RESPIRATORY TRACT INFECTIONS

Kolářová M., EPI Spring 2018

Upper Respiratory Infections: Common Cold, Sinusitis, Pharyngitis, Epiglottitis and Laryngotracheitis, Otitis externa, Otitis media

Pathogenesis: Organisms gain entry to the respiratory tract by inhalation of droplets and invade the mucosa. Epithelial destruction may ensue, along with redness, edema, hemorrhage and sometimes an exudate.

Etiologic agents include **viruses** :

Rhinoviruses with more than 100 serotypes - causing at least 25% of colds in adults. Coronaviruses may be responsible for more than 10% of cases. Parainfluenza viruses, respiratory syncytial virus, adenoviruses and influenza viruses.

Type A coxsackieviruses can cause a severe ulcerative pharyngitis in children (herpangina), and adenovirus and herpes simplex virus, although less common, also can cause severe pharyngitis. Pharyngitis is a common symptom of Epstein-Barr virus and cytomegalovirus infections.

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Etiologic agents include **bacteria** :

The most common bacterial agents responsible for acute sinusitis are *Streptococcus pneumoniae, Haemophilus influenzae*, and *Moraxella catarrhalis*. Other organisms including *Staphylococcus aureus, Streptococcus pyogenes*, gram-negative organisms and anaerobes have also been recovered.

For otitis externa, the skin flora such as *Staphylococcus epidermidis, Staphylococcus aureus*, diphtheroids and occasionally an anaerobic organism, *Propionibacterium acnes* are major etiologic agents. In a moist and warm environment, a diffuse acute otitis externa (Swimmer's ear) may be caused by *Pseudomonas aeruginosa*.

For otitis media, the commonest causative bacteria are *Streptococcus pneumoniae, Hemophilus influenzae* and beta-lactamase producing *Moraxella catarrhalis*.

Upper Respiratory Infections: Common Cold, Sinusitis, Pharyngitis, Epiglottitis and Laryngotracheitis, Otitis externa, Otitis media

Group A beta-hemolytic streptococcus or *Streptococcus pyogenes* is the most important bacterial agent associated with acute pharyngitis and tonsillitis. *Corynebacterium diphtheriae* causes occasional cases of acute pharyngitis, as do mixed anaerobic infections (Vincent's angina), *Corynebacterium haemolyticum, Neisseria gonorrhoeae*, and *Chlamydia trachomatis*. Outbreaks of *Chlamydia pneumoniae* (TWAR agent) causing pharyngitis or pneumonitis have occurred in military recruits.

Mycoplasma pneumoniae and *Mycoplasma hominis* have been associated with acute pharyngitis. *Candida albicans*, which causes oral candidiasis or thrush, can involve the pharynx, leading to inflammation and pain.

Haemophilus influenzae type b is the most common cause of epiglottitis, particularly in children age 2 to 5 years. Epiglottitis is less common in adults.,

2. Lower Respiratory Infections: Bronchitis, Bronchiolitis and Pneumonia

Pathogenesis: Organisms enter the distal airway by inhalation, aspiration or by hematogenous seeding. The pathogen multiplies in or on the epithelium, causing inflammation, increased mucus secretion, and impaired mucociliary function; other lung functions may also be affected. In severe bronchiolitis, inflammation and necrosis of the epithelium may block small airways leading to airway obstruction.

Etiology: Causative agents of lower respiratory infections are viral or bacterial. Viruses cause most cases of bronchitis and bronchiolitis.

In community-acquired pneumonias, the most common bacterial agent is *Streptococcus pneumoniae*. Atypical pneumonias are cause by such agents as *Mycoplasma pneumoniae, Chlamydia spp, Legionella, Coxiella burnetti* and viruses. Infections due to *Haemophilus influenzae* (usually nontypable) and *Klebsiella pneumoniae* are more common among patients over 50 years old who have chronic obstructive lung disease or alcoholism.

The most common agents of nosocomial pneumonias are aerobic gram-negative bacilli that rarely cause pneumonia in healthy individuals. *Pseudomonas aeruginosa, Escherichia coli, Enterobacter, Proteus*, and *Klebsiella* species are often identified. Less common agents causing pneumonias include *Francisella tularensis*, the agent of tularemia; *Yersinia pestis*, the agent of plague; and *Neisseria meningitidis*, which usually causes meningitis but can be associated with pneumonia, especially among military recruits. *Xanthomonas pseudomallei* causes melioidosis, a chronic pneumonia in Southeast Asia.

Mycobacterium tuberculosis can cause pneumonia. Atypical *Mycobacterium* species can cause lung disease indistinguishable from tuberculosis.

Air-borne diseases

Climatic factors such as absolute humidity have been associated with risk of lower respiratory tract infection.

Respiratory syncytial virus (RSV) is one of the most important viral respiratory pathogens especially for infants. The epidemic activity of RSV infection is related to meteorological conditions and thus to latitude: persistently **high temperature and humidity** results in epidemic peaks in summer and early autumn, while in temperate climates RSV infection peaks in the winter. A causal link with temperature seems inconsistent based on these climatic data, but the RSV infection season in England and Wales has ended earlier and its duration has shortened as the climate has become warmer.

