RESPIRATORY TRACT INFECTIONS

Kolářová M., EPI Autumn 2017

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. On the basis of the articles reviewed here, it is not possible to draw conclusive inferences about the link between airborne diseases and climate change, but it might shorten the transmission season.

INFLUENZA VIRUSES

Kolářová Marie,ÚOPZ, Autumn 2016

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.

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.

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.

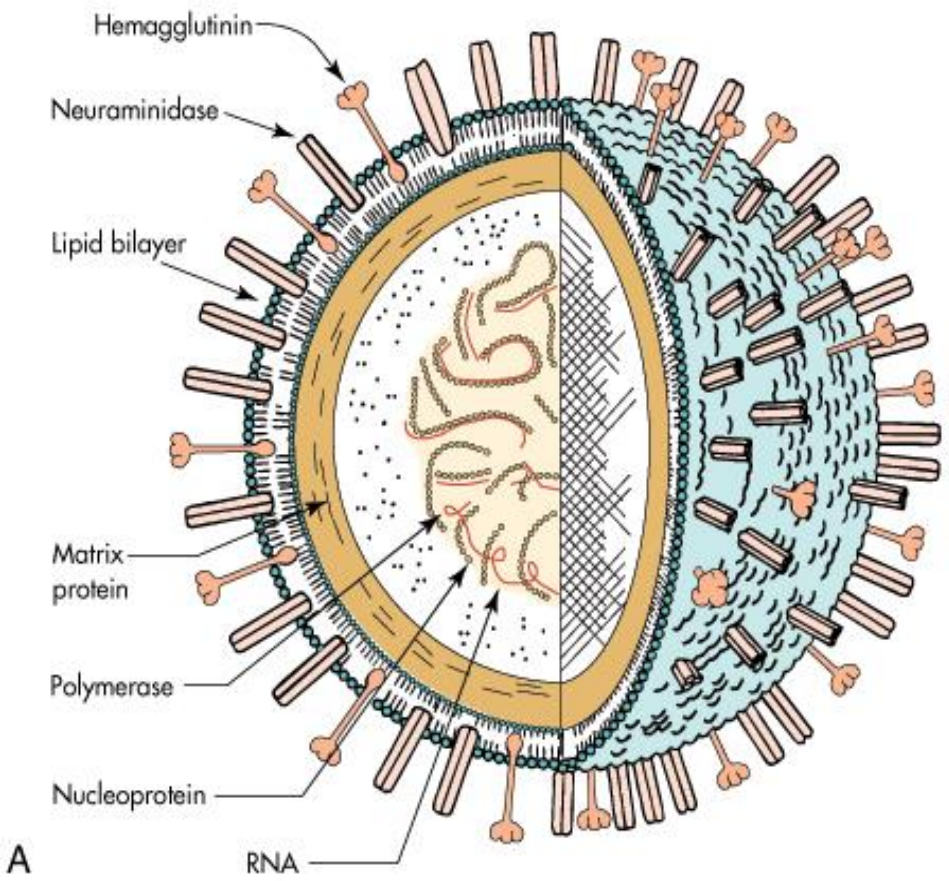
The generation of genetic reassortments in animals (e.g. duck) that are co-infected with human and animal influenza viruses is a proposed mechanism for antigenic shifts that led to theemergence of pandemic disease.

