

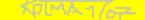
# RESPIRATORY TRACT INFECTIONS

Kolářová M., EPI Autumn 2021



## **INFLUENZA VIRUSES**

Kolářová Marie, EPI, Autumn 2020



## **INFLUENZA**

## **Etiology:**

# The source of infection

# Route of transmission



### ORTHOMYXOVIRUSES - INFLUENZA VIRUSES A,B,C (D

The body enter is the mucous membrane of respiratory tract.

The incubation time for seasonal influenza is on average two days, but ranges from one to four days.

Source is the human from the ende of incubation period to 5. days after the onset of the symptoms.

The replication of the viruses in the epitelial cells of the respiratory tract is very prompt after cca 4 hours with maximum the first 2 – days

The matured viruses consenquently attack a other susceptible cells; cells decay – the beginning of fever.

On average an infectious person will infect less than two non-immune people.

### Influenza spreads:

- \* predominantly via the droplet and contact routes when people cough and sneeze,
- \* and by indirect spread through respiratory secretions on hands, tissues, etc.

If the infected person doesn't cover his or her mouth and nose people within a range of two meters can be infected. There is also some evidence that infectious aerosols may play a role in influenza transmission.

However, immunity to influenza viruses and vaccines wane over time and a large part of the population is susceptible each season.

# Influenza – Case definition

### Clinical Criteria

Any person with at least one of the following clinical forms:

Influenza-like illness (ILI) — Sudden onset of symptoms

AND: — at least one of the following four systemic symptoms: — Fever or feverishness — Malaise — Headache — Myalgia

AND: — At least one of the following three respiratory symptoms: — Cough — Sore throat — Shortness of breath Acute respiratory infection (ARI) — Sudden onset of symptoms

AND — At least one of the following four respiratory symptomms: — Cough — Sore throat — Shortness of breath — Coryza

AND — A clinician's judgement that the illness is due to an infection

### **Laboratory Criteria**

At least one the following four: — Isolation of influenza virus from a clinical specimen — Detection of influenza virus nucleic acid in a clinical specimen — Identification of influenza virus antigen by DFA test in a clinical specimen — Influenza specific antibody response Sub typing of the influenza isolate should be performed, if possible

### **Epidemiological Criteria**

An epidemiological link by human to human transmission

### Case Classification

- A. Possible case Any person meeting the clinical criteria (ILI or ARI)
- B. Probable case Any person meeting the clinical criteria (ILI or ARI) with an epidemiological link
- C. Confirmed case Any person meeting the clinical (ILI or ARI) and the laboratory criteria

## INFLUENZA A/H5N1 – Case definition

#### Clinical Criteria

Any person with one of the following two: — Fever AND signs and symptoms of acute respiratory infection; — Death from an unexplained acute respiratory illness.

### **Laboratory Criteria**

At least one of the following three: — Isolation of influenza A/H5N1 from a clinical specimen; — Detection of influenza A/H5 nucleic acid in a clinical specimen; — Influenza A/H5 specific antibody response (four-fold or greater rise or single high titre).

### **Epidemiological Criteria**

At least one of the following four: — Human to human transmission by having been in close contact (within 1 metre) to a person reported as probable or confirmed case; — Laboratory exposure: where there is a potential exposure to influenza A/H5N1; — Close contact (within 1 metre) with an animal with confirmed A/H5N1 infection other than poultry or wild birds (for example, cat or pig); — Reside in or have visited an area where influenza A/H5N1 is currently suspected or confirmed AND at least one of the following two: — Having been in close contact (within 1 metre) with sick or dead domestic poultry or wild birds in the affected area; — Having been in a home or a farm where sick or dead domestic poultry have been reported in the previous month in the affected area.

#### Case Classification

- A. Possible case Any person meeting the clinical and the epidemiological criteria
- B. Probable case Any person with a positive test for influenza A/H5 or A/H5N1 performed by a laboratory which is not a National Reference Laboratory participating in the EU Community Network of Reference Laboratories for human influenza (CNRL)
- A. Nationally confirmed case Any person with a positive test for influenza A/H5 or A/H5N1 performed by a National Reference Laboratory participating in the EU Community Network of Reference Laboratories for human influenza (CNRL)
- B. WHO confirmed case Any person with a laboratory confirmation by a WHO Collaborating Centre for H5

- Influenza virus type A was first cultivated in the 1930s. Thus this agent was first of the respiratory viruses to be cultivated in the laboratory.
- There are three major antigenic types –A,B,C based on antigenic differences between their nucleocapsid and matrix proteins.
- Subtypes differences are based on antigenic differences in the hemagglutinin (HA) and neuraminidase (NA) surface proteins.
- The segmented genome of influenza viruses is a key features that alows for the genetic reassortment and creation of major antigenic changes (antigenic drift and shift) seen with influenza A viruses.