Seasonality has been documented for a number of other respiratory infections including tuberculosis, and seasonal fluctuations of El Niño-southern oscillation in California are associated with the impact of influenza epidemics (hospital admissions or mortality profiles;) but a direct link to climate change has not been established.

Furthermore, increased **use of cooling towers** during heat waves might increase the risk for exposure to *Legionella spp*, although appropriate public health measures should be able to contain this risk.

INFLUENZA VIRUSES

Case definition

Influenza

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 symptoms:
- — 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) and with an epidemiological link
- C. **Confirmed case**
- Any person meeting the clinical (ILI or ARI) and the laboratory criteria

INFLUENZA

Etiology:

ORTHOMYXOVIRUSES - INFLUENZA VIRUSES A,B,C

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

The source of infection

In human - a high infectivity from the onset of the disease (1st - 5th day), in infants from the 7th day.

The animals: pigs, birds and ducks, who may, after genetic changes, be reservoirs for new human subtypes (genetic reassortment).

Route of transmission

A) Directly - by close contact with the sick, airborne. Most frequently in crowded, closed rooms where a high concentration of the infectious aerosol occurs due to sneezing, coughing and nose-blowing.

B) Indirectly - by objects contaminated with the secret of the sick.

Susceptibility

General, **the highest in children and young adults without specific antibodies**.

Immunity is long-term after recovery from the disease. it is **strictly type- and strain-specific** - antibodies don´t protect against the disease by a new virus variant.

Preventive measures:

Immunization against influenza is the basis of prevention.

For a vaccine to be effective it must contain the surface antigens of the circulating influenza viruses - the topical drift variants.

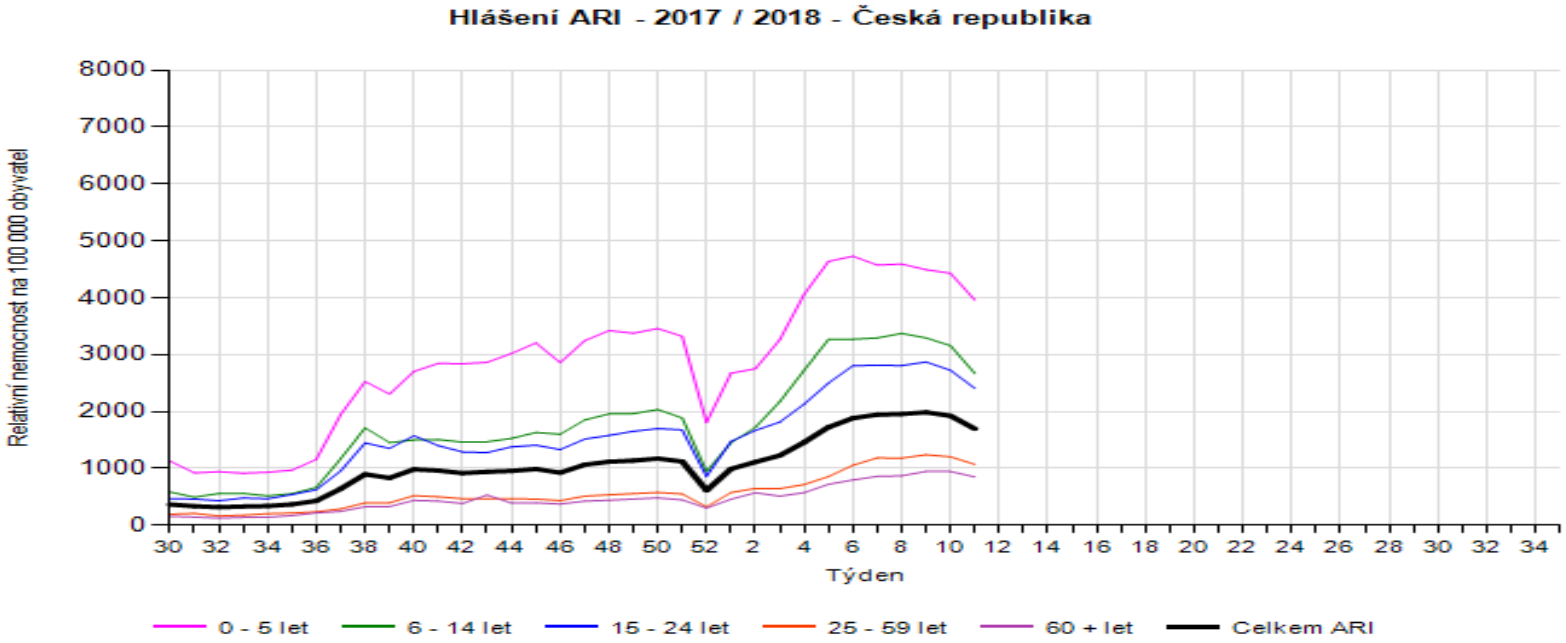
Seasonal influenza

Seasonal influenza is a vaccine-preventable disease that each year **infects approximately ten to thirty per cent of Europe's population,**

and **causes hundreds of thousands** of hospitalisations **across Europe**.