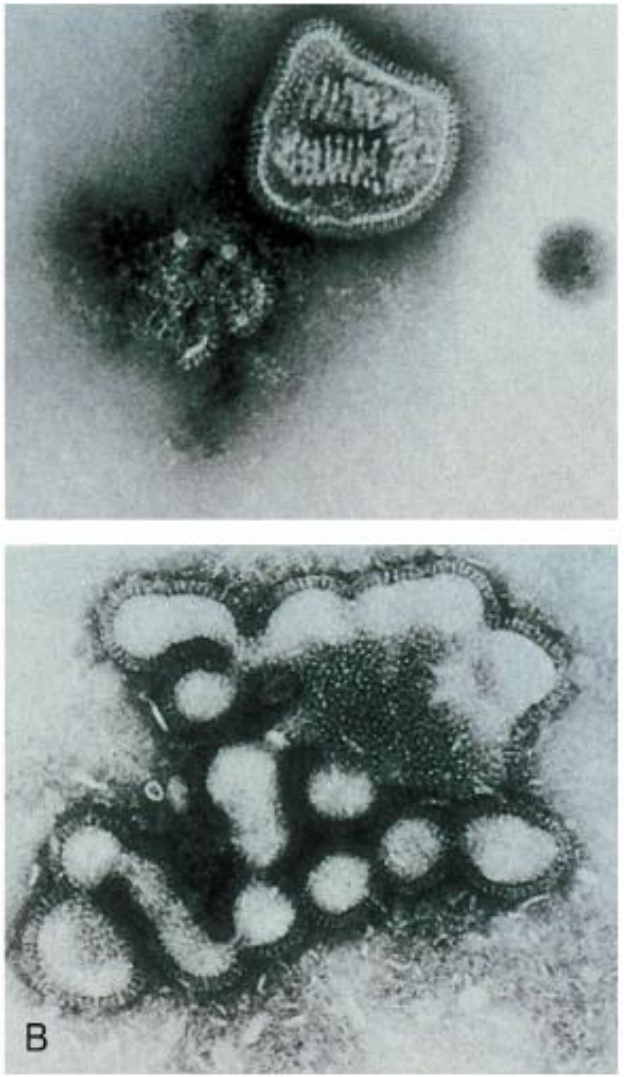
A outbreak of avian influenza A (H5N1) in Hong Kong yeilded isolates with exclusively avian genomes. In this case as well transmissibility of these isolates was minimal.

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.

Schema


Hemagglutinin
Neuraminidase
Lipid bilayer
Matrix protein
Polymerase
Nucleoprotein
RNA
A


B

ORTHOMYXOVIRUSES - INFLUENZA VIRUSES

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).

ORTHOMYXOVIRUSES - INFLUENZA VIRUSES

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.

ORTHOMYXOVIRUSES - INFLUENZA VIRUSES

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 inlfuenza B infection has a lower asssociation with severe disease and hospitalization.

Although most people appear to have experiend **influenza type C infection** 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

