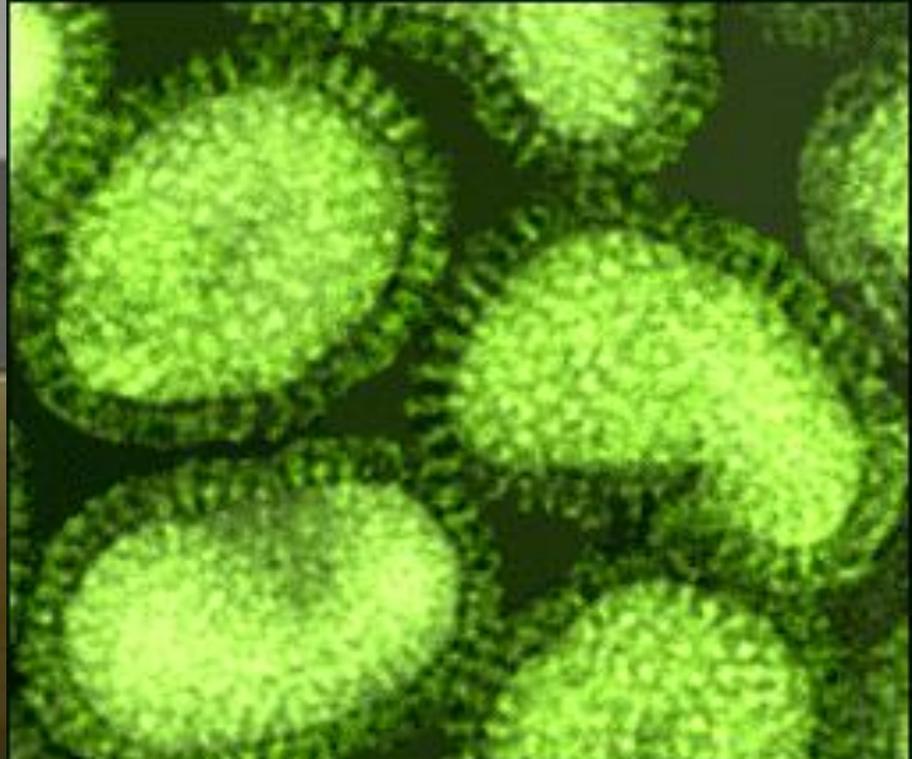
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Diagnosis

- Laboratory diagnosis is accomplished by isolation of the virus from throat swabs, nasopharyngeal washes, or sputum.
- Virus usually is detected in **tissue culture** or less commonly is found in the **amniotic cavity of chick embryos** within 48 to 72 h after inoculation.
- Viral antigens may be detected by **immunofluorescence (IFA), Immunochromatographic assay**
- **Indirect hemagglutination (IHA) or Complement fixation (CF) test** for diagnosis require comparison of antibody titers in sera obtained during the acute illness with those in sera obtained 10 to 14 days after the onset of illness and are useful primarily in retrospect. Fourfold or greater titer rises are diagnostic of acute infection.
- **ELISA, Western blot**
- **RT-PCR, Real-time RT-PCR, NASBA, RT-LAMP**



BSL-2 laboratory

- Diagnostic work on clinical samples from patients who are suspected cases of swine/avian influenza should be conducted in a **BSL-2 laboratory**
 - All sample manipulations should be done inside a **biosafety cabinet (BSC)**
- Viral isolation on clinical specimens from patients who are suspected cases of swine/avian influenza should be performed in a BSL-2 laboratory with BSL-3 practices (enhanced BSL-2 conditions)
- **Additional precautions include:**
 - recommended personal protective equipment (based on site specific risk assessment)
 - respiratory protection - N95 respirator or higher level of protection
 - shoe covers
 - closed-front gown
 - double gloves
 - eye protection (goggles or face shields)

3M N95 filtering facepiece respirator (8612F, 8670F)



Treatment

- Bed rest, drink plenty of liquids
- Paracetamol (acetaminophen) for the relief of headache, myalgia, and fever (**use of salicylates - 'aspirin' is contraindicated**)
- **Cough suppressants** (codeine-containing compounds) **are not indicated because of alveolar flooding**
- Specific antiviral therapy:
 - **Amantadine and rimantadine are not effective**
 - Ribavirin (effective against both influenza A and B virus when administered as an aerosol)
 - **Tamiflu (oseltamivir) or Relenza (zanamivir)**
- Antibacterial drugs should be reserved for the therapy of bacterial complications

	Oseltamivir (Tamiflu)		Zanamivir (Relenza)	
	Treatment	Prophylaxis	Treatment	Prophylaxis
Adults	75 mg capsule twice per day for 5 days	75 mg capsule once per day	Two 5 mg inhalations (10 mg total) twice per day	Two 5 mg inhalations (10 mg total) once per day
Children	15 kg or less: 60 mg per day divided into 2 doses	30 mg once per day	Two 5 mg inhalations (10 mg total) twice per day (age, 7 years or older)	Two 5 mg inhalations (10 mg total) once per day (age, 5 years or older)
	15–23 kg: 90 mg per day divided into 2 doses	45 mg once per day		
	24–40 kg: 120 mg per day divided into 2 doses	60 mg once per day		
	>40 kg: 150 mg per day divided into 2 doses	75 mg once per day		