Older people, younger children and those with chronic conditions suffer the most, but everyone is at risk of developing serious complications—which include pneumonia, myocarditis and encephalitis—that may result in death.

Weekly acute respiratory infections morbidity by age group per 100000 population, 2017 / 2018 The Czech Republic

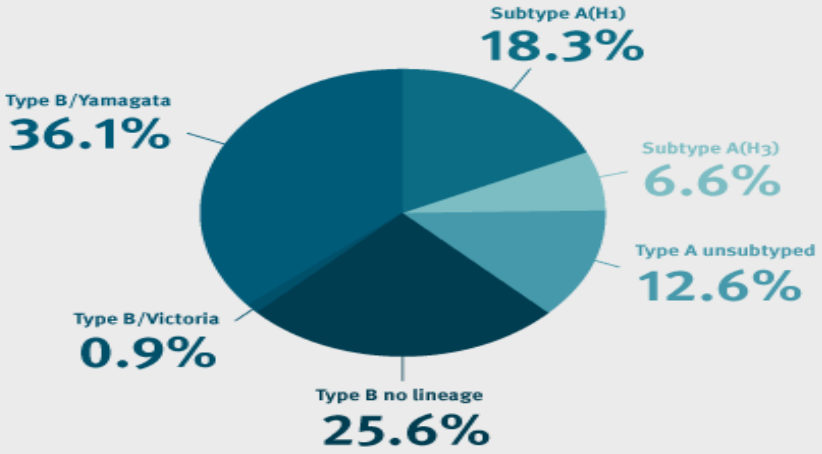


Influenza in Europe

Data from EU and EEA countries for the 2017–18 season
Week 9 (26 February–4 March 2018)

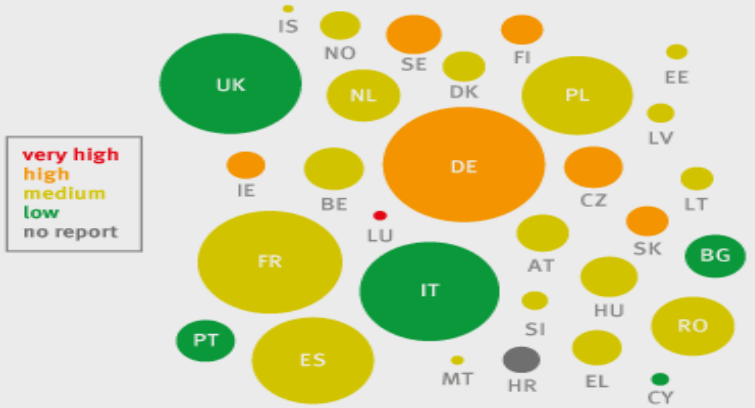
Influenza viruses circulating in 2017–2018

Only sentinel specimens are included



Influenza intensity in week 9

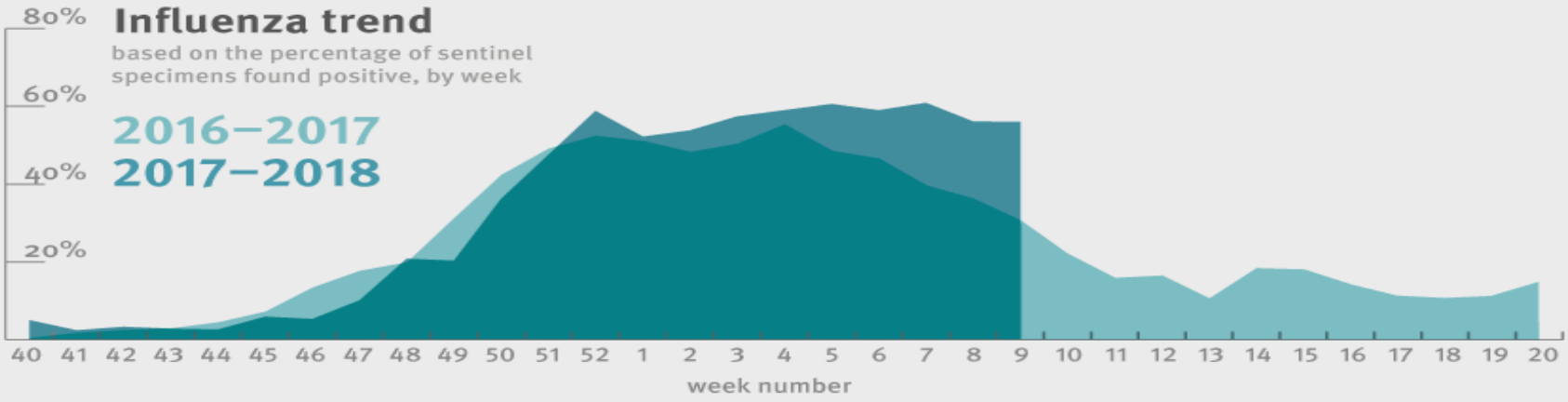
based on sentinel reports of influenza-like illness and/or acute respiratory infections



