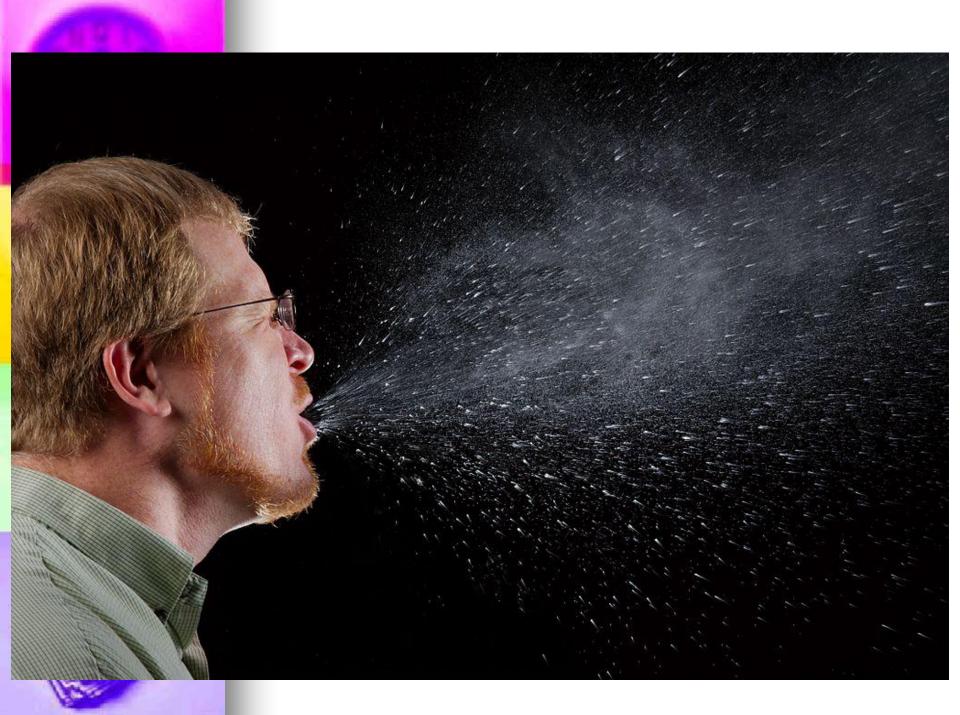


RESPIRATORY TRACT INFECTIONS

aBFEP051p – October 23, 2020 Kolářová M., mkolar@med.muni.cz





Bacterial infections

it is usually a mixture of bacterial infections or followed by viral infections

Tuberculosis Streptococci – group A,C and G Streptococcus pneumoniae Staphylococcus aureus Neisseria meningitis Haemophillus influenzae Pertussis Diphteria Mycoplasma pneumoniae Legionella pneumoniae

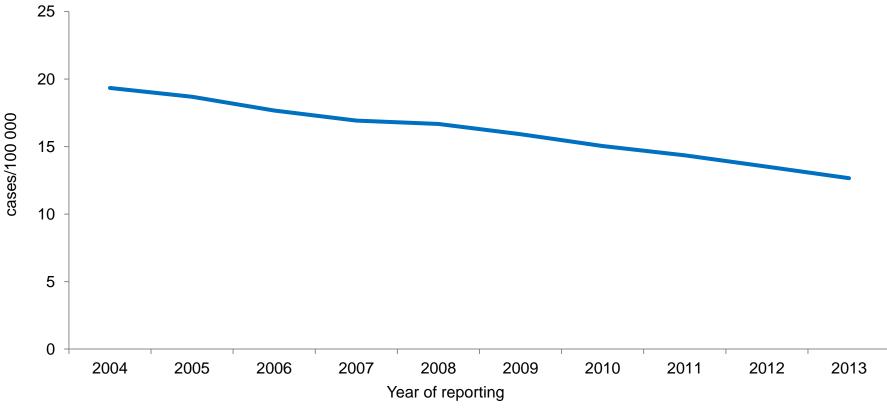
Tuberculosis

The most important causative agent of tuberculosis is Mycobacterium tuberculosis. M. tuberculosis, together with M. bovis, M. africanum and M. microti, form the 'M. tuberculosis complex', which is a group within the genus Mycobacterium. This genus also includes many different nontuberculous mycobacteria of which M. leprae and M. avium are best known.