- Antigenic shift involving the HA protein are critical because antibodies to this surface glycoprotein are associated with neutralization of viral infectivity. The generation of genetic reassortments in animals (e.g. duck) that are co-infected with human and animal influenza viruses is a proposed mechanism for antigenic shifts that led to theemergence of pandemic disease.
- A outbreak of avian influenza A (H5N1) in Hong Kong yeilded isolates with exclusively avian genomes. In this case as well transmissibility of these isolates was minimal.
- A recent outbreak of "pigs" inluenza A was H1N1.
- Minor antigenic changes (antigenic drift) occurs as the results of mutation in the surface HA and NA proteins, which provide a means for the virus to escape existing immunity.

Although distinct antigenic variants of inluenza B viruses cocirculate, antigenic shift among these agents and the existence of different subtypes has not been observed.

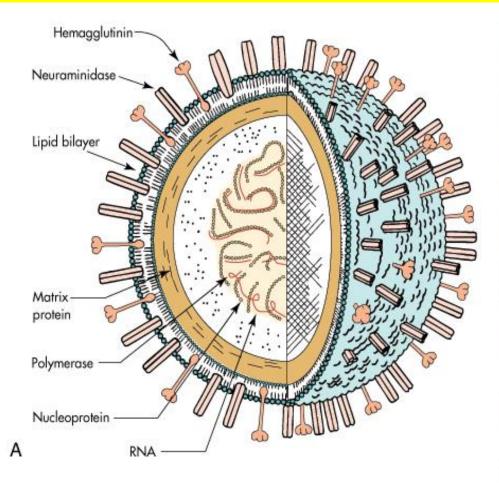
Inluenza A serves as the prototype strain and has organizational similarity to inluenza B with eight RNA segments.

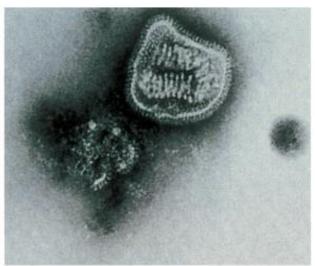
## Gene products include:

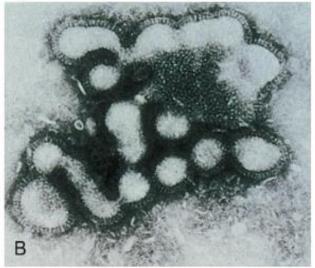
- two surface glycoproteins (HA,NA);
- the major nucleocapsid protein (NP), which associated with tree other proteins (PA,PB1 and PB2) to form the transcription complex;
- matrix proteins (M1 and M2);
- nonstructural proteins (NS1 and NS2).

- The hemagglutinins, of which three are associated with humann inluenza type A (H1, H2,H3), are responsible for viral attachment to sialis acid-containing cell receptors and fusion of viral and cellular membranes.
- The neuraminidases, of which two are associated with human influenza type B (N1, N2), are associated with cleavage of sialic acid residues and viral release.
- The M1 protein is the most abundant protein and underlies the viral membrane. The M2 protein forms an ion channel that is blocked by the antiviral drug amantadine.
- Influenza C has only a single surface glycoprotein, lacks neuraminidase activity and has one less RNA segment.
- In contrast to replication of other RNA viruses, inluenza virus replication involves the nucleus of infecte cells.