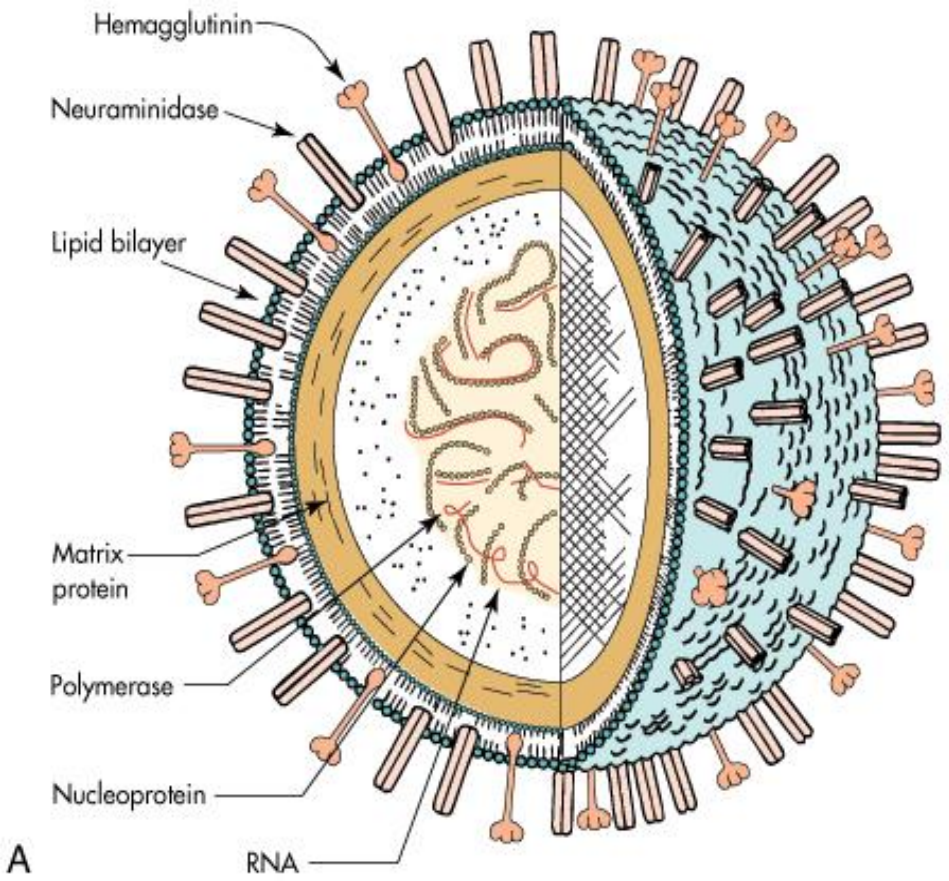
Bubble size is indicative of country population

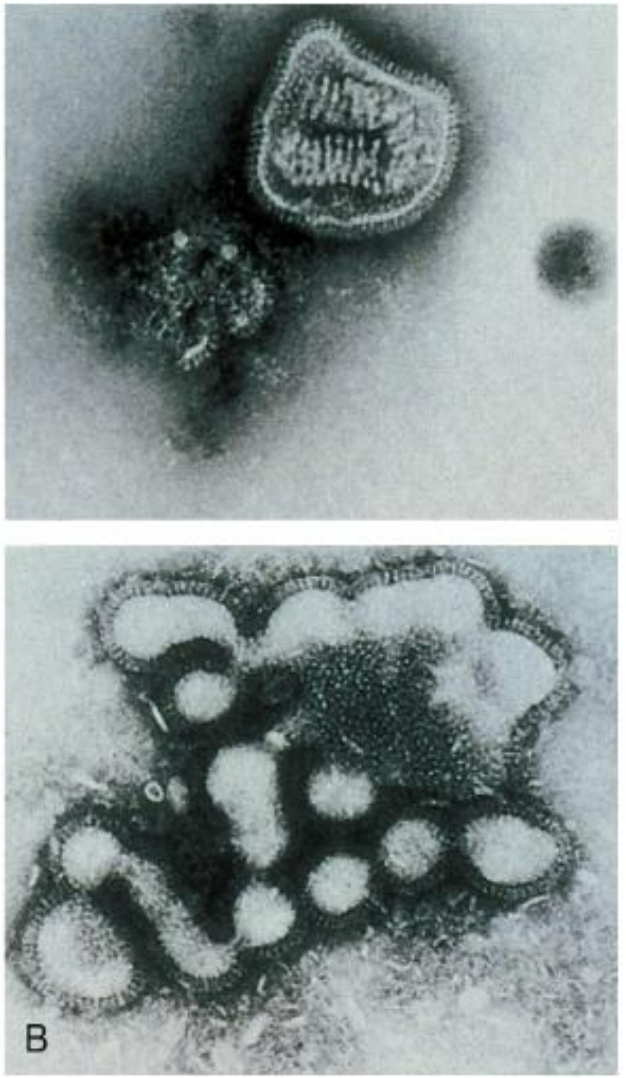
Influenza trend

based on the percentage of sentinel specimens found positive, by week



Schema


Hemagglutinin
Neuraminidase
Lipid bilayer
Matrix protein
Polymerase
Nucleoprotein
RNA
A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ORTHOMYXOVIRUSES - INFLUENZA VIRUSES

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 16 types) and neuraminidase (NA 9 types) 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.