Dosing recommendations for antiviral treatment of children younger than 1 year using oseltamivir. Recommended treatment dose for 5 days. <3 months: 12 mg twice daily; 3-5 months: 20 mg twice daily; 6-11 months: 25 mg twice daily

Dosing recommendations for antiviral chemoprophylaxis of children younger than 1 year using oseltamivir. Recommended prophylaxis dose for 10 days. <3 months: Not recommended unless situation judged critical due to limited data on use in this age group; 3-5 months: 20 mg once daily; 6-11 months: 25 mg once daily




oseltamivir phosphate 



peramivir and laninamivir

PREVENTION

- **Immunization** is the most effective measure for preventing influenza and reducing the impact of epidemics
- **Pre- and Post-exposure chemoprophylaxis**
- **Personal Protective Equipments** while treating suspected case of HPAI H5N1
 - N95 respirator
 - Eye protection (goggles or eye shield)
 - Non sterile gloves and gown while going closer to the patients.

- The organism of a healthy human acquires **full immunity already 7–10 days after vaccination**. Immunity is maintained for up to 12 months.
- Based on information of 112 National Influenza Centres in 83 countries responsible for monitoring the influenza viruses circulating in humans and rapidly identifying new strains, **WHO recommends annually a vaccine that targets the 3 most virulent strains in circulation**.
- Typically, this vaccine includes material **from two influenza A virus subtypes and one influenza B virus strain**. A vaccine formulated for one year may be ineffective in the following year, since the influenza virus changes rapidly over time, and different strains become dominant.

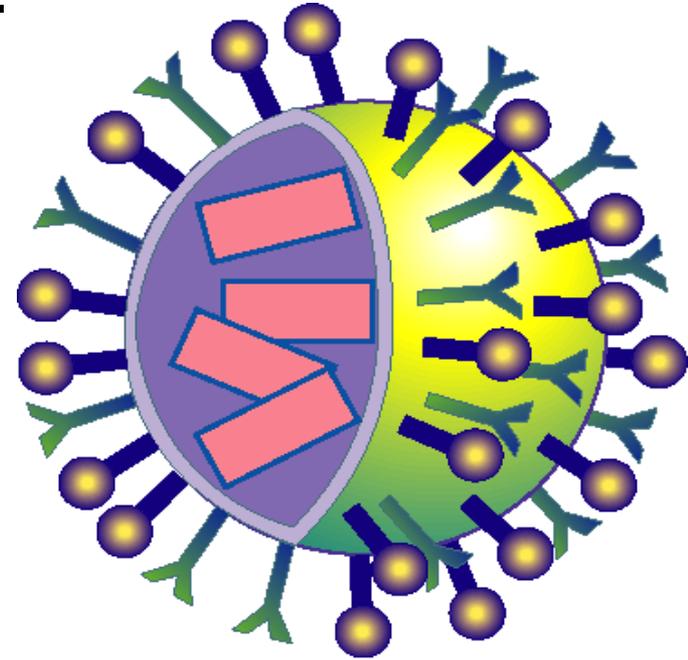
It is recommended that vaccines for
use in the **2012-2013** influenza
season
(northern hemisphere winter)
contain the following:

A/California/7/2009 (H1N1)pdm09;
A/Victoria/361/2011 (H3N2);
B/Wisconsin/1/2010

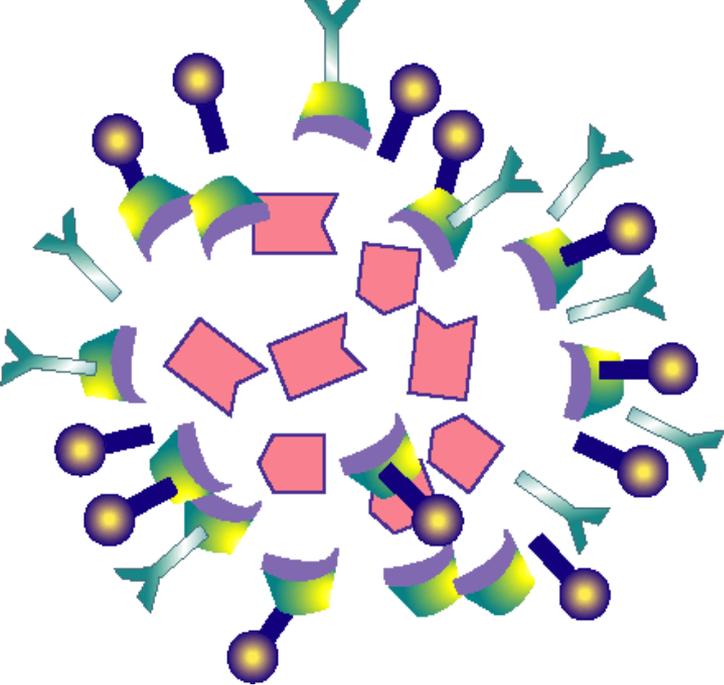
- **Who should get the influenza vaccine**
 - Anyone 50 years of age or older
 - Children 6 months to 5 years of age
 - Residents of long-term care facilities
 - Adults and children who are 6 months of age or older and who have diabetes, a chronic heart or lung disorder, kidney failure, certain blood disorders, or a weakened immune system
 - Family members and caregivers of people in the above groups
 - Family members and caregivers of children less than 6 months of age
 - Doctors and health care workers
 - All pregnant women
 - Children who are younger than 18 years of age and regularly take aspirin (who are at risk of Reye's syndrome if they develop influenza)