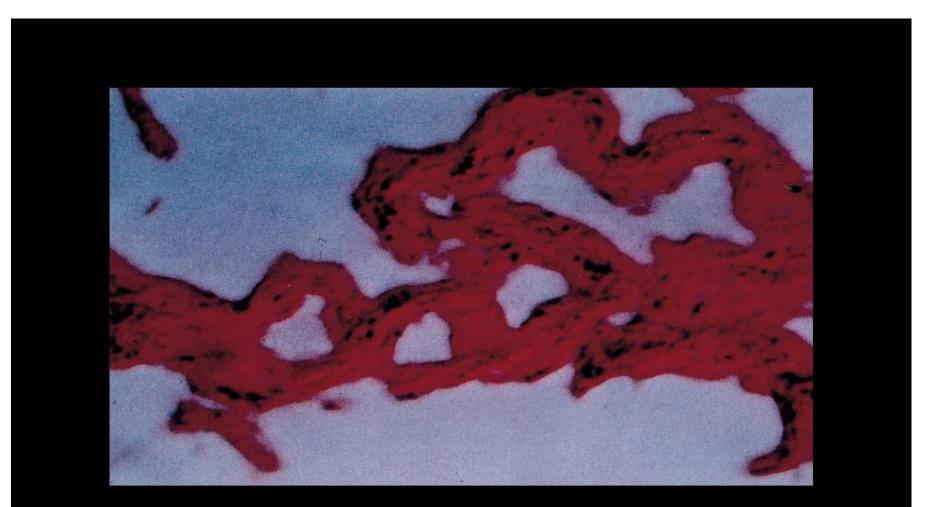
TB notification rate over time

•The TB notification rate has decreased from 19.3 per 100 000 population in 2004 to 12.7 in 2013.

Figure 2: TB notification rate per 100 000 population in EU/EEA 2004–2013



Ziehl-Neelsen stain of 'cords' of *Mycobacterium tuberculosis* isolated from a broth culture. Tubercle bacilli aggregate end to end and side to side to form serpentine cords, especially in broth cultures.





Clinical features and sequelae

- Infection with M. tuberculosis is asymptomatic. The symptoms that occur when TB disease develops are usually not very specific. Often there are complaints of tiredness, listlessness, loss of weight, sub-febrile body temperature and night sweating.
- In the case of pulmonary TB, usually a cough has been present for weeks or even months, possibly accompanied by haemoptysis. Localisation in the vertebral column (spondylitis tuberculosa) can, apart from back pain, also present itself as an abscess with vertebral collapse. Lymphadenitis tuberculosa usually presents itself by painless lymph node enlargement in the neck. Blood in the urine (haematuria) can present as the only symptom of TB of the kidney.
- In cases of co-infection with HIV, the clinical presentation can be less typical. This atypical presentation is usually seen in a more advanced stage of the HIV infection and is the result of impaired cellular immunity. HIV-infected patients show disseminated forms of TB relatively often.
- In the pre-chemotherapy era, case-fatality from tuberculous meningitis approached 100 per cent. Pulmonary TB accounted for the majority of deaths. Sputum smear-positive TB has a much higher fatality than sputum smear-negative TB. Untreated sputum smear-positive TB leads to death in about 30–40 per cent of cases within one year and cumulatively kills about 50–70 per cent of cases within 5 to 7 years5.