# Schema



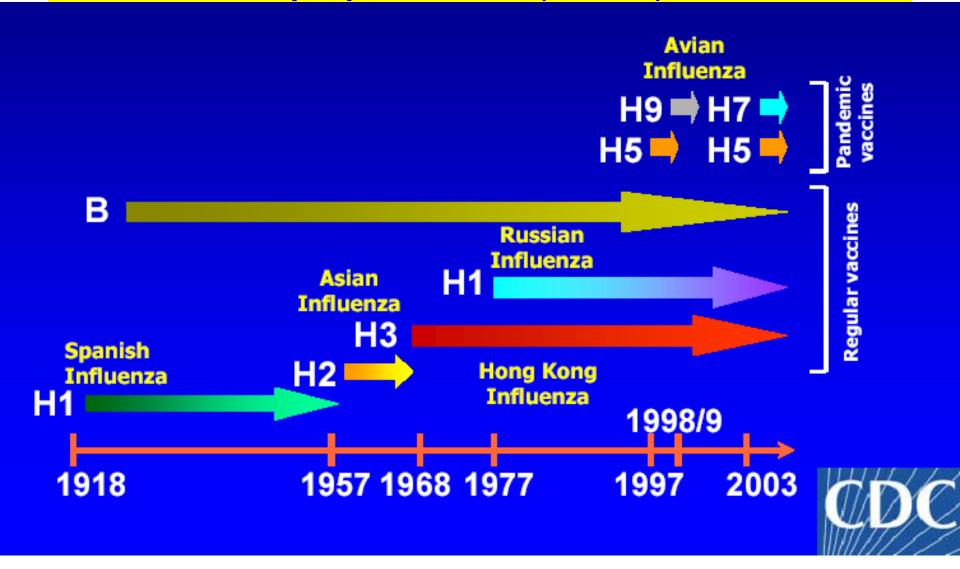




# History

- From the 17. and 18. century are reports about the epidemics in the towns and viliges too.
- Consecutive some epidemics aflicted all continents except Austrálie
- "archeologic sérology" detected:
- A (H2N2) in the 1889-1892 and
- A (H3N8) in the 1898-1901
- A (H1N1) in the 1918-1920 "Spanish flu"

# Incidence subtypes Flu A at human population (CDC)



# SPREAD OF H2N2 INFLUENZA IN 1957 "ASIAN FLU"



## **Epidemiology:**

- Inluenza is an a seasonal virus that infects all age groups.
- **Inluenza type A** is the most clinicaly important, followed by types B and C.
- Influenza B infection is associated with the same disease spectrum as influenza A but influenza B infection has a lower association with severe disease and hospitalization.
- Although most people appear to have experiend <u>influenza type C</u> <u>infection</u> by early adulthood, this agentsis associated with mild sporadic upper respiratory tract infections and is rarely associated with lower respiratory tract disease.

- The source is the human from the ende of incubation period to 5. days after the onset of the symptoms.
- The body enter is the mucous membrane of respiratory tract
- The replication of the viruses in the epitelial cells of the respiratory tract is very prompt after cca 4 hours with maximum the first 2 – days
- The matured viruses consenquently attack a other susceptible cells; cells decay – the beginning of fever

After 5. days is very difficult the isolation of viruses

# Epidemiologie

The reasons of explosive spreading:

- ✓ High infectitivity low infectious dosis
- ✓ Short the incubation period
- ✓ Fast replication of the virus
- ✓ General susceptibility of the population

# Risks groups of people

- Old people more than 65 years
- Pacients wit chronic diseases of lung (CHOPN, bronchial astma, cystic fibrosis)
- Chronic diseases of hepar or decreased function of kidney
- Metabolic diseases (DM)
- Neutropenie, malignit processes, defects of immunity (HIV +, after transplantation, chronic immunosupression)

# **Diagnostics**

- Routine laboratory diagnostics for influenza are usually performed by detecting the virus antigen or genome in specimens from the respiratory tract. Sampling can e.g. consist of swabbing the nose and nasal cavity.
- The tests performed in laboratories include RT-PCR, enzyme-linked immunoassay, immunofluorescence, and virus culture. Except for virus culture these results can be available within approximately 1-2 days, and can help adjust the treatment.
- There are also rapid point of care tests (quick test) that require less time. However these tests generally have a low sensitivity but high specificity, and do not allow subtype determination.

# **Therapy**

- Mainly symptomatic
- By the risks patients antivirotics
- Aplication in the first two days:
  - 1. generation amantadin a rimantadin ⇒
     effectivity only by the influenza types A
  - 2.generation zanamivir (inhalation) and
     oseltamivir (p.o.) ⇒ effectivity for types A i B.

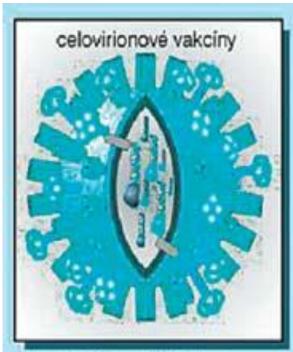
For the best clinical benefit, treatment with antivirals should be given early in the infection, within 48 hours, (the earlier the better).

