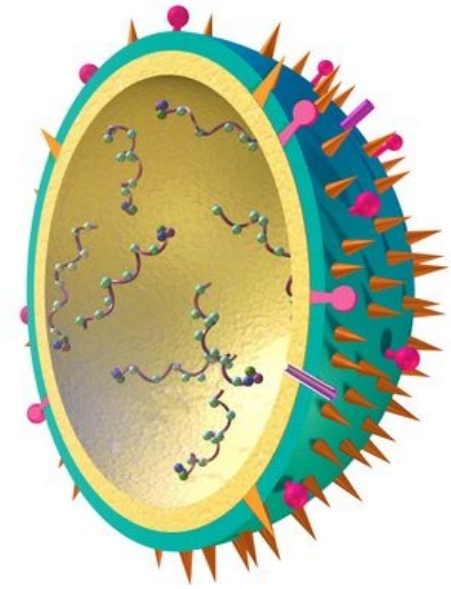
Flu

Influenza is *a* highly infectious disease of viral etiology that primarily affects the airways.



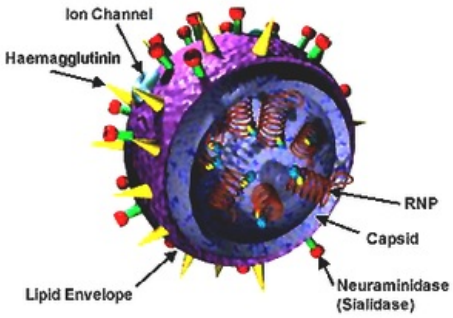
Influenza virus structure

Influenza is caused by two types of RNA viruses from the *Orthomyxoviridae* family : *Myxovirus influenzae* type A and B (there is also *type C* , which forms a special genus).

Not only humans but also other mammals (pigs, horses, some marine mammals) and birds are susceptible to influenza.

Influenza virus is a pleomorphic particle of spherical or fibrous shape. The viral RNA is stored in a helicoid capsid, the nucleocapsid is enveloped by a lipid membrane. Replication takes place (unlike other RNA viruses) in the nucleus. The virus has two surface (species and subtype specific) antigens (glycoproteins):

- hemagglutinin (H, mediates that the virus sticks to the cell, membranes fuse);
- neuraminidase (N, reduces the viscosity of the mucus).



These surface antigens are the main sources of the pathogenicity of the virus, as they facilitate its multiplication. Nucleocapsid (NP) protein and membrane protein (MP) are species specific and relatively invariant. To date, 16 types of influenza A virus hemagglutinin (6 in humans) and 9 types of neuraminidase (2 in humans) have been identified . Individual types are further divided into subtypes. The mutual composition of these antigens (or their variants) creates various (even new) genetic mutations that can cause an epidemic in a population of susceptible individuals. They also determine the danger of the disease (infectivity and course).

The virus replicates in the ciliated epithelium of the airways. Influenza virus

Influenza virus mutations

Influenza has a segmented genome consisting of 7 (type C) or 8 (type A and B) ribonucleic acid segments, so point mutations and amino acid sequence changes are possible . According to the extent, we divide antigen changes into drifts and shifts . Mutations provide the influenza virus with greater success in infecting the body.

Antigen drift

Changes in antigenic structure in influenza It arises from the selection pressure of the growing immunity of the population in relation to already existing forms. There are point mutations in the virus and single amino acid substitutions. It means a smaller change in the antigenic characteristics of the virus. The resulting subtypes are the cause of recurring small epidemics in two- to three-year cycles, which allows the reinfection of people who have already contracted the disease. It occurs in influenza A and B.

Antigen shift (break)

It is a more severe type of antigen change and is caused by genetic recombination between human and animal viruses . There is a significant change in one or both antigens, and a virtually new type of virus is emerging that is responsible for large-scale pandemics affecting all age groups. This change occurs after 10 or more years. Antigenic shifting occurs only with influenza A viruses . The reservoir of new antigenic types of influenza A are mainly birds and pigs . New combinations of the virus are very dangerous, usually causing more serious forms of the disease, and are spreading rapidly in susceptible human populations (especially in large, high-density cities).

Influenza B causes disease only in humans, drift changes are rare and pandemics do not. It can also occur with a predominance of gastrointestinal disorders such as the so-called intestinal flu.

Type C only causes sporadic diseases. It is pathogenic for both humans and animals, but only rarely for animals, and small children are a sensitive group in humans, the course is very mild, it does not cause epidemics or pandemics. It most often occurs as a so-called cold disease.

