RESPIRATORY TRACT INFECTIONS

Kolářová M., EPI Spring 2016

INFLUENZA VIRUSES

Kolářová Marie,ÚOPZ

INFLUENZA

ORTHOMYXOVIRUSES - INFLUENZA VIRUSES A,B,C

Etiology:

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.

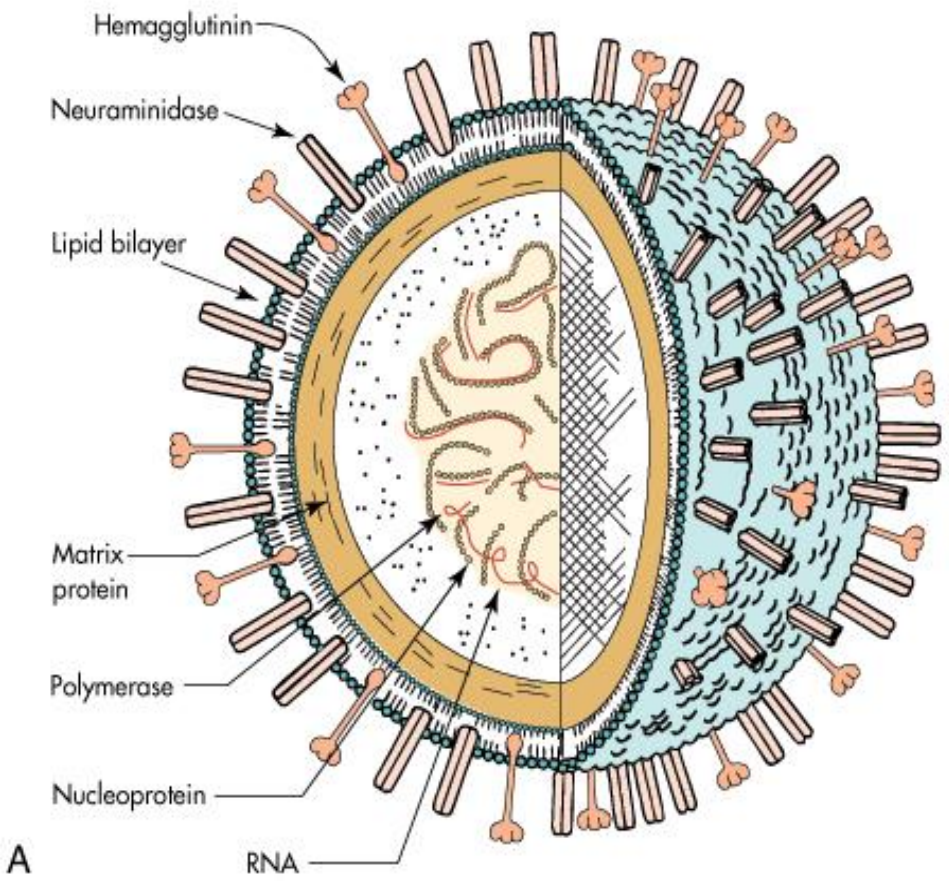
The generation of genetic reassortments in animals (e.g. duck) that are co-infected with human and animal influenza viruses is a proposed mechanism for antigenic shifts that led to theemergence of pandemic disease.

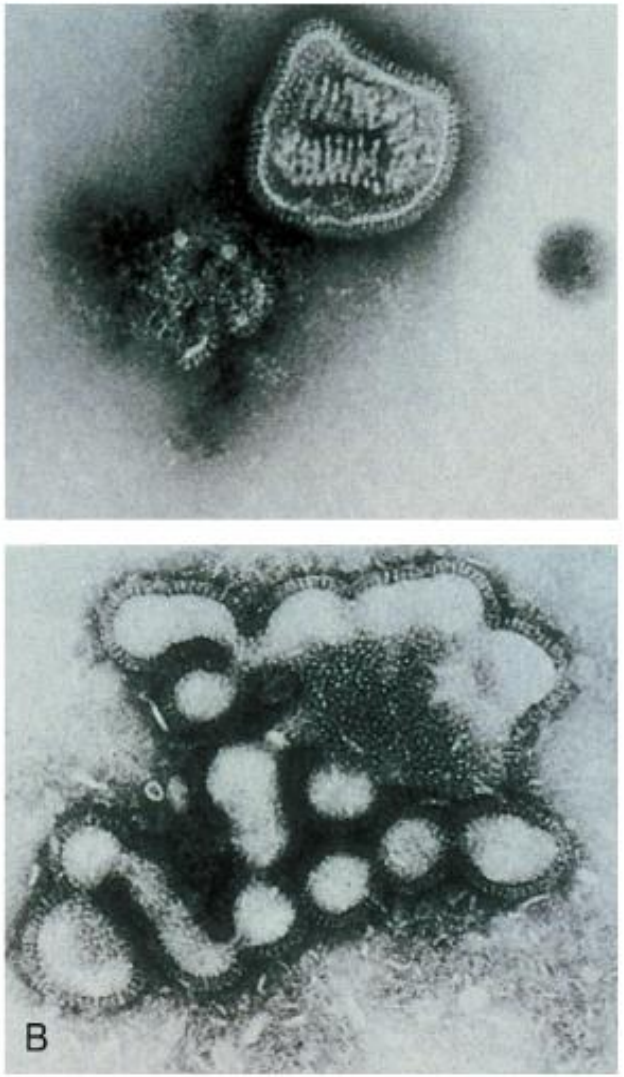
A outbreak of avian influenza A (H5N1) in Hong Kong yeilded isolates with exclusively avian genomes. In this case as well transmissibility of these isolates was minimal.