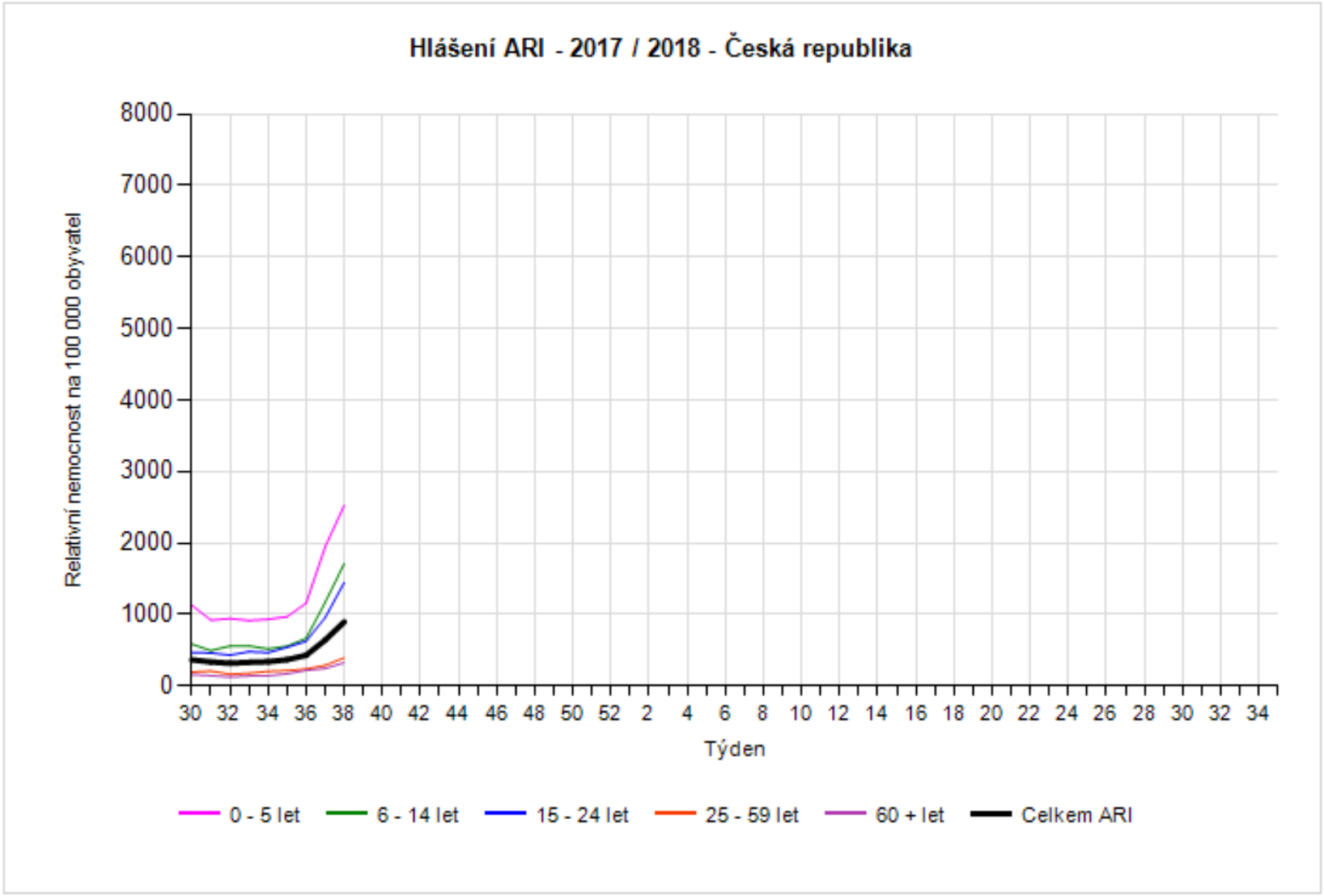
- ***The reasons of explosive spreading:***

✓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)

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



In the Czech Republic
Current information on the flu vaccination for the upcoming 2016/2017 season using the "recommended procedure for vaccination against seasonal flu" of National Immunization Committee.

Based on epidemiological analyses and discussion of the situation in Europe, influenza vaccine is recommended to be given every year to the following two population groups:

- 1) persons aged 65 years and over;
- 2) persons at any age (including children) with chronic conditions from any of the categories listed below:
- chronic diseases of the respiratory tract including bronchial asthma;
- chronic cardiovascular diseases;
- chronic kidney and liver diseases;
- chronic metabolic diseases including diabetes mellitus1;
- immune system deficiency (congenital or acquired); and
- impaired bronchial and pulmonary function (including impaired respiratory function due to brain or spinal cord injury, seizure conditions, and other neurological or muscular disorders).

- In these cases, influenza vaccination including vaccine is fully covered by the health insurance

In the Czech Republic
Seasonal influenza vaccination guideline

In addition, influenza vaccine is recommended to:

- • pregnant women at any stage of pregnancy and women planning to become pregnant during the influenza season;
- • persons who may increase the risk of infection to the groups listed above, namely:
- persons providing care to high-risk individuals (health professionals and social workers);
- persons living with high-risk individuals; and
- persons in contact with high-risk individuals (employees of posts, shops, services, schools, public transport, etc.).