ORTHOMYXOVIRUSES - INFLUENZA VIRUSES

Antigenic shift involving the HA protein are critical because antibodies to this surface glycoprotein are associated with neutralization of viral infectivity.

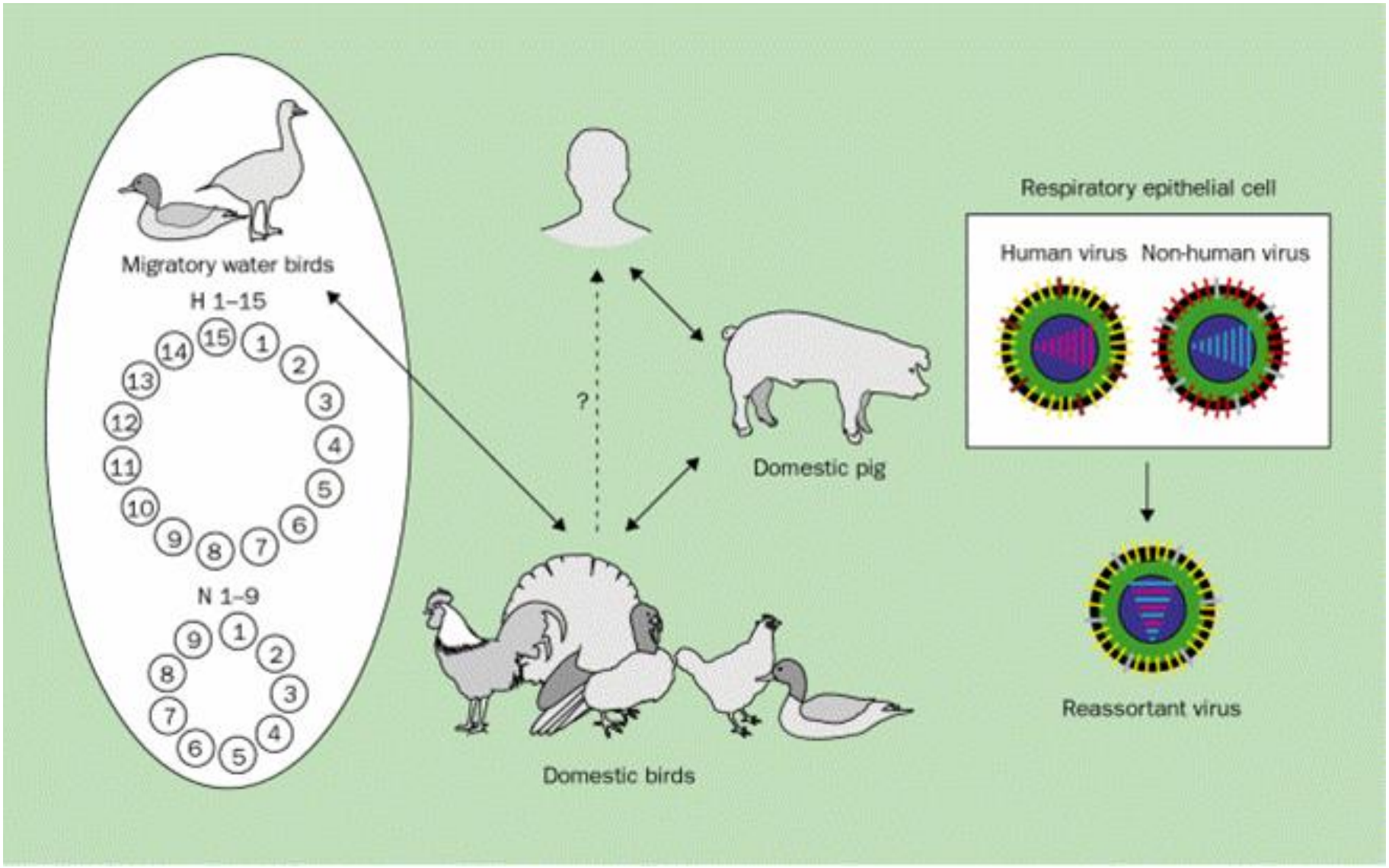
The generation of genetic reassortments in animals (e.g. duck) that are co-infected with human and animal influenza viruses is a proposed mechanism for antigenic shifts that led to theemergence of pandemic disease.

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.