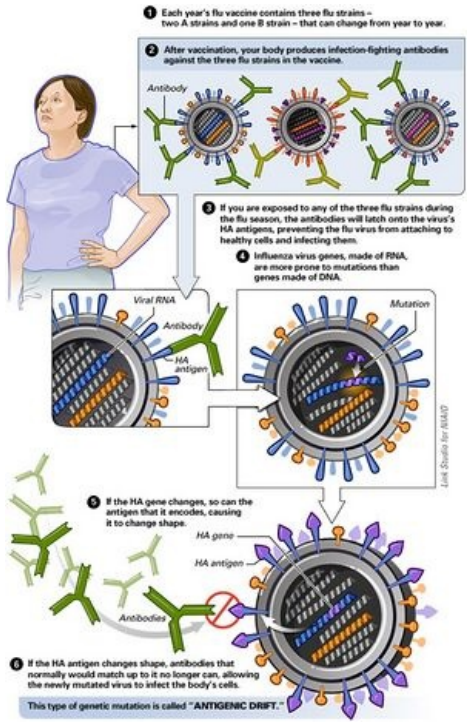
Influenza epidemiology

Type A

Influenza A virus causes diseases of several animal species (especially pigs, birds), not only humans. Type A viruses have caused all major epidemics and pandemics (see the history chapter). These arise at ten- and multi-year intervals with the emergence of a new antigenic shift. In the case of antigenic drift, epidemics are usually smaller.

Type B

Type B virus causes minor epidemics, especially in children's groups (typically kindergartens). Type B antigen shift was not observed. The disease is seasonal, occurs mainly in winter and early spring. The seasonal occurrence of influenza is not yet sufficiently explained. One possible explanation is that in the winter, people spend more time indoors and come into closer contact with each other. The travel factor during the winter holidays in the Northern Hemisphere is also considered. Another factor is that low temperatures lead to dry air, which can dry out the mucus. The virus also survives on contaminated surfaces in cold environments. Aerosol transmission of the virus is highest in cold conditions (less than 5 ° C) and at low relative humidity. Nevertheless, the seasonal occurrence also occurs in the tropics and in some countries it is highest, especially during the rainy season. Robert Edgar Hope-Simpson tried to explain in 1965, who assumedvitamin D (lack of sunlight when people stay inside).



Transmission

2 to 3 virions are sufficient to cause infection . Most of those infected will develop an obvious form of the disease with flu-like symptoms, which in turn contribute to the further spread of the flu. Young children get the disease most often and spread the infection.

After the introduction of the influenza A virus into the family, 20–60% of those exposed have virological or serological signs of infection, half of whom suffer from symptoms that we refer to as influenza.

Source

The source of the infection is the person at the end of the incubation period and in the first days of the acute disease (it is stated that the person is most infectious between the second and third day after the infection and that the infection lasts about 7-10 days). Children are much more contagious than adults (they spread the virus from the asymptomatic period and up to two weeks after the infection). If the flu is complicated by pneumonia , the virus is released into the environment for 10-12 days. Patients with an asymptomatic course of the disease pose a great risk to the environment.

Infectiousness

Influenza infectivity decreases with the level of immunity of the exposed population, which is mainly due to the presence or absence of antibodies to neuraminidase, hemagglutinin, or both antigens of the virus.

Transmission

Transmission occurs by droplet infection (by air or indirectly by objects contaminated with the secretions of sick persons, eg door handle, public transport handrail, banknotes, light switches) from the patient to the susceptible individual .

The gateway to the infection is the airways (possibly a placental infection). The virus is at the peak of the disease in large amounts in the secretions of the airways and is eliminated by talking, coughing and sneezing.

The transmission therefore takes place in three main ways:

1. directly - the infected person transmits mucus to the eyes, nose or mouth of the susceptible individual by sneezing;
2. inhalation of aerosols - produced by the patient during coughing, sneezing, etc .;
3. hand-to-mouth transmission - contaminated areas, handshake.

The relative importance of each route of infection is unclear, all of which may contribute to the spread of the virus. When transmitted by air, droplets are 0.5 to 5 µm in diameter, so inhalation of even one of them may be sufficient to cause infection. Although up to 40,000 droplets are released in one sneeze, most of them are too large and settle quickly. The survival time of the virus in the air depends on air humidity and UV radiation.

Incubation time

The incubation period is short, lasting 18-24 (sometimes up to 72) hours . Susceptibility is general, immunity is long-lasting, but strictly type and strain specific.