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)

4 December 2015

Main conclusions and options for response

- Highly pathogenic avian influenza (HPAI) of the subtypes A(H5N1) and A(H5N2) have been detected in birds in a backyard and in two poultry farms in the Dordogne region of France.
- The HPAI A(H5N1) virus detected in France is not related to the A(H5N1) viruses circulating in other parts of the world, but appears to have evolved from a low pathogenic avian influenza virus circulating in Europe.
- No human case has been reported related to the HPAI A(H5N1) virus detected in France.

No human case has been reported related to any HPAI A(H5N2) virus worldwide.

4 December 2015

• When avian influenza viruses circulate in poultry, sporadic infections or small clusters of human cases are possible in people exposed to infected poultry or contaminated environments, especially in households and at live bird markets in areas where the viruses are circulating. Sustained human-to-human transmission of influenza A(H5N1) virus and its highly pathogenic reassortants have never been observed.

• The risk of foodborne transmission, e.g. through the consumption of eggs or meat is considered extremely low.

• People having direct contact with diseased birds or poultry, or their carcasses (e.g. farmers, veterinarians and labourers involved in the culling and rendering) are at a potential risk of infection. Persons at risk of exposure should therefore wear personal protective equipment.

• People who have been exposed to the HPAI A(H5N1) or A(H5N2) virus should be monitored for at least 10 days.

• Animal and public health authorities should be prepared for a possible introduction of HPAI A(H5N1) or A(H5N2) virus into other European countries, although the risk is considered low.

- **Recommended composition of influenza virus vaccines for use in the 2015-2016 northern hemisphere influenza season**
- **26 February 2015**
- It is recommended that trivalent vaccines for use in the 2015-2016 influenza season (northern hemisphere winter) contain the following:
- an A/California/7/2009 (H1N1)pdm09-like virus;
- an A/Switzerland/9715293/2013 (H3N2)-like virus;
- a B/Phuket/3073/2013-like virus.
- It is recommended that quadrivalent vaccines containing two influenza B viruses contain the above three viruses and a B/Brisbane/60/2008-like virus.

In the Czech Republic
Seasonal influenza vaccination guideline

In the Czech Republic, seasonal influenza vaccination is provided on a non-compulsory, voluntary basis.

Based on the surveillance data from the Czech Republic and policies applied by other countries, the National Immunisation Committee (NIKO) recommends the following vaccination strategy for the Czech Republic:

Vaccination against seasonal influenza is intended for persons in whom it is desirable to reduce the risk of influenza and possible complications associated with influenza.

In the Czech Republic
Seasonal influenza vaccination guideline

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.).