The rise of the pandemic strain



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

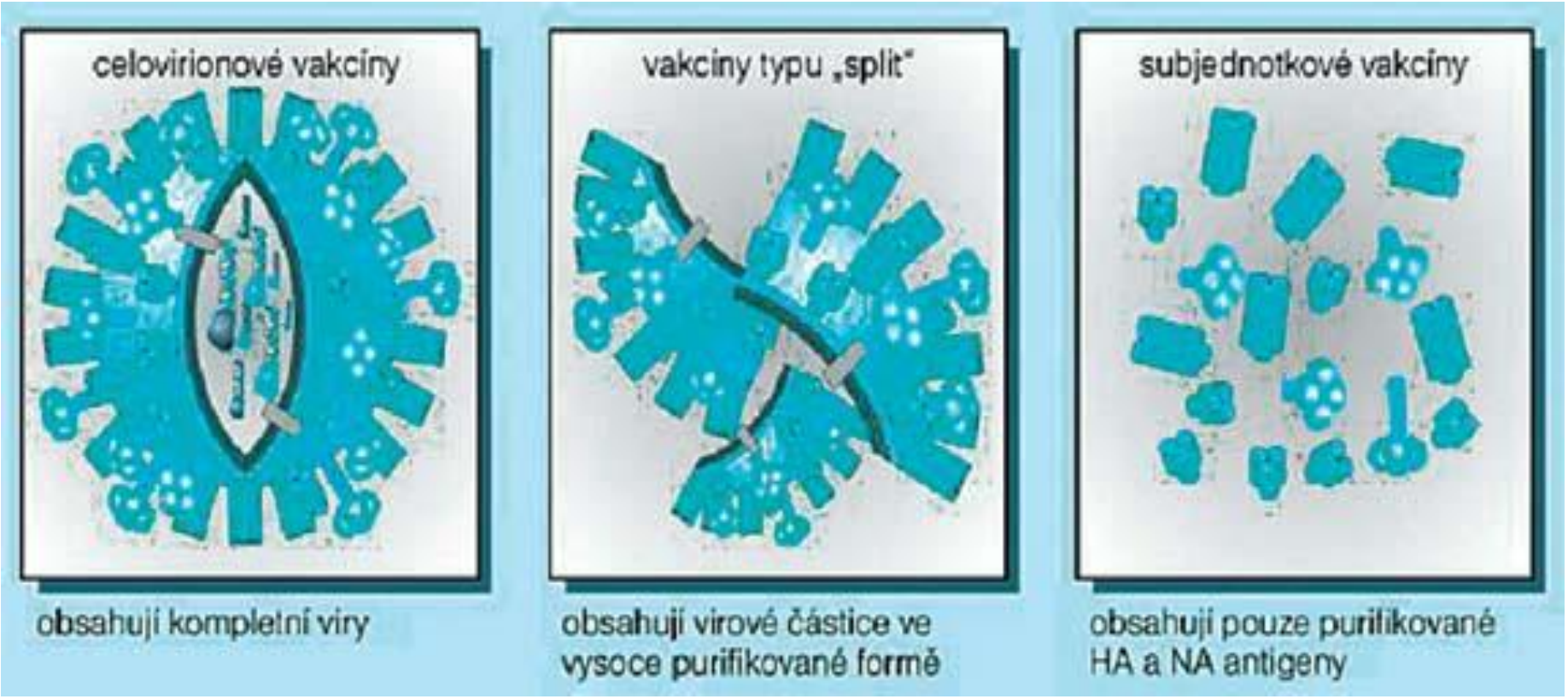
- ***The reasons of explosive spreading:***

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

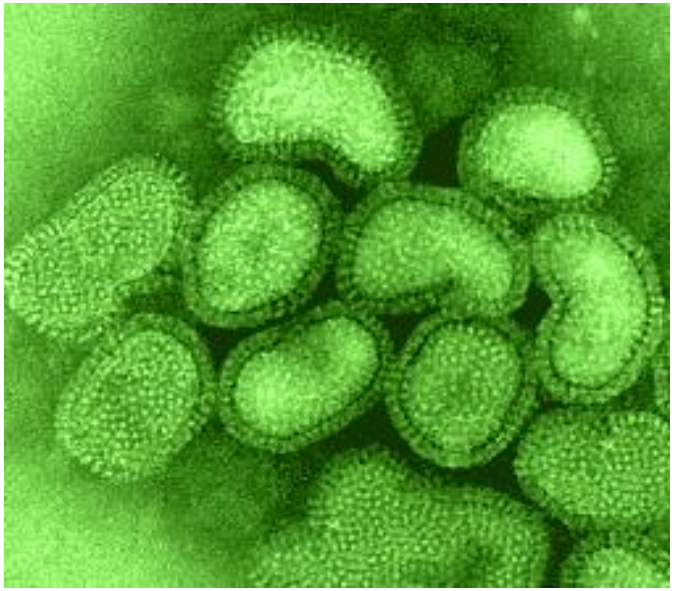
Risks groups of people

- 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)

Types of the vaccine



Influenza and H5N1



Interhuman transmission ?