- **Who should not get the influenza vaccine**
 - People with a severe allergy to eggs
 - People who have had a severe reaction to an influenza vaccination in the past
 - People who have had Guillain-Barré syndrome
 - People who currently have a disorder that causes fever (other than a mild cold)

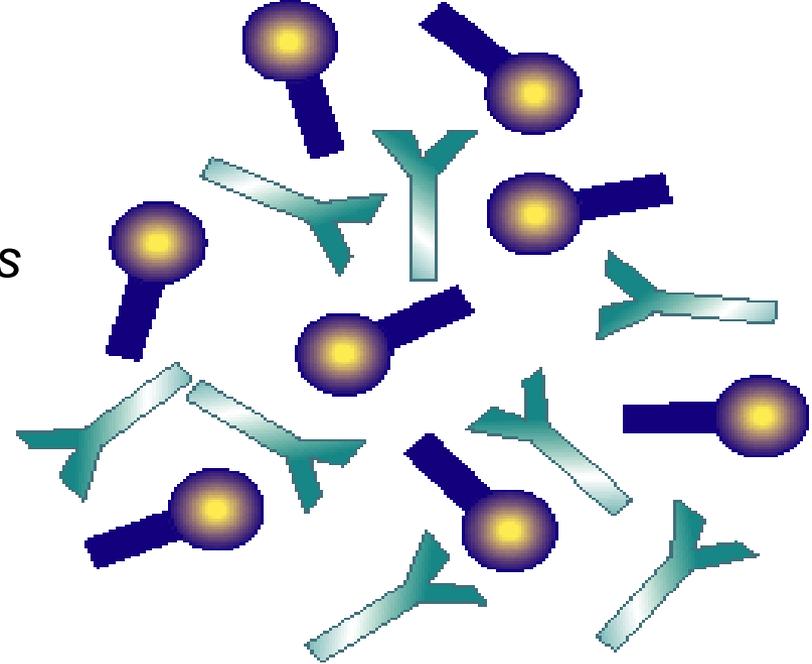
- There are two kinds of influenza vaccines:
- The nasal vaccine is known by the trade name of **FluMist**. It contains weakened, live viruses, and is sprayed into both nostrils.



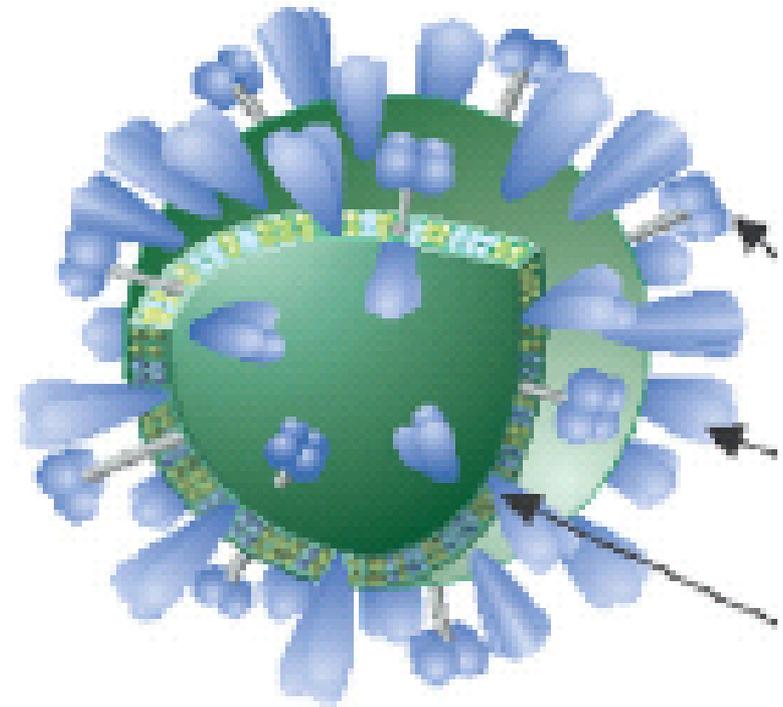
- The flu shot contains inactivated, or killed, influenza viruses.



SUBUNIT
Influvac
solvay
pharmaceuticals
(Netherlands)



SPLIT
Fluarix
glaxosmithkline
biologicals
(Germany)
Vaxigripp
sanofi pasteur
(France)



VIROSOMAL
Inflexal V
berna biotech ltd.
(Switzerland)

PREVENTION IS BETTER THAN CURE