# **Therapy**

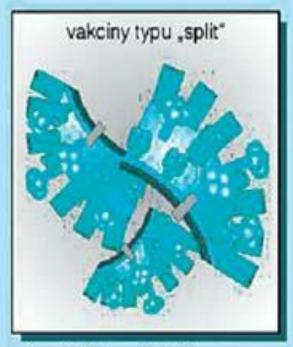
- Resistance to antivirals
- Pre-exposure prophylaxis with influenza antivirals can be prescribed for longer or shorter time periods when an exposure is expected, for example in healthcare settings.
- Post-exposure prophylaxis with influenza antivirals, for example for an at-risk unvaccinated person, is dependent on timely prescription given that the incubation period is 1-4 days. It is usually not prescribed for more than 10 days.

TOLMA 1/07

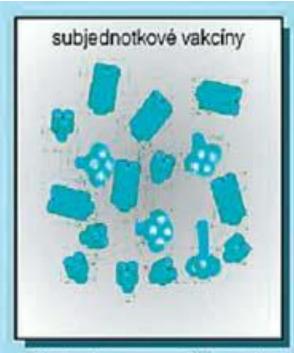
# Types of the vaccine



obsahují kompletní viry



obsahují virové částice ve vysoce purifikované formě



obsahují pouze purifikované HA a NA antigeny

## Pandemic Preparedness and Response Plan for:

#### Date:

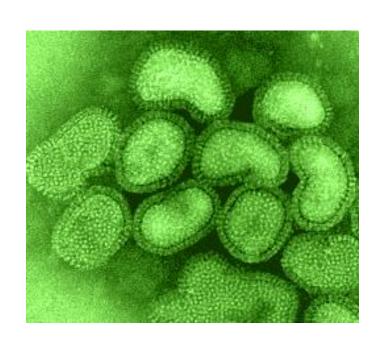
#### Introduction

In preparation for a potential pandemic, all individuals, government and business entities, and community organizations and agencies should take appropriate measures to minimize the impact of a pandemic. This *Pandemic Preparedness and Response Plan* recommends a series of action steps that our faith-based organization should take in response to a potential pandemic in our community.

### Steps to Developing a Pandemic Preparedness and Response Plan for Your Faith-based Organization<sup>1</sup>

- **Step 1** Establish a Pandemic Planning Committee with the responsibility to develop, maintain and put into action a pandemic preparedness and response plan.
- Step 2 Determine the potential impact of a pandemic outbreak on your organization's usual activities and services.
- Step 3 Develop contingency plans for the performance of all critical functions of your faith-based organization during a pandemic.
- **Step 4** Develop plans to extend timely and factual information about the pandemic to your staff, organizational members and people in the communities.
- **Step 5** Develop plans for crisis communications during a pandemic. Develop tools to communicate information about pandemic status and your organization's actions.
- **Step 6** Identify people with special needs (e.g. elderly, disabled, limited English speakers), and include their needs in your response and preparedness plan.
- **Step 7** Develop plans to coordinate your pandemic preparedness and response plans with external organizations and agencies. This includes working with public health agencies, emergency responders, local health care facilities, and other faith-based and community organizations.
- Step 8 Share information about your pandemic preparedness and response plan with staff, organizational members
- 1 These eight steps listed are modified from:
- Flu.gov (2014). Faith-Based and Community Organizations Pandemic Influenza Preparedness Checklist.
- www.flu.gov/planning-preparedness/community/faithbaseedcommunitychecklist.pdf