Epidemiology

- The average notification rate in the European Union (EU) and European Economic Area (EEA) region is 16.7 per 100 000 population (2008 data).
- In low-incidence countries (reporting a notification rate below 20 per 100 000), TB is predominant in vulnerable populations. Examples of vulnerable populations include individuals from high incidence countries, prisoners, contacts of contagious patients, persons who have previous had TB, drug addicts, alcoholics, illegal immigrants and the homeless. In some of these risk groups the incidence is increased due of ongoing

Transmission

- Humans are the main reservoir for M. tuberculosis and M. africanum. For M. bovis, cattle are the most important host. Cases of TB can occur sporadically in monkeys and some other mammals.
- Transmission of TB is aerogenic. After coughing, sneezing, speaking or singing, infected sputum droplets can dry and form into droplet nuclei of approximately 6–18 µm. These droplet nuclei can float in the air for a longer period and penetrate into the alveoli of the host after inhalation. In moist warm air, the droplet nuclei can survive for hours.
- The lifetime risk of developing TB for people outside of the risk groups is approximately ten per cent11. For HIV-infected persons this risk is much higher, amounting to 8–10 per cent per year.
- Patients with a negative culture of sputum ('closed' TB) and cases of extrapulmonary TB are not considered to be contagious.
- In general, in patients with a positive Ziehl-Neelson slide and/or positive culture of their sputum, the start of coughing complaints is considered to be the start of the period of infectiousness.

Transmission II

The incubation period (between infection and the first signs of illness) varies between eight weeks to a lifetime. The greatest chance of progressing to disease is within the first two years after infection, with half of all cases of disease occurring within five years of the original infection. However, a lifelong risk of progression to disease remains for all those people with 'dormant' organisms.

People in whom infection progresses to disease are only a minority of all infected persons.

- People with latent TB infection are never infectious.
- The risk of transmission in cases of active TB is determined by patient factors and the type of contact made with their surroundings.
- The level of contagiousness of TB patients depends on the concentration of bacteria in the sputum, the severity of the cough and the coughing hygiene practiced by the patient. In general, the closer and/or more frequent the contact, the higher the chance of transmission. Characteristics of the place of contact may also play an important role (e.g. size of the room, ventilation). Usually, intimate contacts (household) are at the highest risk of being infected14.

• Prevention

- The vaccine currently available is the BCG-vaccine (Bacille Calmette Guérin). This is a live, weakened strain of M. bovis. It mainly gives protection against severe forms of the disease, like meningitis TB and miliary TB, in children under five years of age.
- The World Health Organization (WHO) advises BCGvaccination for all newborns in countries with a high incidence of TB within the framework of the Expanded Program of Immunization (EPI).
- Within the EU, the policy on BCG-vaccination varies between countries. Low incidence countries commonly vaccinate only persons with an increased risk of TB; for example, children whose parents come from high incidence countries and who travel regularly to their home country.
- BCG-vaccination should not be given to the immunosuppressed (e.g. HIV, leukaemia, chemotherapy) due to the increased risk for complications. Also, BCG-vaccination during pregnancy should be avoided, even though no harmful effects on the foetus have been observed.

Prevention II

- Practising cough hygiene will decrease the spread of all types of infections that are spread through the air.
- Preventing the transmission of the disease is the foundation for effective TB control programmes. Preventive measures focusing on the early diagnosis and immediate effective treatment of people with contagious TB is therefore essential. Many factors have been shown to be associated with a delay in diagnosis including old age, low education/awareness, poverty, negative sputum smear, extrapulmonary TB, female sex and a history of immigration.
- Passive case finding is defined as the detection of TB cases among patients attending healthcare facilities because they have symptoms. Active case finding focuses on the screening of high-risk groups (immigrants, drug addicts, homeless people and prisoners) for TB. It aims to identify and treat TB cases at an early stage and to provide preventive treatment to those at the highest risk for developing active TB.