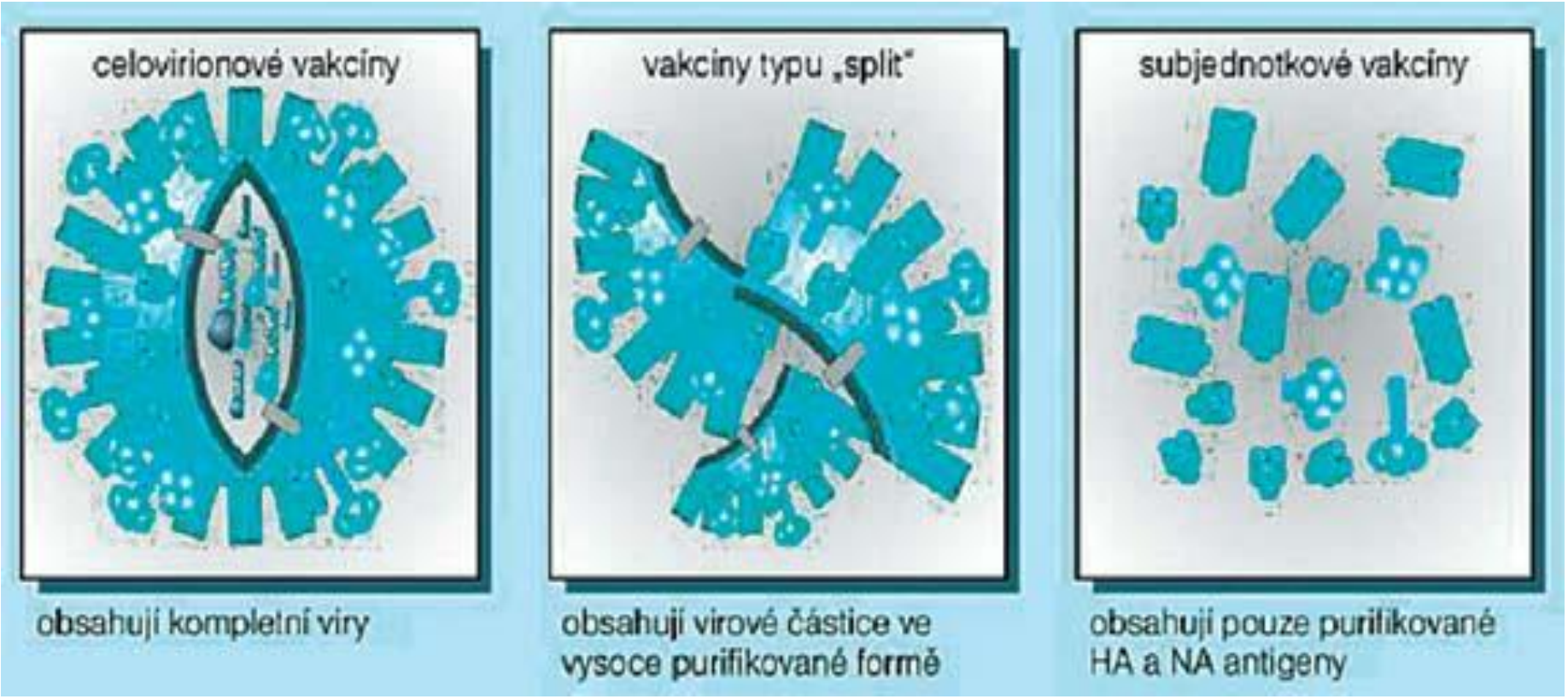
Specific profylaxis

- ***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

Types of the vaccine



History

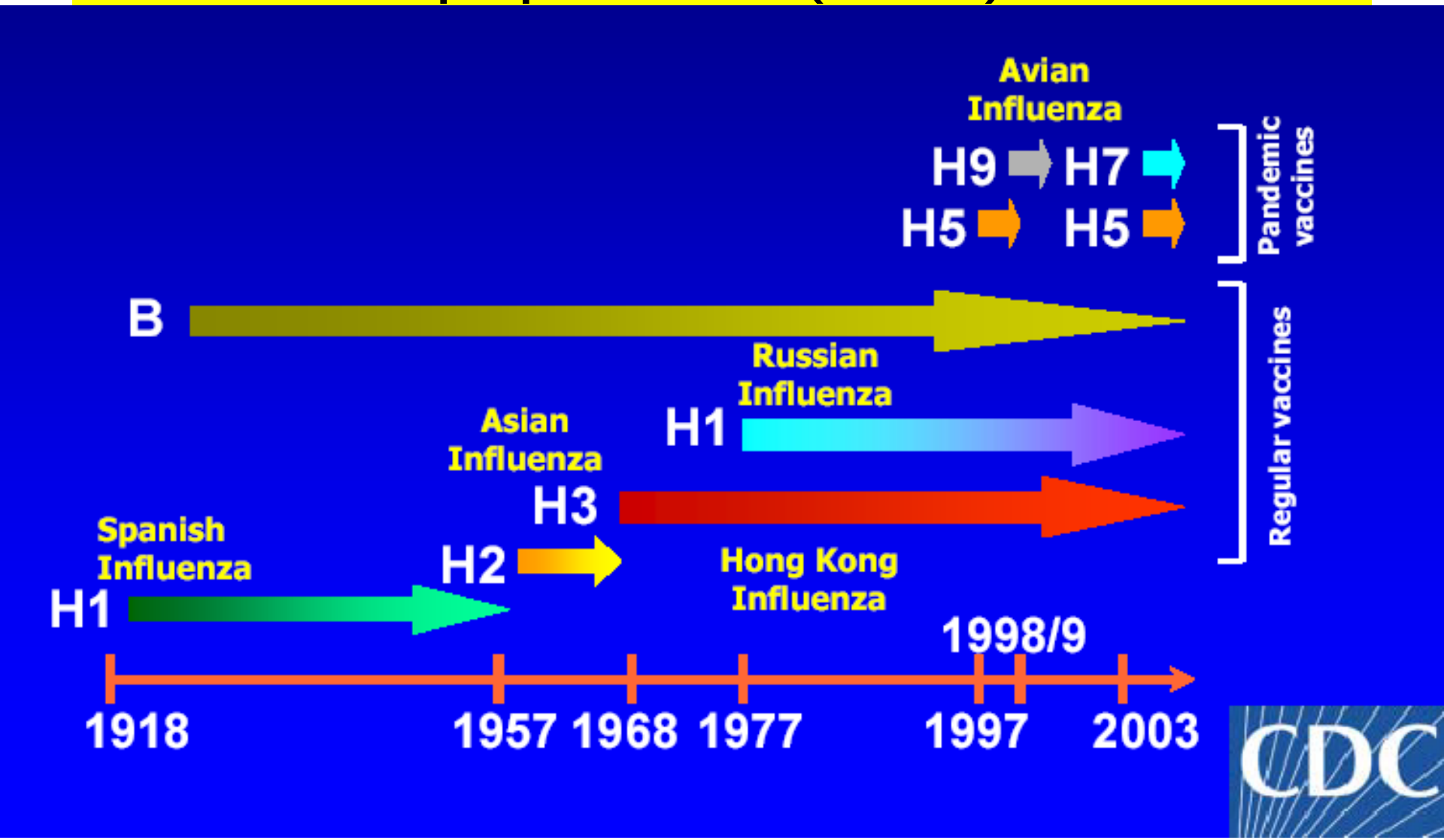
- From the 17. and 18. century are reports about the epidemics in the towns and viliges too.
- Consecutive some epidemics aflicted all continents except Austrálie
- „archeologic sérology“ detected:

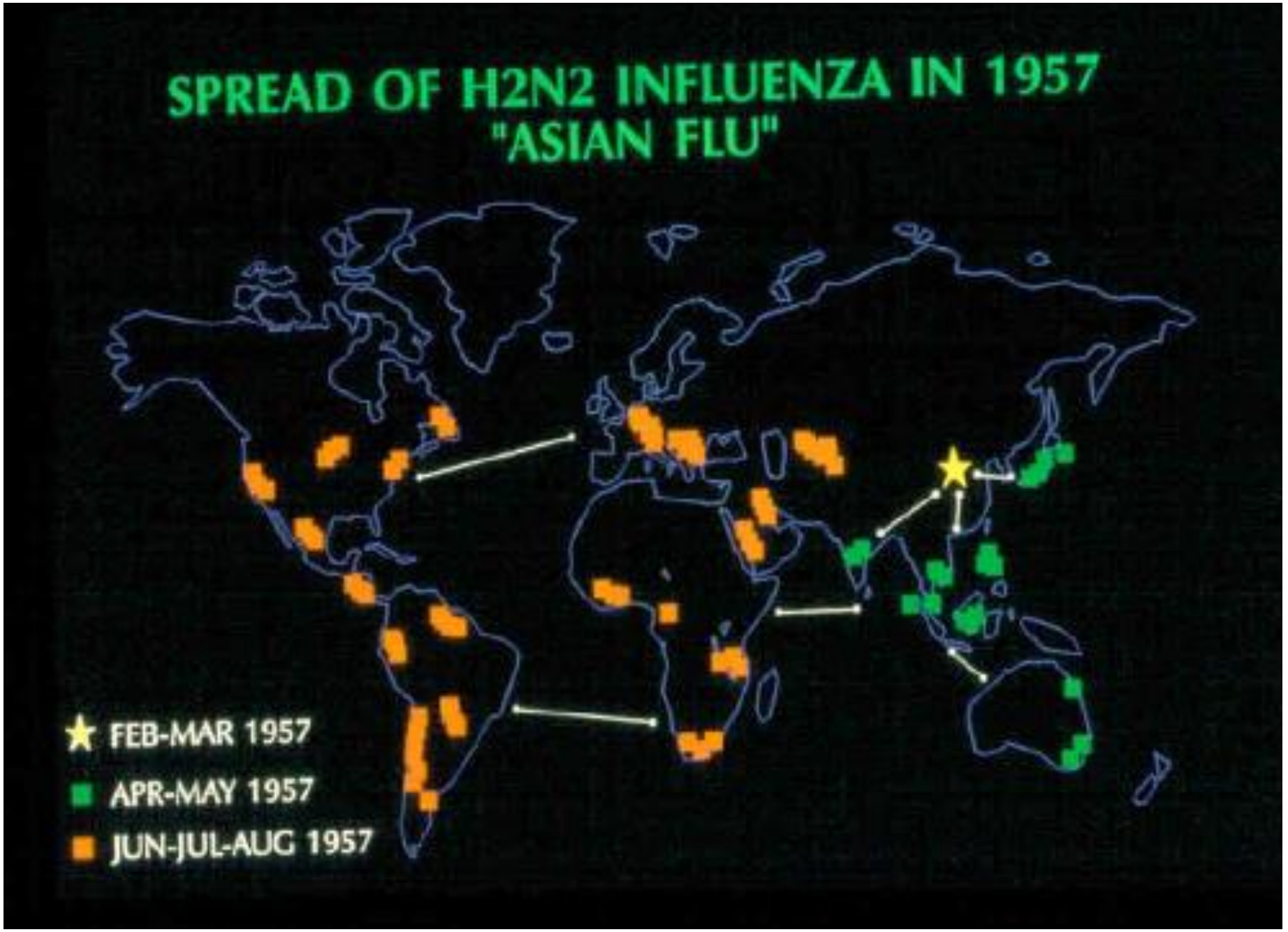
A (H2N2) in the 1889-1892 and

A (H3N8) in the 1898-1901

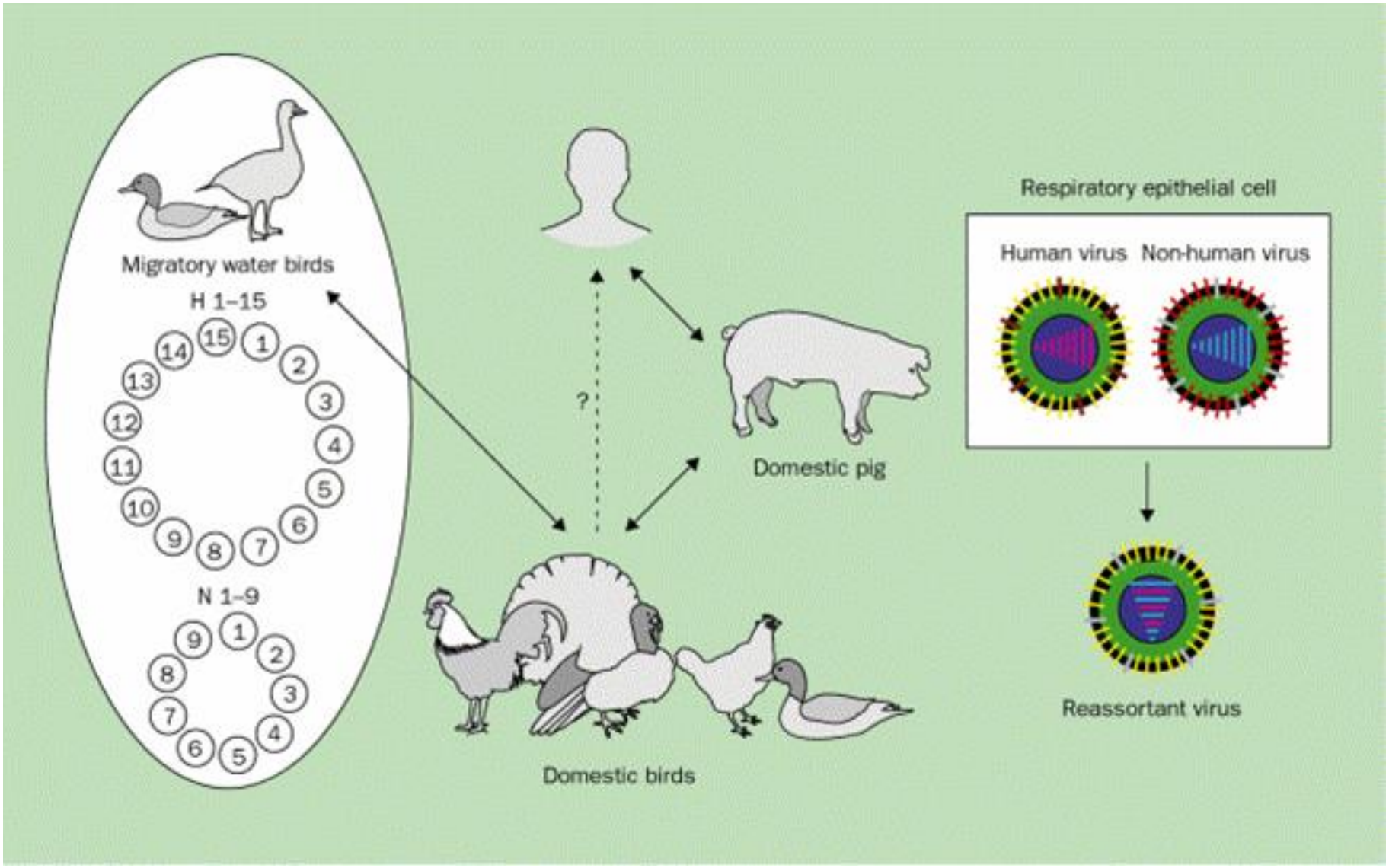
A (H1N1) in the 1918-1920 – „Spanish flu“