1. dosis content:

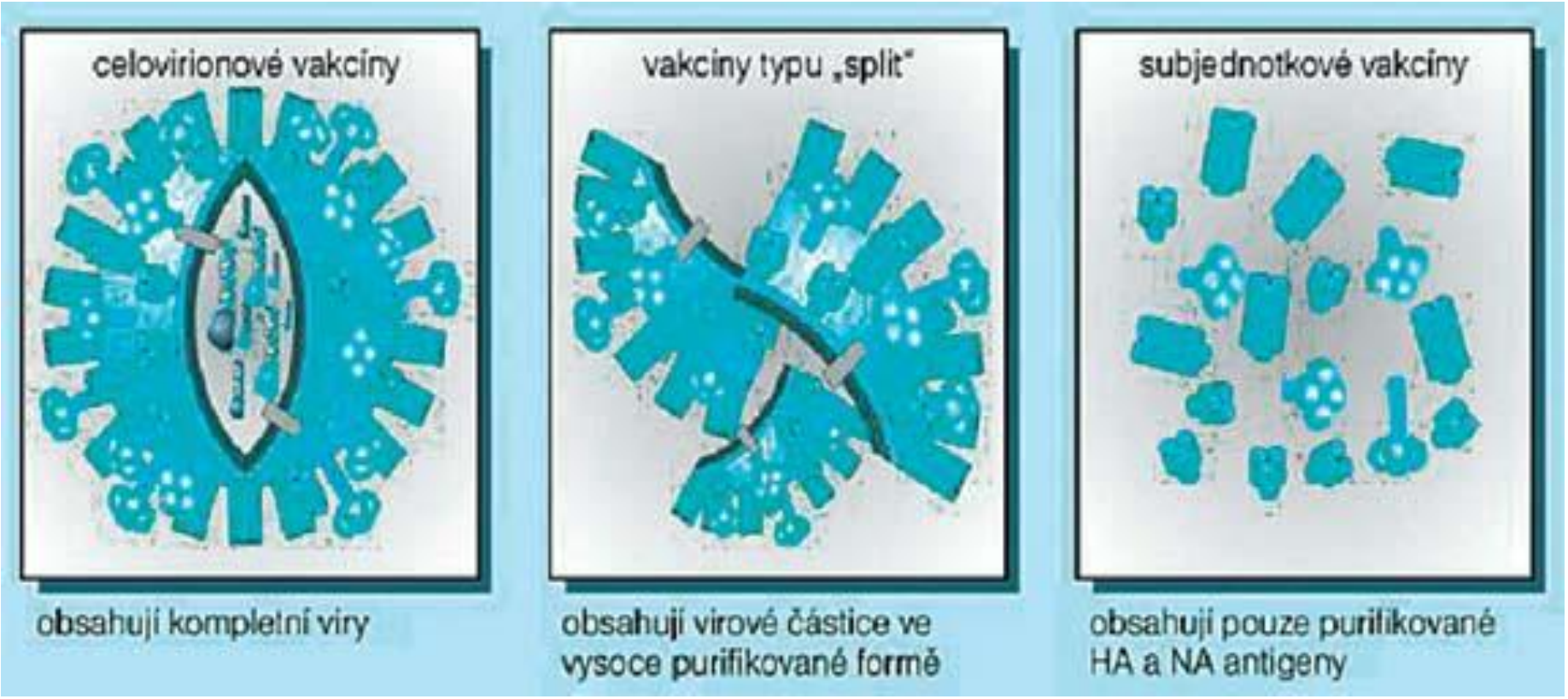
Každá dávka je tří- nebo čtyř-valentní a obsahuje:

- Haemaglutininum A (H_3N_2)
- Haemaglutininum A (H_1N_1)
- Haemaglutininum B – 1x nebo 2x
-

Antigenní složení chřipkových vakcín je každoročně upravováno podle doporučení Světové zdravotnické organizace. Pro období 2017/2018 obsahuje trivalentní vakcína následující typy a subtypy kmenů:

- A/Michigan/45/2015 (H1N1)pdm09 – varianta,
- A/Hong Kong/4801/2014 (H3N2) – varianta,
- B/Brisbane/60/2008 – varianta.
-
- Čtyřvalentní vakcína obsahuje navíc kmen:
- B/Phuket/3073/2013 – varianta

Types of the vaccine



Specific profylaxis

- ***Inactivated cracked (split) vaccine***
- Produced from the inactivated virions elements, that are divided and reactive lipides from the envelope take out
- **Begrivac, Fluarix, Vaxigrip.**
- Aplication: to adults 1. dosis i.m.
- For children from 3 months (under redommendation of the producer)