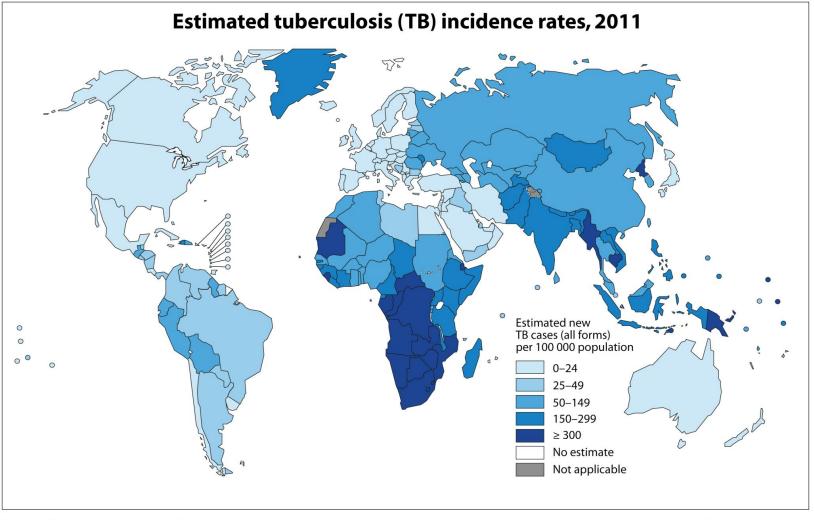
Management and treatment

- Notification of TB cases is compulsory in most EU countries6.
- Cases of respiratory TB require infection control precautions until infectivity has been eliminated by effective chemotherapy; this often requires two weeks treatment with drugs to which the infecting strain is sensitive19,20.
- Contact investigation can be performed as soon as a contagious patient with TB has been diagnosed. The aim of this activity is to identify secondary cases of TB and/or newly infected persons. If a secondary case is identified through the contact investigation, this patient can be diagnosed early which then reduces the chance of further transmission21.
- Newly infected persons can be offered prophylactic treatment in order to reduce their chance of progression from latent to active disease1.
- The treatment of active TB has two phases: an initial intensive phase and a continuation phase. The recommended standard regimen by the WHO for all new cases is an intensive phase of two months with isoniazid, rifampicin, pyrazinamide and ethambutol and a continuation phase of four months with isoniazid and rifampicin.
- Drug resistance is increasing in many countries, and treatment failure and relapse are strongly associated with initial drug resistance23. Individual risk factors include history of previous treatment for TB, recent contact with drugresistant case and HIV infection24.
- Persons at a high risk for developing TB (cases with recent M. tuberculosis infection and those with clinical conditions associated with progression to active TB like HIV, for example) will be given prophylactic treatment25,26.

• Areas of uncertainty

- Use of interferon gamma-release assays (IGRA): IGRA, a new diagnostic tool, is gradually being introduced in circumstances in which the tuberculin skin test is currently used.
- Caution is necessary when testing certain populations because of limited data in the use of IGRAs. More data are necessary on their use in younger age groups, among persons recently exposed to M. tuberculosis, and in immunocompromised persons (e.g. cases of HIV, users of immunosuppressive drugs, selected haematological disorders, those with specific malignancies along with cases of diabetes, silicosis and chronic renal failure). Limited data are available on the use of IGRA to determine who is at risk for developing active TB.
- Treatment and prophylaxis of MDR TB and XDR TB cases: There is little evidence regarding the treatment of MDR TB and XDR TB. In the absence of controlled trials, expert opinions prevail and perspectives differ according to personal experience. As a result, significant discrepancies are found in the guidelines published by scientific societies29,30. Success rates for the treatment of MDR TB patients vary between 50–80 per cent, depending on the treatment setting.
- Also, evidence for the effects of latent TB infection treatment in people exposed to MDR TB is extremely limited both in quantity and quality. For the treatment of MDR TB at present, we see a great variety in recommended treatment.
- Further studies are required on the level of recurrence of TB following successful treatment from real-life directly observed treatment, short-course (DOTS) programmes.