Incidence subtypes Flu A at human population (CDC)

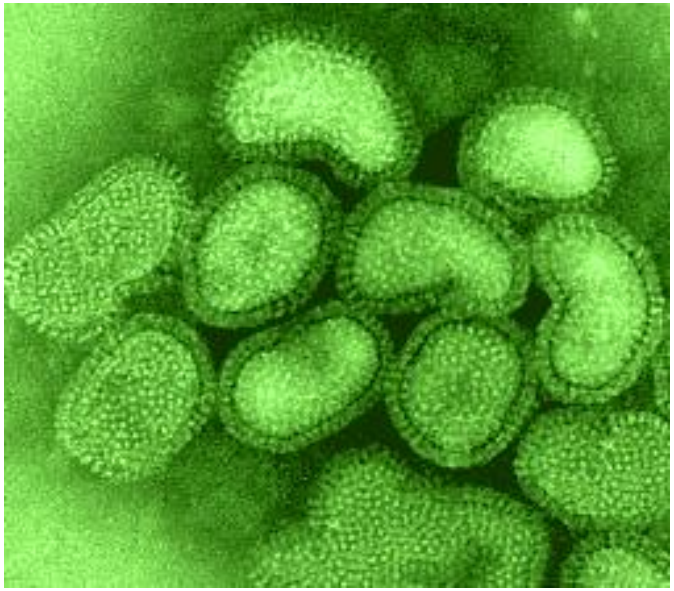



SPREAD OF H2N2 INFLUENZA IN 1957
"ASIAN FLU"
FEB-MAR 1957
APR-MAY 1957
JUN-JUL-AUG 1957

The rise of the pandemic strain

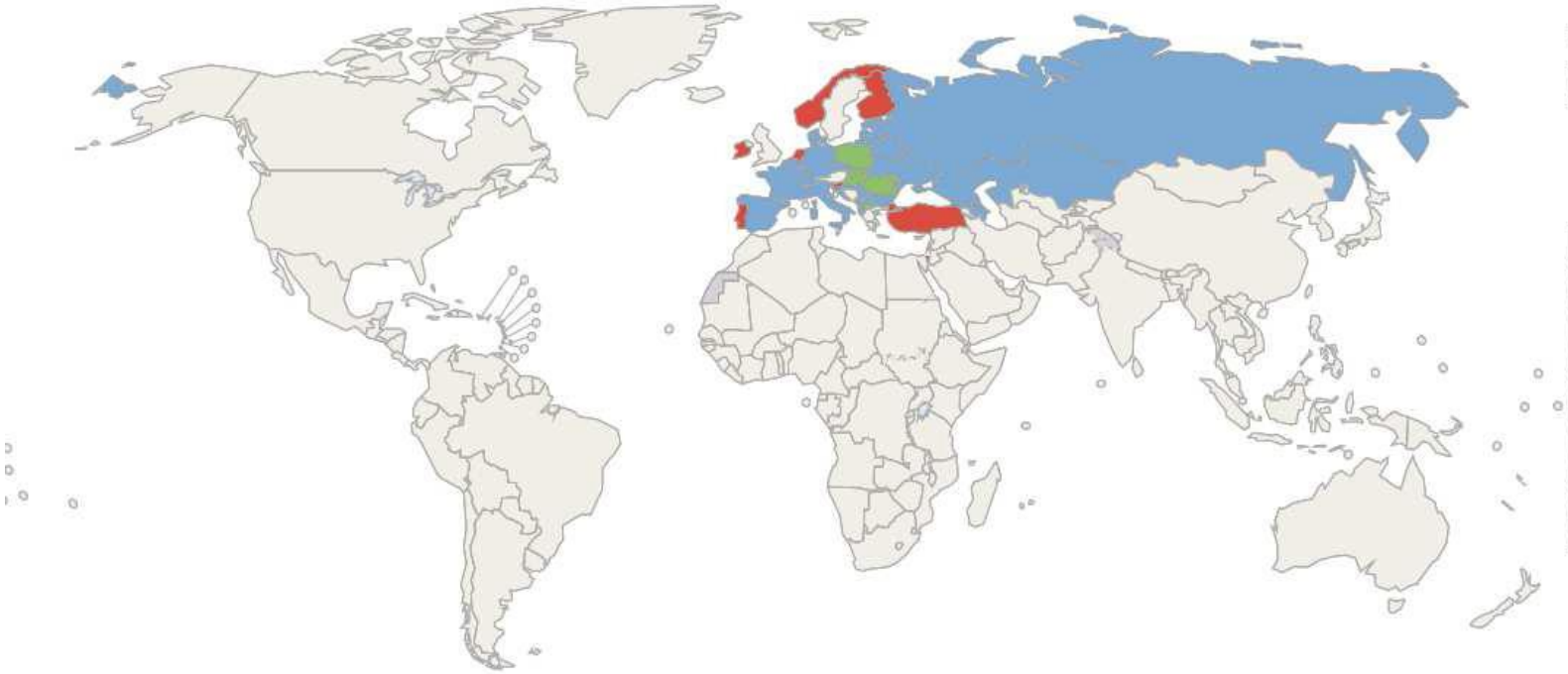


Influenza and H5N1



Influenza qualitative indicators: Geo Spread

Menu



Indicator selection:

Geo Spread

Year

1996	1997
1998	1999
2000	2001
2002	2003
2004	2005
2006	2007
2008	2009
2010	2011
2012	2013
2014	2015
2016	

Week selection:

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53

World Health Organization

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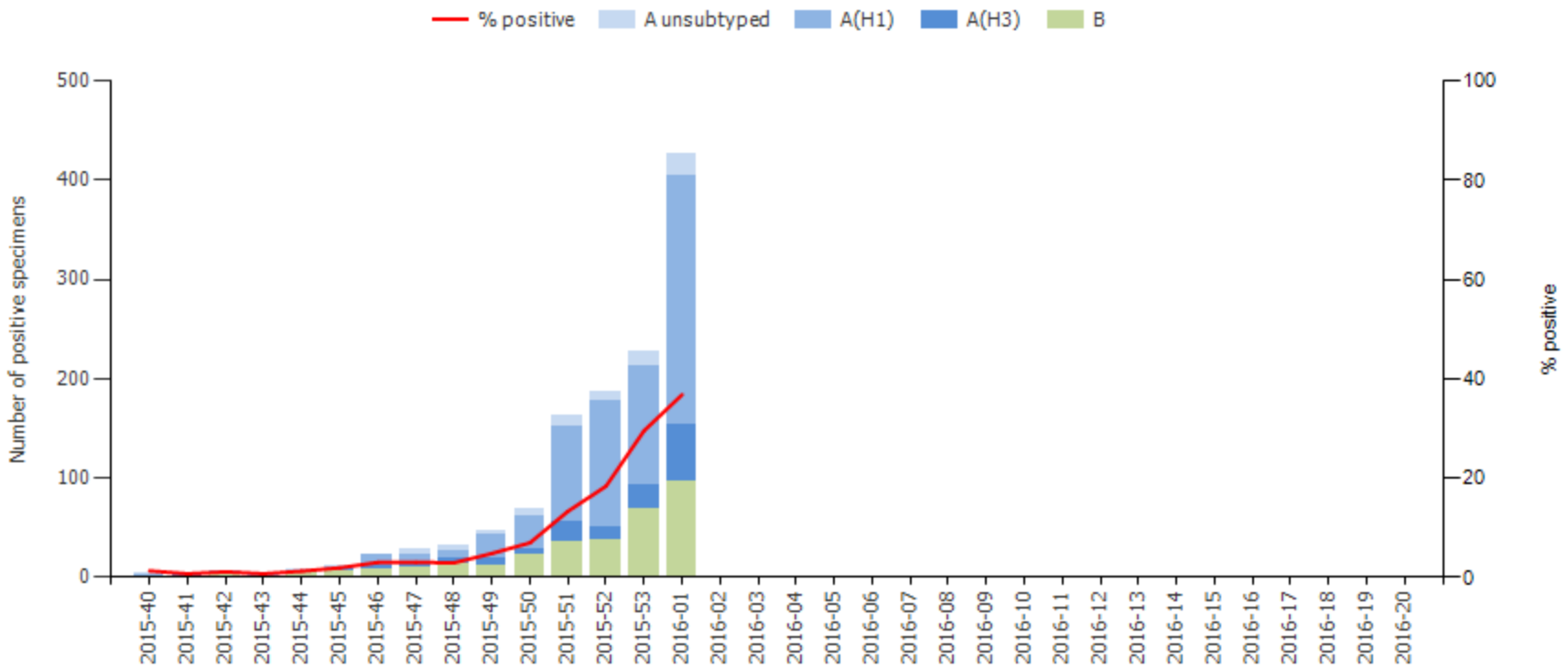
% positive
A unsubtyped
A(H1)
A(H3)
B
Number of positive specimens
% positive
500
400
300
200
100
0
100
80
60
40
20
0
2015-40
2015-41
2015-42
2015-43
2015-44
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2016-19
2016-20