Infectivity factors

Factors influencing an influenza pandemic are as follows:

- high contagiousness of the disease;
- ease of transmission of the infection (the disease is transmitted directly: by droplet path, contact, stained objects, the gateway of the agent is the respiratory epithelium of the airways, but transmission through other mucous membranes is also possible);
- shift variant of the virus, absence of antibodies in the population and therefore general susceptibility;
- similarity with other respiratory diseases (limits early diagnosis of the first cases).

The threat of a pandemic spread of influenza is not so much in the severity and mortality of the disease, but in the societal importance of the emergence and spread of the disease, which is expected to be very high morbidity and incapacity for work with rapid onset, which could jeopardize the state, paralyzing its infrastructure and some necessary services.

Clinical signs

The flu has many clinical symptoms. The most important are 🌡 fever, which is often accompanied by chills and severe headaches , followed by arthralgia , myalgia , eye, back and leg pain, which can be accompanied by nausea and even vomiting. Over the next few days, the symptoms of respiratory problems increase : runny nose, sore throat and dry, irritating cough.

The acute phase of the disease, which lasts, with a normal course of about 10 days, may be followed by a phase of increased fatigue of varying lengths (one month or more). If the patient has a weakened immune system or is possibly associated with other diseases, the disease often has a much more dramatic course and prognosis, which can be fatal (primary or secondary pneumonia, myocarditis and others).

Seasonal flu

It is a disease caused by the influenza A or B virus. It often occurs together with other viral respiratory diseases, typically from autumn to spring. The virus circulates in the population and part of it has antibodies against it. In the twentieth century, there were three influenza pandemics that cost the lives of tens of millions of people. They have always been associated with the emergence of a new type of virus. According to some studies, a type with the same virulence as the one that occurred in 1918 (Spanish flu, H1N1) could kill 50 to 80 million people today.

According to long-term surveillance (influenza surveillance), approximately 33% of the population is infected with the influenza virus every year , of which 26% become ill, of which 1% are hospitalized and about 8% die from hospitalizations due to influenza (its complications or due to pre-existing disease). The prevalence of influenza in the world has two peaks , in the northern and southern hemispheres, the time of influenza is different (associated with the winter season). Therefore, the WHO annually determines two different vaccine formulations for seasonal influenza vaccination, ie for the southern and northern hemispheres. There is currently a mix of influenza A H3N2 and H1N1 types in the world. During an epidemic, the number of cases of influenza and acute respiratory diseases multiplies by about 10 to 20 times. All age groups are affected, but with a different risk of a severe course.

About 20% of unvaccinated children and 10% of unvaccinated adults are infected each year, and 340 million to 1 billion people become infected worldwide. The form of the disease is from mild to severe and can even result in death. Hospitalization resulting in death occurs mainly in high-risk groups. It is estimated that seasonal influenza epidemics worldwide result in about 3 to 5 million cases of severe disease and about 290,000 to 650,000 deaths due to the disease. Seasonal flu mortality in the European Union ranges from 8 to 44 per 100,000 people, depending on the size and severity of the epidemic. Worldwide, mortality is estimated at 4 to 8 per 100,000 people. Per EU populationthat's 40,000-220,000 deaths during the flu season. In the United States , an average of 41,400 people died of influenza between 1979 and 2001 each year. In the Czech Republic, according to epidemiological studies for the period 1982–2000 , it is estimated that influenza deaths account for an average of 2.17% of all deaths and 2.57% of cardiovascular deaths.

Selected influenza strains that have caused pandemics and large-scale epidemics

Strain	Season	
A H1N1	2009-2010	"Pig", "Mexican", "California"
A H5N2		"Bird"
A H3N2	1968–1969	"Hong Kong"
A H2N2	1957–1958	"Asian"

Bird flu

It is an infection with the influenza A virus, which has a possible anthropozoonotic spread. The virus is not normally human-to-human transmission and animal-to-human transmission is rather rare. However, virulent and pathogenic types of viruses can also occur. H9N2 and H5N2 are referred to as low pathogenicity viruses. Viruses that can be expected to have a significant pandemic risk with high pathogenicity and mutational ability are reported as

H5N1and H7N7. In most of the cases described so far, these were people who were and lived in very close contact with birds (especially frequent exposure to bird droppings). The H5N1 strain, which infected a large number of poultry in Hong Kong in 1997, did not cause epidemics because these strains were less infectious to humans, even though the population was not immune to them.

There are concerns that the virus may mutate (eg by exchanging antigens with seasonal influenza virus) and develop a new variant of the virus, highly virulent and pandemic.