- In 2011, the countries of the WHO European Region
- reported 295 968 new episodes (new and relapses)
- of TB (33 per 100 000 population) out of an estimated
- 380 000 (range 321–437 000), which would correspond
- to 42 cases per 100 000 population (range 36– 49).
- More than 85% of them were in the 18 high priority



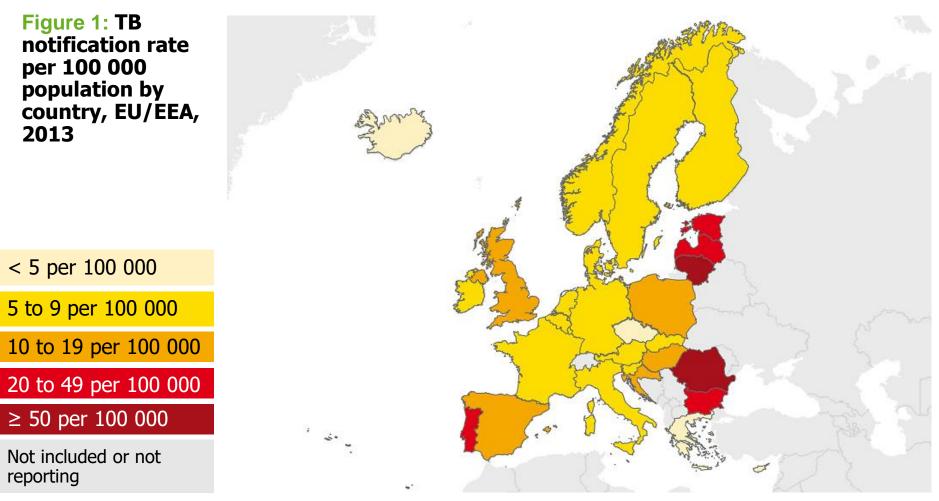
The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers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

Source: *Global Tuberculosis Report 2012*. WHO, 2012.

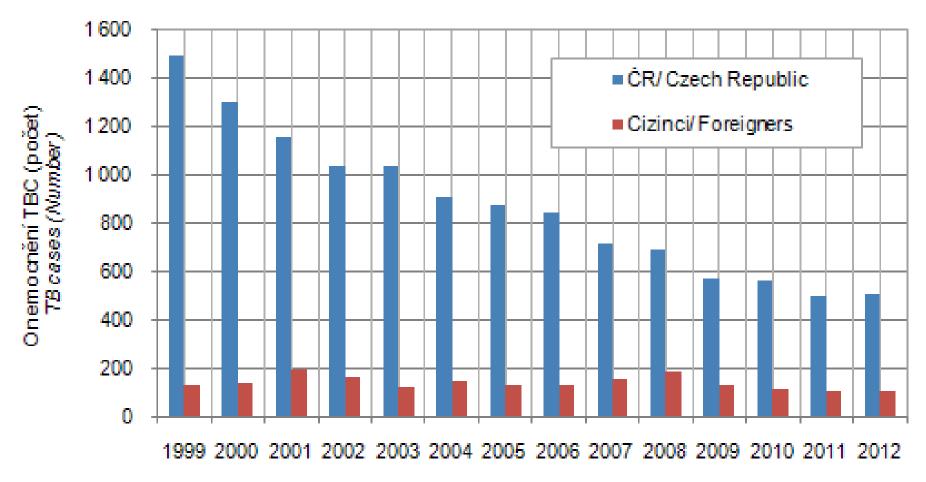


•In 2013, 64 844 TB cases were reported in the EU/EEA.

•The notification rate was 12.7 per 100 000 population (range 3.4-83.5).