Specific profylaxis

- ***Subdosis trivalent vaccine***
- contens only external antigens **H** and **N**, witout MATRIX and NP antigens
- = low reaktivity and good immunogenity.
- **Agrippal S1, Influvac a Fluad**
- For children from 6 months

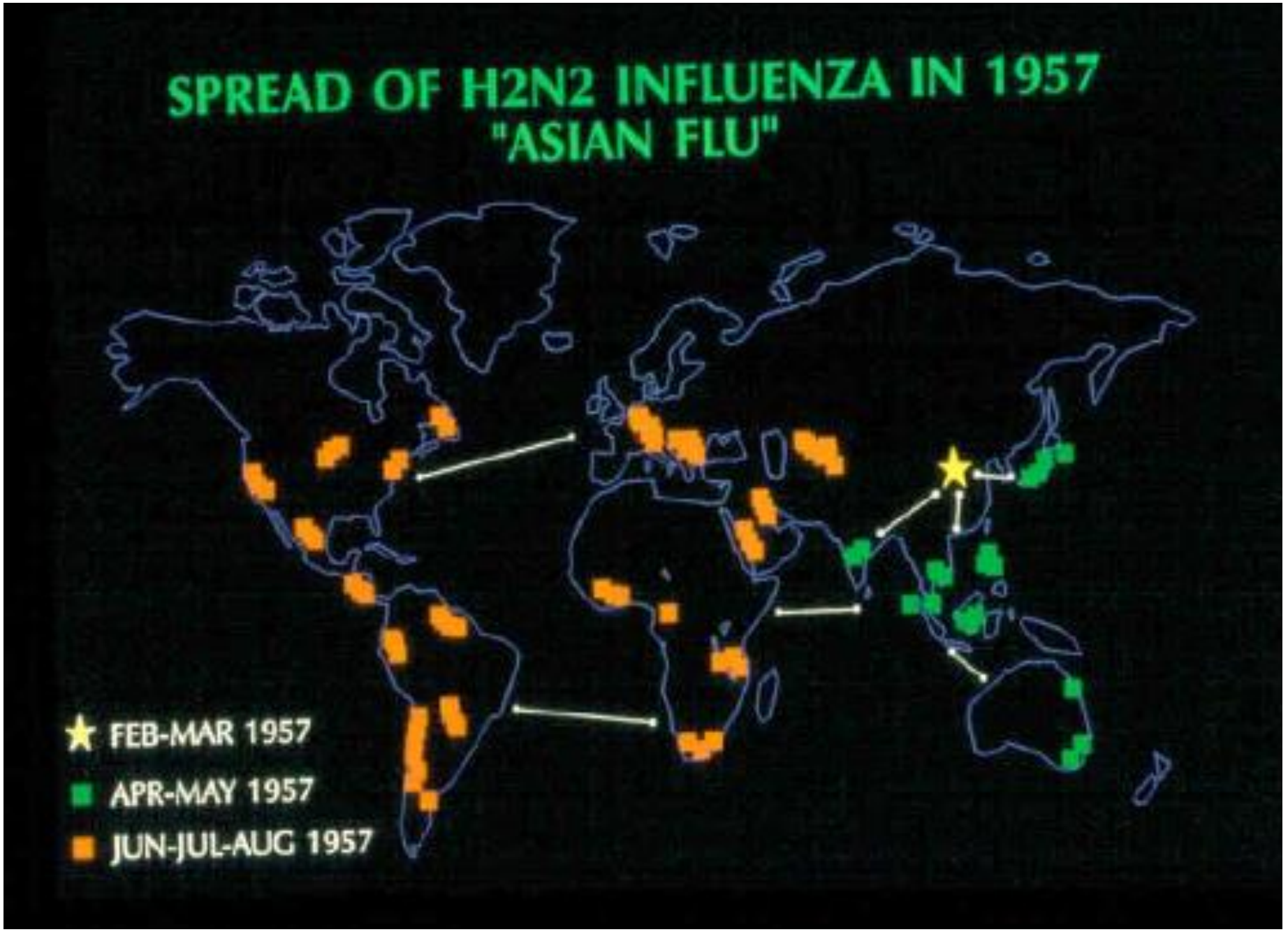
History

- 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:

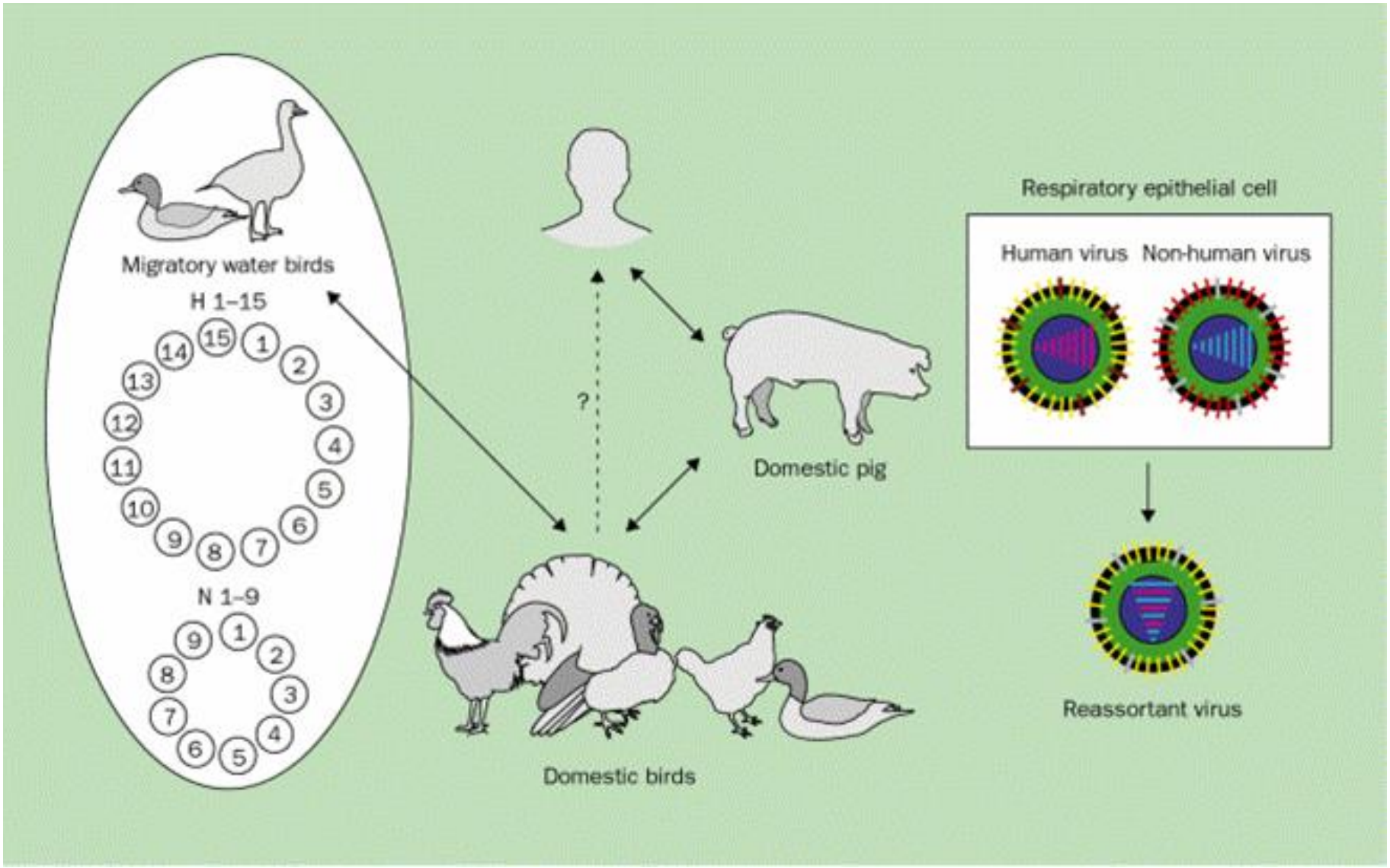
A (H2N2) in the 1889-1892 and

A (H3N8) in the 1898-1901

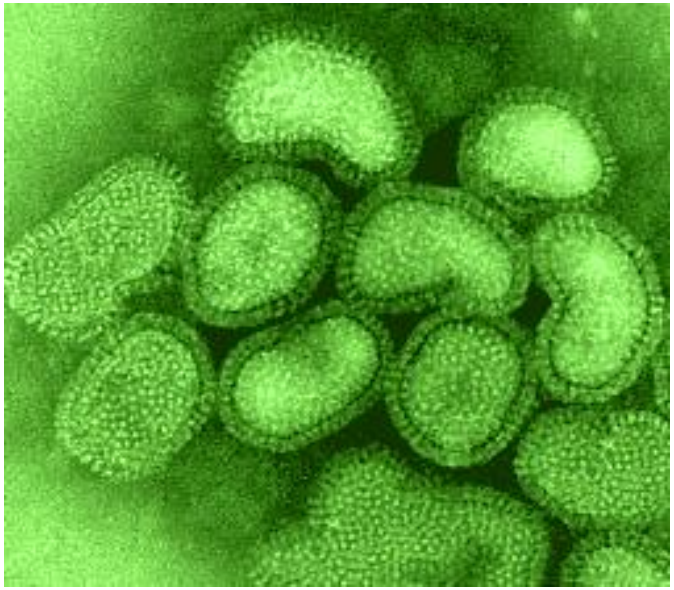
A (H1N1) in the 1918-1920 – „Spanish flu“


SPREAD OF H2N2 INFLUENZA IN 1957
"ASIAN FLU"
FEB-MAR 1957
APR-MAY 1957
JUN-JUL-AUG 1957

The rise of the pandemic strain



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'.

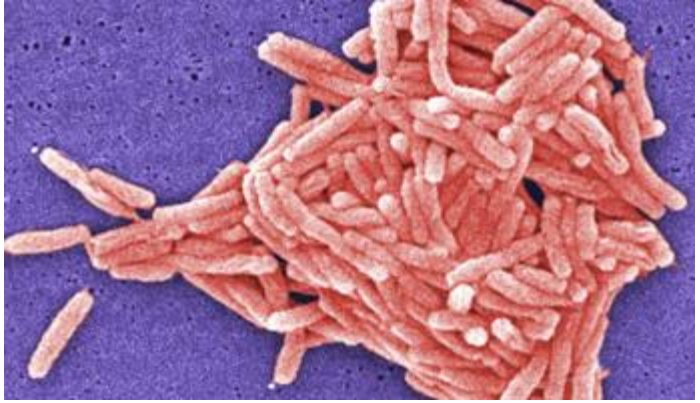
In animals the viruses infect the respiratory and gastrointestinal systems as well as occasionally affecting the liver and the neurological systems.

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 L.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.