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

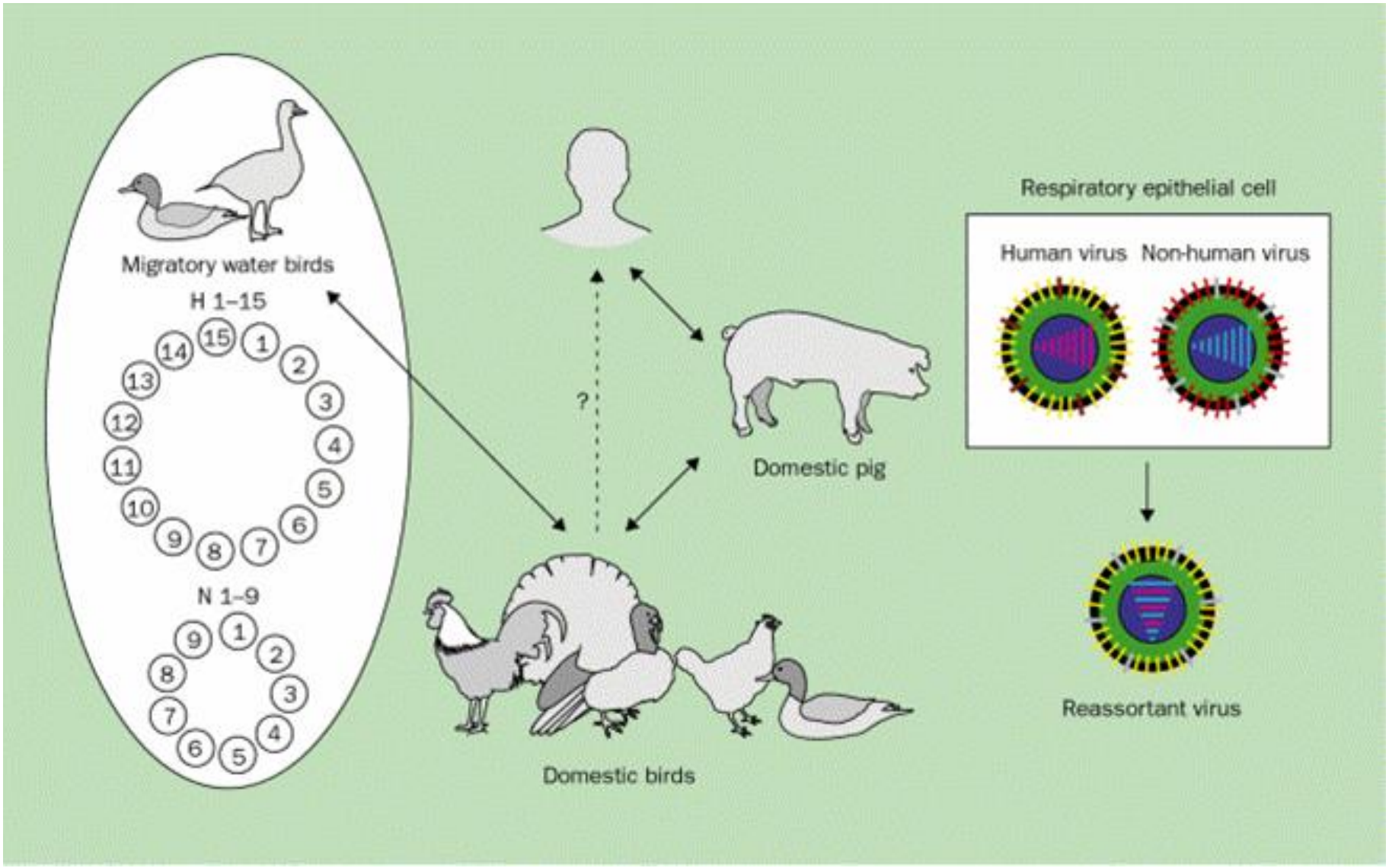
- očkováni proti chřipce popř. záznam o tomto očkování chybí. Věk pacientů se pohyboval
- v rozmezí 35 let – 82 let..

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

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

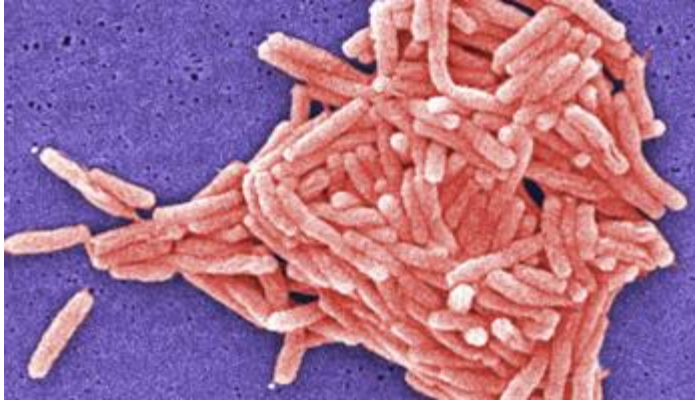
The rise of the pandemic strain



Interhuman transmission ?

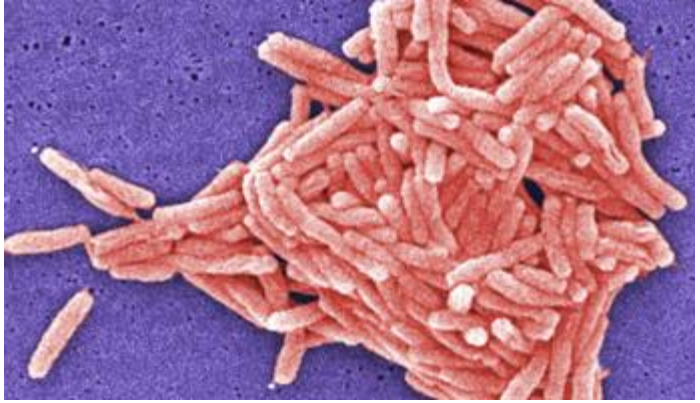
Farm by Hanoi, 2002 (CDC)

Legionellosis



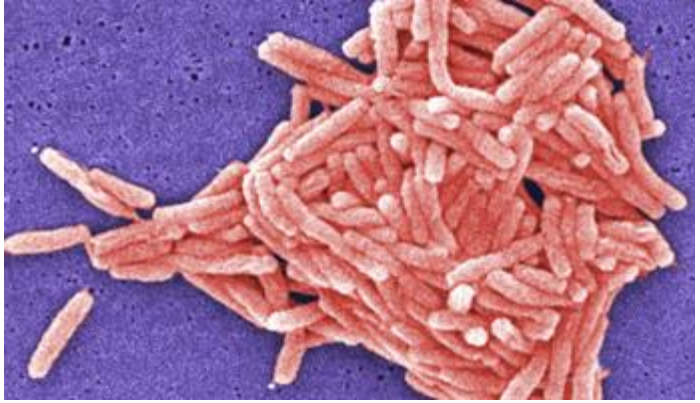
- People over the age of 50 are more at risk than younger people, and males are more at risk than females. Effective antibiotic treatment is available if the diagnosis is made early in the illness. Deaths occur in about 5-15% of travellers who get the disease, depending on their age and individual health 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.
-