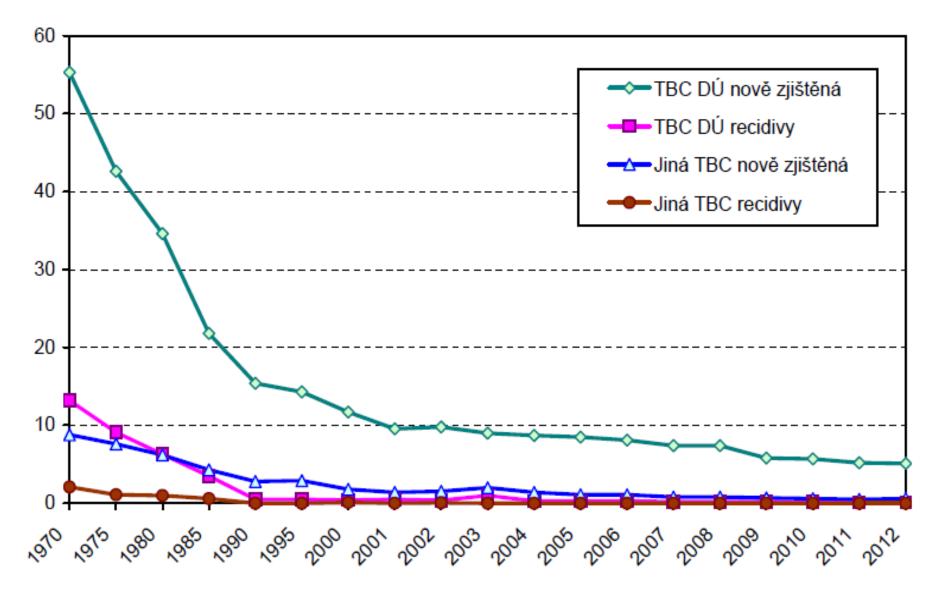


Nově hlášená onemocnění TBC v ČR, 1999-2012 New notified TB cases in the CR; 1999-2012

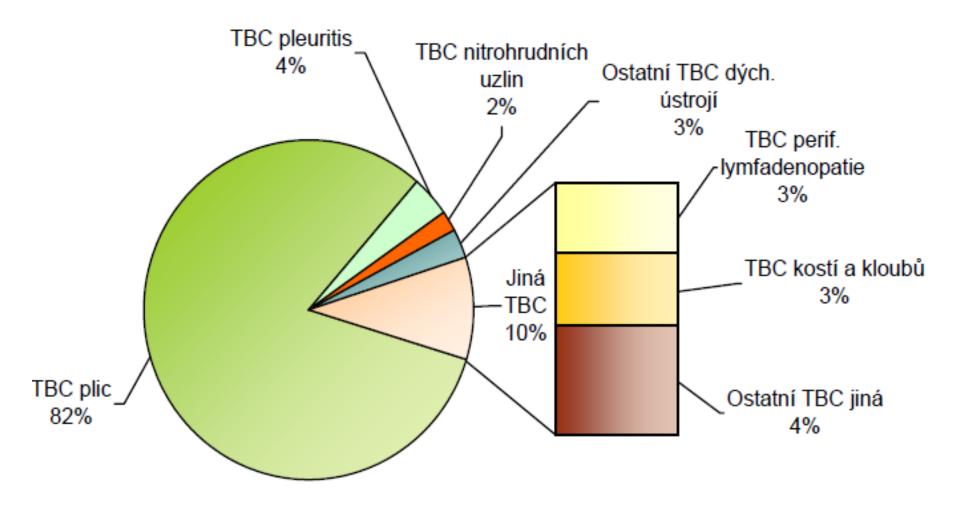


Rok/ Year

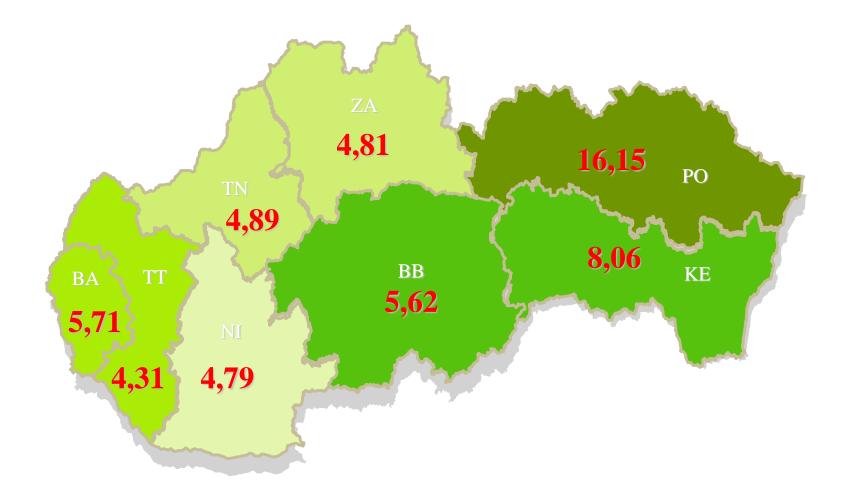
Vývoj počtu hlášených TBC/100 tis.obyvatel,ČR