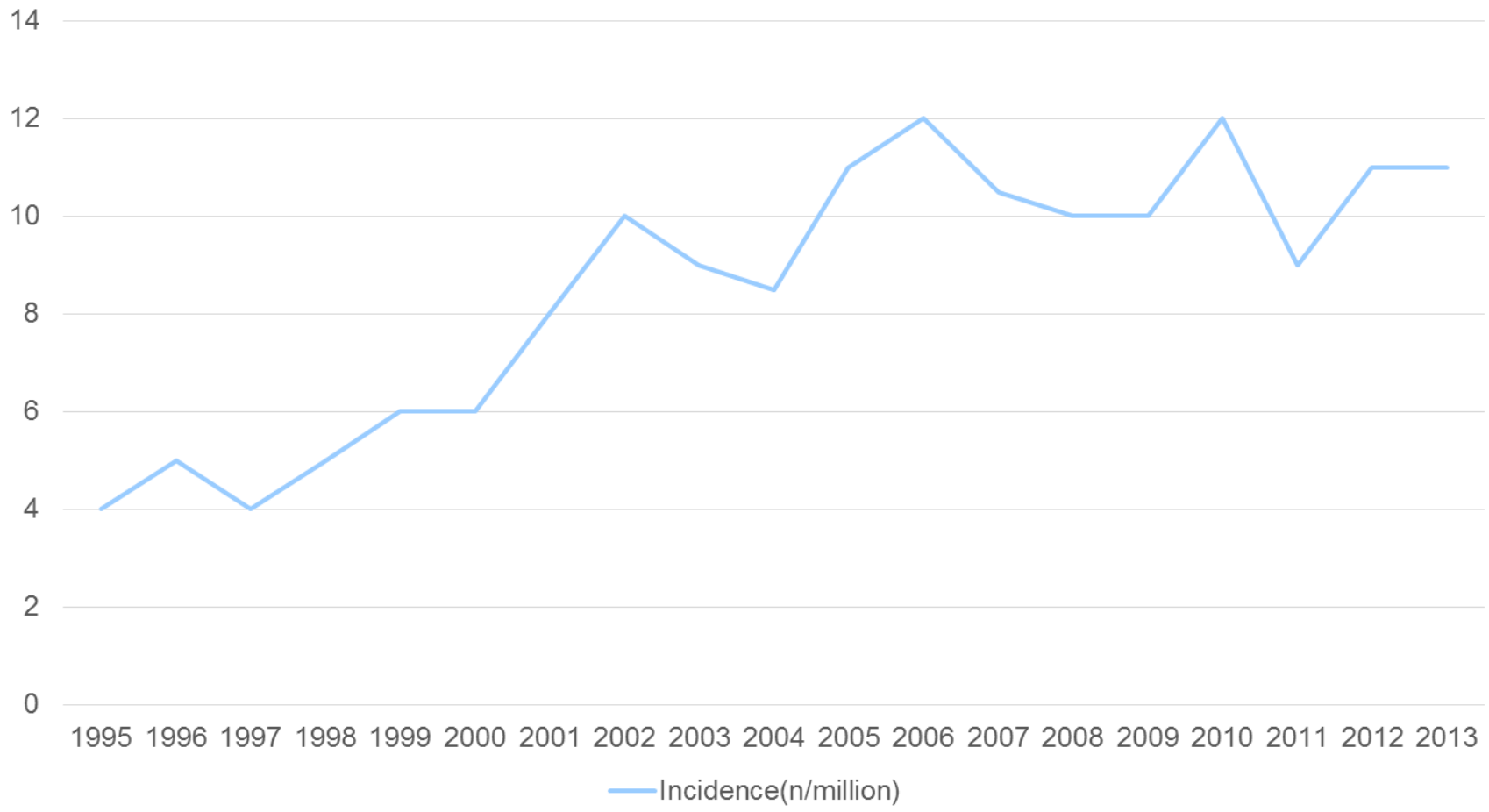
The male-to-female ratio was 2.4:1.

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.

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.

- This novel coronavirus differs from the previously identified coronaviruses such as the SARS coronavirus (SARS-CoV), which caused the 2003 SARS outbreaks.
- There is still much to be investigated, but it is considered likely that this virus originated from an animal source.

Coronavirus infections
Middle East respiratory syndrome coronavirus

- 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.

Coronavirus infections
Middle East respiratory syndrome coronavirus

- 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.

Coronavirus infections
Middle East respiratory syndrome coronavirus

- The five coronaviruses types which affect humans are alpha (229E and NL63), beta (OC43), HKUI1 and SARS-CoV - although the latter is best considered an animal virus that has only rarely infected humans.
- 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.
- There are currently no vaccines or specific treatments for the coronaviruses. Hence, in order to reduce the risk and prevent the spread of infections, simple preventative measure are: good respiratory hygiene, including washing hands; avoiding touching one's eyes, mouth and nose; sanitary disposal of oral and nasal discharges as well as avoiding contact with sick people.