# Influenza and H5N1





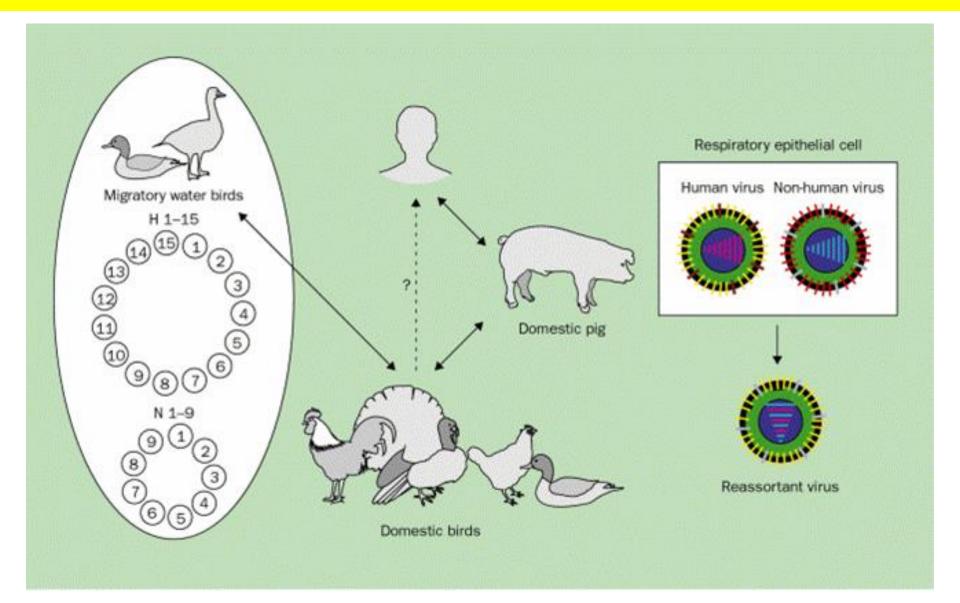


- Fifteen subtypes of influenza virus are known to infect birds,
- thus providing an extensive reservoir of influenza viruses potentially circulating in bird populations.
- To date, all outbreaks of the highly pathogenic form have been caused by influenza A viruses of subtypes H5 and H7.

Within a country, bird flu can spread easily from farm to farm. Large amounts of avian flu is secreted in bird droppings, therefore contaminating dust and soil. An airborne virus can spread bird flu from bird to bird, causing infection when the avian flu is inhaled.

Bird flu viruses <u>do not usually infect</u> <u>humans</u>, however, several cases of human infection with bird flu viruses have occurred since 1997.