Pandemic H1N1 2009

The first cases of infection with a new type of influenza A (H1N1 , originally considered, and still used today), were Mexican or swine flu.) were confirmed in a laboratory in the USA on April 17, 2009 by two Californians. Subsequently, there was an explosive increase in reported cases, especially in the case of reports from Mexico. Most of the reported cases did not require hospitalization and home treatment, including possible Tamiflu therapy (high-risk cases, neuraminidase inhibitor) was sufficient. Therefore, the course of the disease is assessed as mild. According to the WHO, the proportion of hospitalized persons is below 10% of confirmed cases. According to the report, the dead almost always had another serious illness. According to preliminary estimates, mortality from this new type of influenza was approximately 0.4% (0.3-1.5%) in the first moments, based on data from Mexico. In July 2009, when the disease spread on a pandemic scale (WHO declared a pandemic on 11 June 2009), the mortality estimate is already significantly lower than 0.29%. The reason for such low mortality may be the availability of modern treatment and early detection of patients. The contagiousness estimate is 1.5 (unlike seasonal flu, where it is about 1.1–1.2 lower). The time of infectivity, the mode of spread and the symptoms are similar to those of seasonal flu. Its incubation period is longer (7 days). Many cases were related to travel to Mexico or the United States. The most affected group are children and younger adults. The United Kingdom and Spain reported the most secondary transmissions (after contact with travelers) in the European Union.

Prevention and prophylaxis

Reliable prophylaxis is not yet available (antivirals can be used : amantadine, rimantadine [these are M2-protein inhibitors of the influenza virus] or the more modern zanamivir [RELENZA inhal.] And oseltamivir [Tamiflu], which are neuraminidase inhibitors). Occurrence, resp. however, the course of the flu can be reduced to some extent. One of the important prevention options is vaccination . A tetravalent influenza vaccine is usually used, which contains purified and inactivated material from 2 subtypes of influenza A and 2 influenza B. In the Czech Republic, the most suitable time for vaccination is from October to December (depending on the epidemiological situation).

General precautionary measures

The good health of the population and hygienic habits (hand washing, non-spitting, covering the nose and mouth when sneezing or coughing) are clearly effective in reducing the transmission of influenza.

- Washing your hands with soap and water (or alcohol-based products) is very effective in inactivating flu viruses. It is these simple hygiene recommendations that are the main way to reduce infection in pandemics.
- Although mouthpieces and other personal protective equipment are a form of prevention in the care of the patient, they are not very effective in protecting the population.
- Smoking increases the risk of the disease, as well as the risk of more severe symptoms. Smokers are therefore responsible for much of the increase in cases during epidemics.
- As the flu also spreads through contaminated surfaces , cleaning and disinfecting it is also a form of prevention. The use of alcoholic detergents is effective, with quaternary ammonium salts prolonging the protective effect.
- The closure of schools, churches, theaters, etc. during pandemics slowed down the spread of the virus, but did not have a significant effect on overall mortality. It is uncertain whether restrictions on public gatherings in schools and workplaces will reduce the transmission of influenza, as the infection will only relocate and similar measures may be very unpopular in the public eye. Conversely, when a small percentage of people are infected, their isolation clearly reduces the risk of further spread.

WHO recommendations for reducing the risk of infection:

- Avoid touching your face and nose.
- Wash hands with soap and water (especially after touching potentially contaminated surfaces).
- Avoid close contact with infected persons.
- If possible, limit the time spent among the crowds.
- Ventilate the living area regularly.
- Practice a healthy lifestyle (enough sleep, nutritious and healthy diet, physical activity).

The hygiene regime must be strictly observed during children's epidemics in children's facilities, polyclinics, hospitals and maternity hospitals.

Influenza diagnosis

Detection of antigen in nasopharyngeal swab

- in the laboratory (ELISA , immunofluorescence) agent capture in 50-80%;
- bed side tests (fast tests in the surgery) capture of agents in 40-70%;

- proper collection and transport of material is important;
- significant in case of virostatic treatment indication .

Detection of RNA in swabs or secretions

- fast very sensitive;
- not commonly available (yet).

Cultivation

- on tissue cultures;
  - the virus grows without cytopathic effect;
  - demonstrated by monoclonal antibodies or hemadsorption;
  - capture depends on the collection and transport of material;
- on a chicken embryo;
  - demonstrated by hemagglutination;
  - the capture depends on the collection and transport of the material.

Serological examinations

- KFR from paired sera;
  - importance mainly for epidemiological purposes;
  - determination of etiological diagnosis;
- HIT ;
  - sensitive test, but also for epidemiological surveillance purposes;
- Detection of IgG , IgM , IgA ;
  - possibility to speed up diagnostics.

Links

related articles

- Cold
- Angina
- Parainfluenza

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