Struktura hlášené TBC podle dg., rok 2012



TBC – in Slovakia - 2013 number of cases/100 000 residents



Source: Doc. MUDr. Ivan Solovič, CSc.

- More than 44 000 (44–46 000) deaths were estimated
- to have been caused by TB in the Region (4.9 per 100 000 population) (range 4.7–5.3).
- Overall, 92% of deaths occurred in the 18 HPC.
- The notification shows a 24% decrease compared to
- 2005, however there is a significant difference in TB
- notification rates among the countries, from 2 to 119
- per 100 000 population.

- In 2011, there were 12 751 (56.5%) TB cases with HIV co-infection detected from the 22 500 (range 18–27 000) estimated in the WHO European Region. Estimated prevalence of HIV infection among incident TB patients was 6% (range 5.6–6.2%), with 3.6% of these cases occurring in the EU/EEA countries and 6.5% in the non-EU/EEA countries.
- Due to the low reporting coverage of HIV testing (60%), only 12 751 (6.2%) of the 205 578 new TB and previously treated cases were found to have HIV co-infections.
- Three countries reported higher rates of HIV positivity among TB patients: Ukraine (18.5%), Malta (16.7%) and Estonia (15%).

- Of the 78 000 estimated MDR-TB cases in the Region, around 30 000 (38%) were detected in 2011.
- In all, 98% of them were reported by 18 HPC. The prevalence of MDR among new TB cases in the Region amounted to 14% and 7.7% among previously treated cases.
- Although testing coverage for XDR has almost doubled in the Region, it is still only at 9%, documenting that 11% of MDR-TB patients are XDR-TB.

In response to the alarming problem of MDR-TB, all 53 Member States have fully endorsed the Consolidated Action Plan to Prevent and Combat Multidrug- and Extensively Drug-Resistant Tuberculosis in the WHO European Region 2011–2015 and its accompanying Resolution EUR/RC61/R7 from the sixty-first session of the WHO Regional Committee for Europe in 2011. The Action Plan includes a set of activities for countries, WHO and partners in order to achieve universal access to prevention and treatment of M/XDR-TB. WHO is currently preparing a detailed report on progress with the implementation of the Consolidated Action Plan to Prevent and Combat Multidrug- and

Haemophilus influenzae type b (Hib).



Other familiar diseases that vaccines protect against include chickenpox, hepatitis A and B, and Haemophilus influenzae type b (Hib). Hib causes meningitis, an inflammation of the fluid-filled membranes that surround the brain and spinal cord. Meningitis can be fatal, or it can cause severe disabilities such as deafness or mental retardation. This disease has nearly disappeared among babies and children in the United States since the Hib vaccine became widely used in 1989.

Invasive Haemophilus influenzae disease

Invasive Haemophilus influenzae disease has become rare; the notification rate in Europe was 0.49 per

100 000 population, with a slightly ascending trend which may be attributed to improved surveillance in most countries.

Country-specific rates were highest in northern Europe and in the United Kingdom;
 age-specific rates were highest in children under one year and adults aged 65 years or over.
 The national immunisation schedules of all EU/EEA countries include the Hib vaccine, which has led to a

progressive reduction of type b serotype infections.