# The rise of the pandemic strain



## Interhuman transmission?



# Farm by Hanoi, 2002 (CDC)



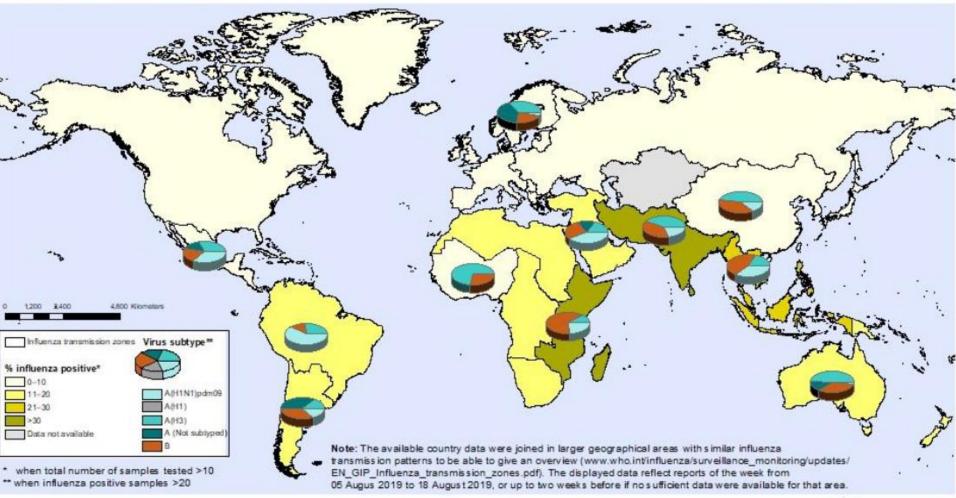






### Percentage of respiratory specimens that tested positive for influenza By influenza transmission zone

Status as of 30 August 2019

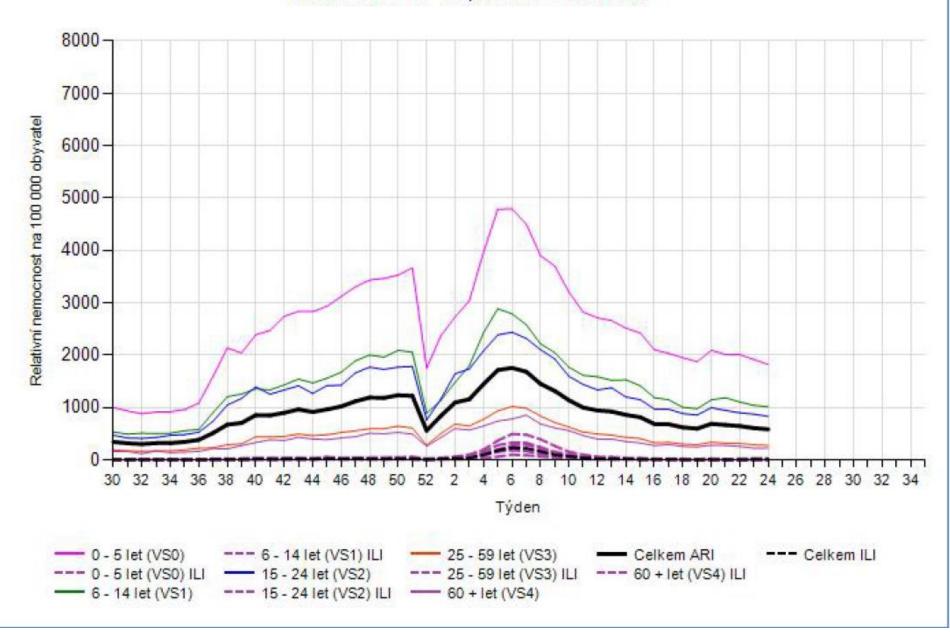


The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: Global Influenza Surveillance and Response System (GISRS), FluNet (www.who.int/flunet)



### Hlášení ARI / ILI - ČR, sezóna: 2018 / 2019



	0-5	6-14	15-24	25-59	60+
Α	2/119 (1,7 %)	2/181 (1,1 %)	0	1/148 (0,7 %)	1/68 (1,5 %)
В	0	0	1/63 (1,6%)	2/148 (1,4 %)	3/68 (4,4 %)
A/H1	19/119 (16,0 %)	43/181 (23,8 %)	4/63 (6,3 %)	26/148 (17,6 %)	8/68 (11,8 %)
A/H3	4/119 (3,4 %)	10/181 (5,5 %)	2/63 (3,3 %)	4/148 (2,7 %)	3/68 (4,4 %)
HRV	22/119 (18,5 %)	24/181 (13,3 %)	13/181 (20,6 %)	21/148 (14,2 %)	11/68 (16,2%)
RSV	19/119 (16,0%)	3/181 (1,7 %)	2/63 (3,3 %)	11/148 (7,4 %)	8/68 (11,8 %)
ADV	5/119 (4,2 %)	11/181 (6,1%)	3/63 (4,8 %)	3/148 (2,0 %)	0
PIV	7/119 (5,9 %)	6/181 (3,3 %)	2/63 (3,3 %)	8/148 (5,4 %)	4/68 (5,9 %)
COV	5/119 (4,2 %)	10/181 (5,5 %)	3/63 (4,8 %)	12/148 (8,1 %)	2/68 (2,9 %)
MPV	2/119 (1,7 %)	5/181 (2,8 %)	1/63 (1,6 %)	0	1/68 (1,5 %)
BOCA	3/119 (2,5 %)	0	0	0	0
SM	12/119 (10,1%)	7/181 (3,9 %)	1/63 (1,6 %)	5/148 (3,4 %)	3/68 (4,4 %)
NEG	19/119 (16,0 %)	60/181 (33,1 %)	31/63 (49,2 %)	22/148 (35,2 %)	24/68 (35,2 %)

## A set of 579 sentinel patients:

HRV - humann rhinovirus PIV - parainfluenza virus BOCA - bocavirus

RSV - resp. syntic. virus COV - coronaviruses

ADV - adenovirus MPV - metapneumovirus

National Influenza Centres (NICs) and other national influenza laboratories from 96 countries, areas or territories reported data to FluNet for the time period from 05 August 2019 to 18 August 2019 (data as of 2019-08-30 04:12:36 UTC). The WHO GISRS laboratories tested more than 37252 specimens during that time period. 2823 were positive for influenza viruses, of which 1698 (60.1%) were typed as influenza A and 1125 (39.9%) as influenza B. Of the subtyped influenza A viruses, 461 (31.3%) were influenza A(H1N1)pdm09 and 1014 (68.7%) were influenza A(H3N2). Of the characterized B viruses, 51 (8.4%) belonged to the B-Yamagata lineage and 555 (91.6%) to the B-Victoria lineage.

#### **Quadrivalent combination vaccines containing:**

- \* two influenza A strains (H1N1 and H3N2 subtypes) and
- \* two influenza B strains (Victoria and Yamagata lineages) as per WHO recommendations.
- Injected quadrivalent inactivated influenza vaccines, available from the 2014/2015 season in some EU/EEA countries

- In 2011, a live attenuated influenza vaccine (LAIV) for intranasal use was approved in the EU/EEA for children and adolescents (2-17 years of age).