Farm by Hanoi, 2002 (CDC)

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

Coronavirus infections
Middle East respiratory syndrome coronavirus

The Middle East respiratory syndrome coronavirus (MERS-CoV) is a new beta virus strain of an animal coronavirus that was first identified in Saudi Arabia in September 2012.

Coronaviruses are enveloped RNA viruses from the *Coronaviridae* family and part of the *Coronavirinae* subfamily. With its characteristic surface, the virions appear as a crown like image under the electron microscope and so the viruses are named after the Latin word *corona*, meaning 'crown' or 'halo'.

In animals the viruses infect the respiratory and gastrointestinal systems as well as occasionally affecting the liver and the neurological systems.

The human coronaviruses mainly infect the upper respiratory and gastrointestinal tract. They often result in upper respiratory tract infections (simple colds) in humans, causing mild illnesses usually of short lasting nature with a rhinitis, cough, sore throat, as well as fever.

Occasionally, the viruses are able to cause more significant lower respiratory tract infections in human with pneumonia; this is more likely in immunocompromised individuals, people with cardiopulmonary illnesses, as well as the elderly and young children. Only very rarely do the humans viruses cause severe disease, like sever acute respiratory syndrome.

In humans, the transmission of coronaviruses between an infected individual and others can occur via respiratory secretions.

This can happen either directly through droplets from coughing or sneezing, or indirectly through touching contaminated objects or surfaces as well as close contact, such as touching or shaking hands.

Legionellosis

The Genus Legionella is

a pathogenic group of Gram-negative bacteria which include *Legionella pneumophila*, the cause of Legionellosis (from 40 types around 20 types are patogenic).

Legionella organisms are aerobic, motile, pleomorphic rods. It may be visulized in a silver stain, or cultured in cysteine rich media such as BCYE(Buffered charcoal yeast extract)

- The organism is found mainly in aquatic medium.
- Freshwater amoebae appear to be the natural reservoir for the organisms
  - **Natural aquatic habitats**
    - Freshwater streams
    - Lakes
    - Water reservoirs
  - **artificial sources**
    - Cooling towers
    - Potable water distribution systems
    - Air conditioning devices

Legionella survive and multiplay in water:

- at temperatures between 20°- 50°C (shower, taps, spa)
- in pipes with little or no water flow (this include unoccupied rooms
- in slime (biofilm) and dirt on the inner surfaces of pipes and tanks.

Legionella was discovered after an outbreak **in 1976** amongst people who attended a Philadelphia convention of the American Legion. Those who were affected suffered from an atypical pneumonia that eventually became known as

Legionnaires' disease.

The bacteria was found in the Colling tower of the AC system.

The total number of cases reported were **211.**

A total of 34 deaths were reported.

- The first identified cases of **Pontiac fever** occurred in 1968 in Pontiac, Michigan, in people who worked at and visited the city's health department.
- It was only when *Legionella* was discovered in 1976 that public health officials were able to show that the same bacterium causes both diseases.

- The incubation period is up to two weeks.
- **Pontiac fever**
  - acute, non fatal respiratory disease that resembles influeza, it resolves spontaneously.
  - Named after Pontiac city, where the first case was recognized in 1968.
- **Legionnaires´s disease**
  - Form of atypical pneumonia, more severe then Pontiac fever.
  - Legionares´s afects mainly immunocompromised and elderly.

EU case definition of Legionnaires' disease

Clinical criteria

- Any person with pneumonia

Laboratory criteria for case confirmation

- At least one of the following three:
- • Isolation of *Legionella spp.* from respiratory secretions or any normally sterile site
- • Detection of *Legionella pneumophila* antigen in urine
- • Significant rise in specific antibody level to *Legionella pneumophila* serogroup 1 in paired serum samples.

Laboratory criteria for a probable case

- At least one of the following four:
- • Detection of *Legionella pneumophila* antigen in respiratory secretions or lung tissue, e.g. by DFA staining
- using monoclonal-antibody-derived reagents
- • Detection of Legionella spp. nucleic acid in respiratory secretions, lung tissue or any normally sterile site;
- • Significant rise in specific antibody level to Legionella pneumophila other than serogroup 1 or other
- Legionella spp. in paired serum samples
- • Single high level of specific antibody to Legionella pneumophila serogroup 1 in serum.

Case classification

- Probable case: Any person meeting the clinical criteria AND at least one positive laboratory test for a probable
- case.
- Confirmed case: Any person meeting the clinical AND the laboratory criteria for case confirmation.

All notified cases

For 2013, 5 851 cases of LD were reported by 28 EU Member States and Norway.

The number of notifications per million inhabitants was 11.4, well within the 2005–2012 range.

Six countries (France, Italy, Spain, Germany, the Netherlands and the United Kingdom) accounted for 83% of all notified cases.

The number of notifications ranged from below 0.1 per million inhabitants in Bulgaria to 39.4 per million in Slovenia.

Most cases were communityacquired (73%), 19% were travel-associated, and 8% were linked to healthcare facilities.

People over 50 years of age accounted for 81% of all cases.