Legionellosis



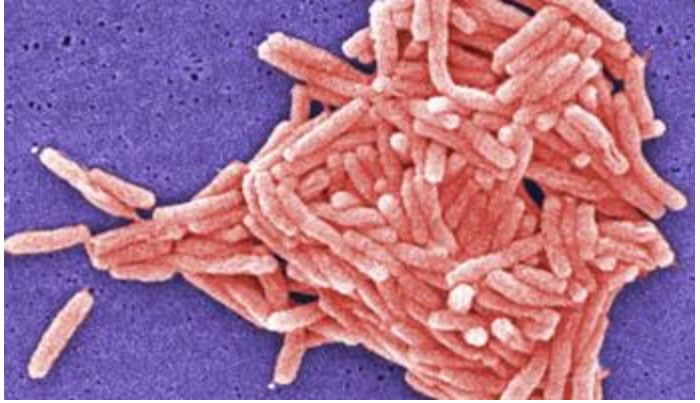
- The bacterium responsible for Legionnaires' disease was identified in 1976, after a large outbreak at a hotel in Philadelphia, USA. The disease got its name from the group of people affected in this outbreak. They were retired American service personnel who were attending a legion convention. Since 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.

Legionellosis



- **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.

Legionellosis



- 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.

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.

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.

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.

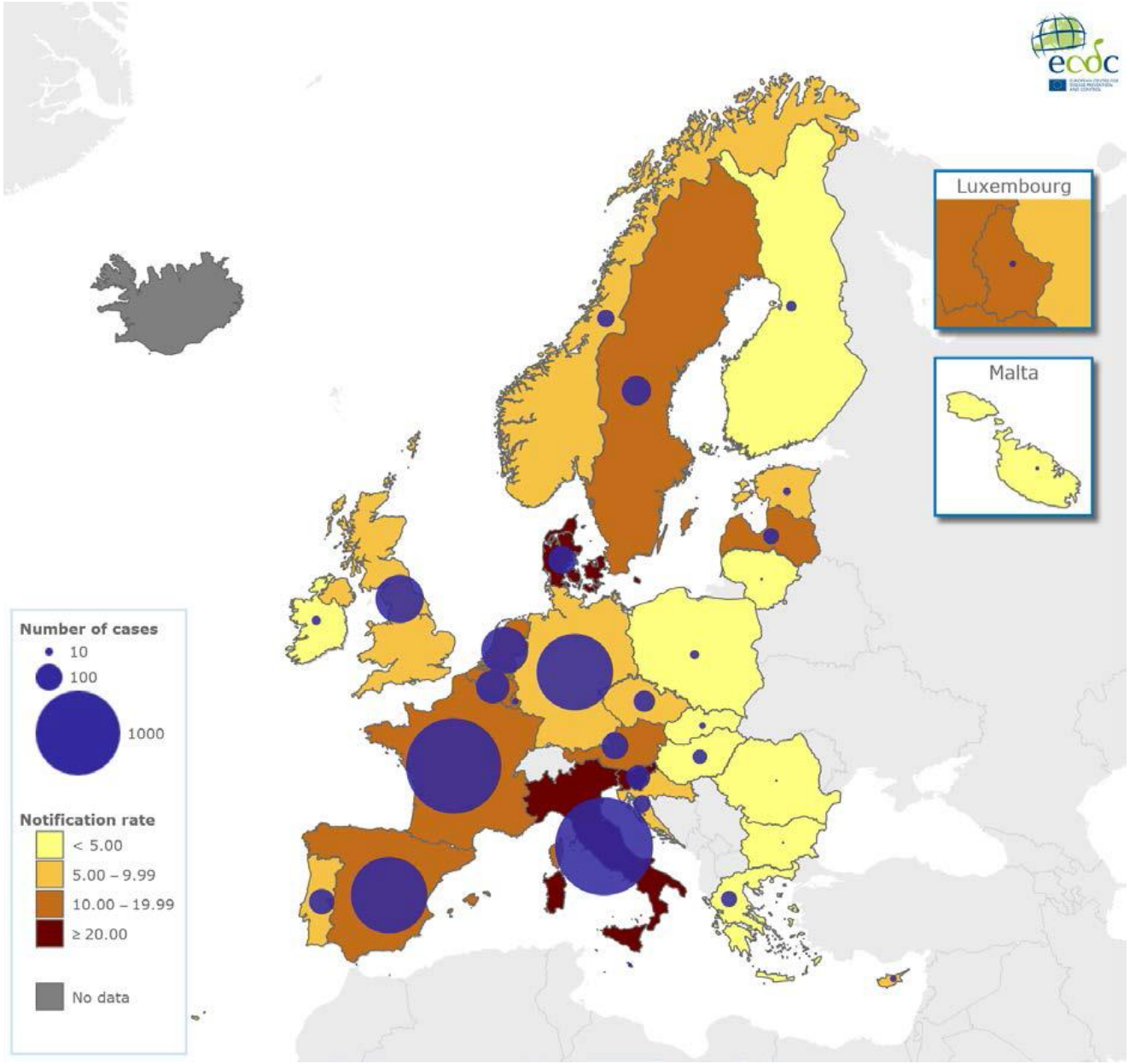
Laboratory criteria for a probable case

- 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.

Figure 5. Reported cases and notifications of Legionnaires' disease per million, by reporting



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.