Most influenza vaccines, both inactivated and live attenuated, are based on production of influenza viruses/antigens in fertilised hens' eggs. These vaccines can therefore not be given to egg-allergic individuals developing severe symptoms upon exposure to egg proteins.

Hence, a few manufacturers have developed cell-based influenza vaccines which can be given to severely egg-allergic individuals.

### Risk groups for severe influenza

### Older adults - cca 65 yers

#### All persons (over six months of age) with chronic medical conditions:

- respiratory system e.g. asthma
- cardiovascular system e.g. coronary artery disease
- endocrine system e.g. diabetes
- hepatic system e.g. liver cirrhosis
- renal system e.g. chronic renal failure
- neurological/neuromuscular conditions e.g. parkinsonism

#### In addition to the above:

- any condition compromising respiratory functions e.g. morbid obesity (BMI > 40), physical handicap in children and adults
- immunosuppression due to disease or treatment including due to haematological conditions and HIV infection

### From 2012 --- new group - pregnant women

- health care workers with patient contact.

### Česká republika - závažné případy chřipky s prokázanou nákazou virem chřipky vč. úmrtí – stav hlášení od 1.9.2015 do 15.1.2016:

V ČR bylo v uvedeném období hlášeno celkem 16 klinicky závažných případů chřipky,

z nichž ve 3 případech došlo k úmrtí.

Jako etiologické agens byl ve 3 případech prokázán virus chřipky typu B,

ve 3 případech se jednalo o virus chřipky A,

v 8 případech se jednalo o subtyp A/H1N1 a

ve 2 případech se jednalo o subtyp viru chřipky A/H3N2.

U všech pacientů bylo v anamnéze některé ze základních chronických onemocnění a nebyli

- očkování proti chřipce popř. záznam o tomto očkování chybí. Věk pacientů se pohyboval
- v rozmezí 35 let 82 let...

Z uvedeného počtu pacientů se jednalo v 5 případech o ženy a v 11 případech o muže. V 9 případech byla do 48 hodin podána antivirotika.

MUDr Martina Havlíčková, CSc, NRL pro chřipku a nechřipková virová respirační onemocnění

### **ECDC**

### In the course of the 2012–13 season,

A(H1N1)pdm09, A(H3N2) and B/Victoria- and B/Yamagata-lineage influenza viruses have co circulated in ECDC-affiliated countries over what was an extended influenza season.

- The relative prevalences of each virus type/subtype/lineage has varied between countries.
  - Type A (~60%) and type B (~40%) viruses have been detected in similar proportions but with type A peaking and declining slightly before type B.

- A(H1N1)pdm09 viruses have been detected at approximately twice the level of A(H3N2) viruses.
- The vast majority of A(H1N1)pdm09 viruses have remained antigenically similar to the vaccine virus, A/California/07/2009, but continued to show genetic drift with an increasing prevalence of genetic group 6 viruses, predominant in the 6C subgroup.
- The vast majority of A(H3N2) viruses have been antigenically and genetically similar to cell-propagated A/Victoria/361/2011, a genetic subgroup 3C virus and the prototype vaccine virus for the 2012–13 influenza season; subgroup 3C viruses have circulated exclusively in recent months, and the recommended vaccine virus for the 2013–14 season, A/Texas/50/2012, is in this genetic group.

- Viruses of the B/Yamagata-lineage have predominated over those of the B/Victoria-lineage.
  - B/Victoria-lineage viruses have remained antigenically similar to cell-propagated reference viruses of the B/Brisbane/60/2008 genetic clade.
  - B/Yamagata-lineage viruses formed two antigenically distinguishable genetic clades: clade 3 represented by B/Wisconsin/1/2010 (the recommended vaccine component for the 2012–13 influenza season) and, in increasing numbers, clade 2 (75% of B/Yamagata detections recently) represented by B/Massachusetts/2/2012 (the recommended vaccine component for the 2013–14 influenza season).

# Zpráva NRL pro chřipku a nechřipkové respirační viry

- 14.10.2013 -- Souhrn epidem. situace v ČR a v Evropě:
- Situace v ČR je ohledně incidence chřipky stále zcela klidná, není zatím evidován ani sporadický výskyt.
- Evropa: hlásí pouze ojedinělé záchyty. Zpráva WISO (Weekly Influenza Surveillance System) za 40. KT uvádí 132 vyšetřených sentinelových vzorků, z nich:
- 3 byly pozitivní 1x H1 (Španělsko) a 2x B (Belgie, Irsko).
- Z nesentinelových zdrojů bylo prokázáno 15 případů chřipky, přičemž u 11 pacientů se jednalo o typ A u 4 pacientů o typ B. U skupiny chřipek A byl 3x dourčen subtyp H3, 1x H1.
- Dále je hlášen jeden případ těžkého průběhu chřipky B typu z Irska (31letá těhotná pacientka).