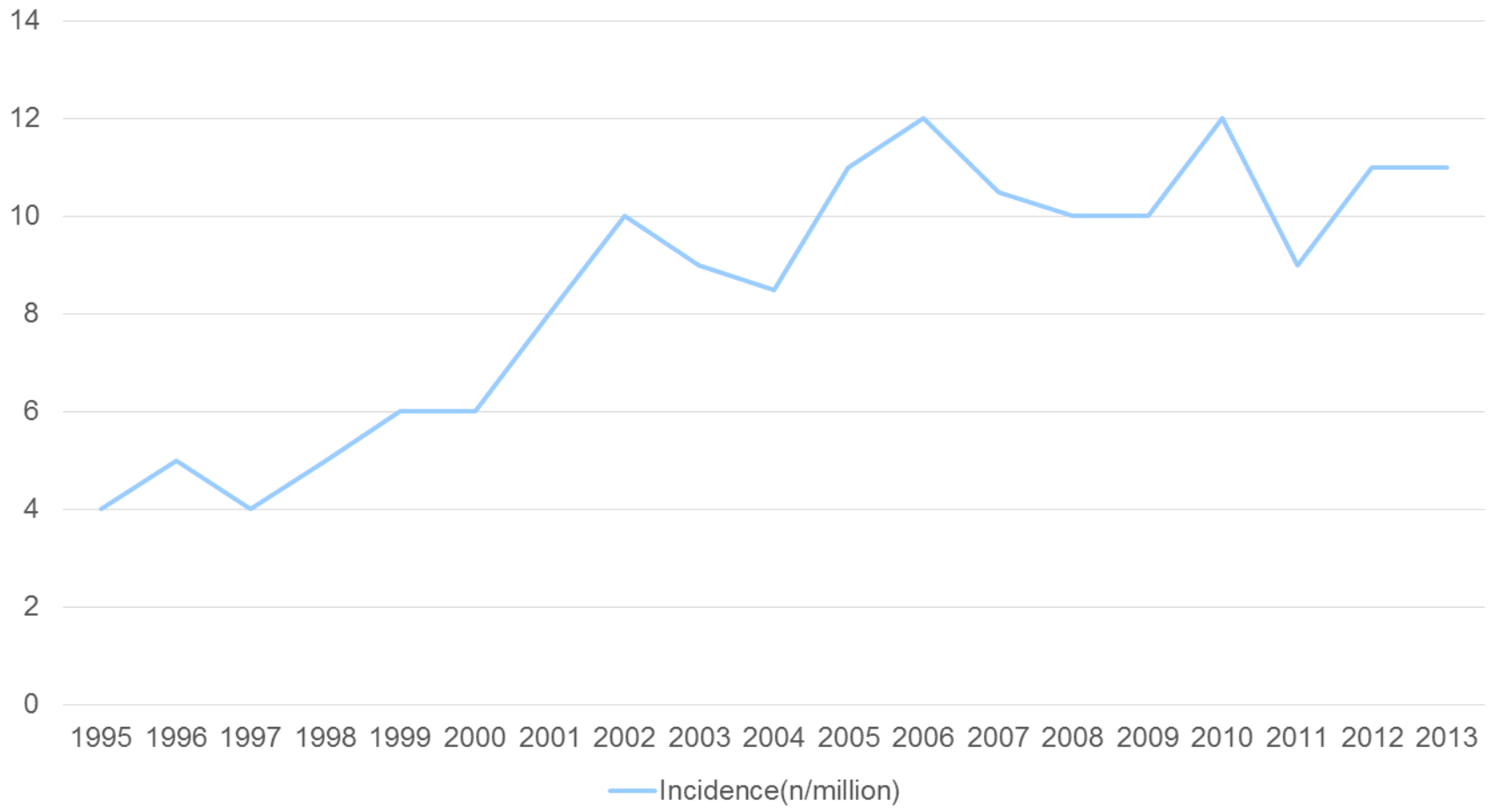
The male-to-female ratio was 2.4:1.

The case-fatality ratio was 10% in 2013, similar to previous years.

Most cases (88%) were confirmed by urinary antigen test, but an increasing proportion of cases are reported to have been diagnosed by PCR.

L. pneumophila serogroup 1 was the most commonly identified pathogen, accounting for 83% of culture-confirmed cases.

Graph 1. Notification rate of legionnaires´s disease in EU by year of reporting, 1995-2013



Rapid risk assessment on the outbreak of Legionnaires' disease in Portugal

14 Nov 2014

The current outbreak of Legionnaires' disease in Vila Franca de Xira, in the Lisbon area of Portugal is one of the largest outbreaks of the disease in the European Union to date.

- As of 12 November, 311 cases have been identified, of which seven have died. Despite the magnitude of the outbreak, this event can be considered a local event and the risk is confined to people in the area or who have travelled to the area in the past three weeks. Investigations are ongoing to discover the source of the outbreak, and cooling towers of major industrial installations in Vila Franca de Xira have been closed as a precaution.
- The risk assessment also looks at the possibility of Legionnaires' disease being transmitted through the transfusion of infected blood, and concludes that this risk is low.