MUDr Martina Havlíčková



- People over the age of 50 are more at risk than younger people, and males are more at risk than females. Effective antibiotic treatment is available if the diagnosis is made early in the illness. Deaths occur in about 5-15% of travellers who get the disease, depending on their age and individual health status. Smokers are more at risk than non-smokers.
- People become infected when they breathe in air that contains tiny droplets
  of water known as aerosols, inside of which are the Legionella bacteria. If
  the bacteria get inhaled into the lungs they can cause infection.
  Legionellosis cannot be got from water you drink that enters your stomach in
  the normal way the bacterium has to get into the lungs through breathing it
  in. The illness is not spread from person to person.

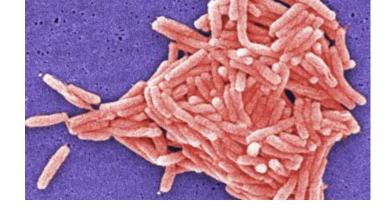
•



The bacterium responsible for Legionnaires' disease was identified in 1976, after a large outbreak at a hotel in Philadelphia, USA. The disease got its name from the group of people affected in this outbreak. They were retired American service personnel who were attending a legion convention. Since the outbreak in 1976, cases and outbreaks have been reported from all countries in Europe, many of them linked to hotels and other types of holiday accommodation.



- What is legionellosis?
- Legionellosis is an uncommon form of pneumonia. The disease has no particular clinical features that clearly distinguish it from other types of pneumonia, and laboratory investigations must be carried out to confirm the diagnosis. It normally takes between two to ten days to develop symptoms (typically five to six days) but very rarely some cases may take two to three weeks to develop symptoms. Patients usually start with a dry cough, fever, headache and sometimes diarrhoea and many people go on to get pneumonia. People over the age of 50 are more at risk than younger people, and males are more at risk than females. Effective antibiotic treatment is available if the diagnosis is made early in the illness. Deaths occur in about 5-15% of travellers who get the disease, depending on their age and individual health status. Smokers are more at risk than non-smokers.



- People become infected when they breathe in air that contains tiny droplets
  of water known as aerosols, inside of which are the Legionella bacteria. If
  the bacteria get inhaled into the lungs they can cause infection.
- Legionellosis cannot be got from water you drink that enters your stomach in the normal way – the bacterium has to get into the lungs through breathing it in.
- The illness is not spread from person to person.
- Where do the Legionella bacteria come from?
- Legionella bacteria are common and can be found naturally in environmental water sources such as rivers, lakes and reservoirs, usually in low numbers. The bacteria are able to survive in the nature at a wide range of temperatures. The bacteria can multiply in man-made aquatic systems like cooling towers, evaporative condensers, humidifiers, decorative fountains, hot water systems and similar systems.



- How do outbreaks occur?
- Experience shows that outbreaks in hotels are mostly associated with hot or cold water
  distribution systems. If the bacteria is in the water in quantities that can cause infection,
  someone taking a shower would inhale the bacteria trapped inside the tiny aerosols that are
  created when the shower water hits the hard surfaces of the shower unit or bath. They may also
  be affected by other water systems that cause aerosols, for example whirlpool spas and
  fountains.
- In contrast, large explosive outbreaks in the community are mostly associated with cooling towers. Cooling towers are devices used to cool buildings. They are also called "wet air conditioning systems" because the process of cooling air involves extensive contact between water and air, thereby creating aerosols. When the Legionella bacteria are present in these systems they can cause Legionnaires' disease. Air conditioning units that use water to cool the air can also pose a risk in hotels.
- However, many air conditioning systems are "dry" and these pose no risk for legionellosis.
- When an outbreak of legionellosis occurs, the source may be found through two types of investigation. One collects information on the activities and whereabouts of the patients with legionellosis to look for links between cases such as staying at or visiting the same places before they became ill. The other involves looking for the Legionella bacteria in the suspected water sources and in clinical specimens from the patients. If the bacteria are found in both, specialised laboratory methods are used to see if they are of the same type.

•