Even though there appears to be a trend towards an increase in disease due to noncapsulated (nontypeable) strains, European data is too scarce to draw conclusions on serotype replacement.

Continued monitoring of strains, together with their associated clinical syndromes, is essential for assessing the effect of interventions.

In 2012, 2 545 confirmed cases of invasive Haemophilus influenzae disease (all serotypes) were reported by 27 countries, 24 of which have surveillance systems with national coverage. Belgium, France and Spain reported data from sentinel surveillance and therefore had to be excluded from the notification rates analysis, while no confirmed cases were reported from Malta for 2012.

Pertussis

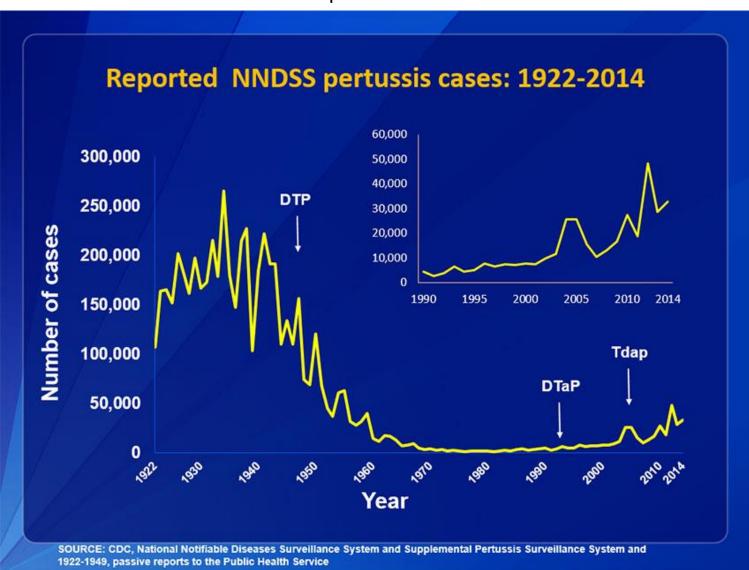


Pertussis is an acute bacterial infection of the respiratory tract, caused by the bacterium *Bordetella pertussis*. The disease is characterised by a severe cough, which can last two months or even longer.

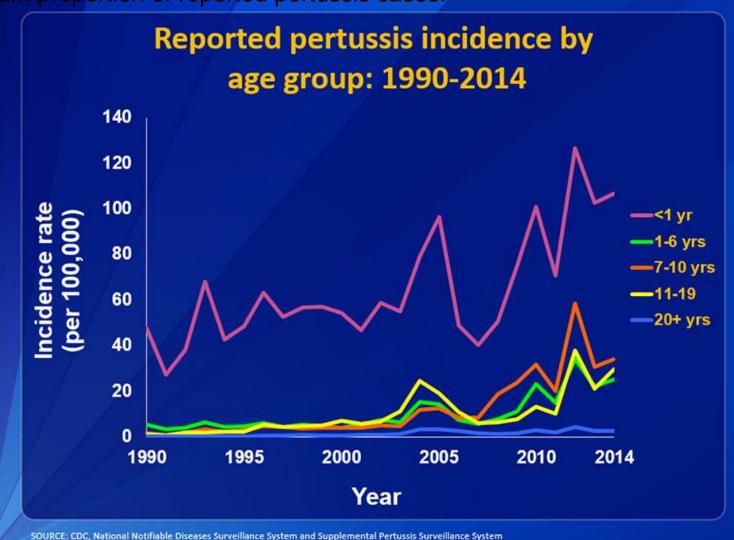
Humans are the only reservoir. Infected adults usually have only mild symptoms, but can shed bacteria for weeks. Following infection (by inhalation of droplets), susceptible individuals develop symptoms after an incubation period of about 10 days. The typical paroxysmal cough is usually seen in young children. Babies less than six months old may not cough, but they manifest dyspnea and paroxysmal asphyxia and are the most likely to die of the disease unless they receive suitable treatment.

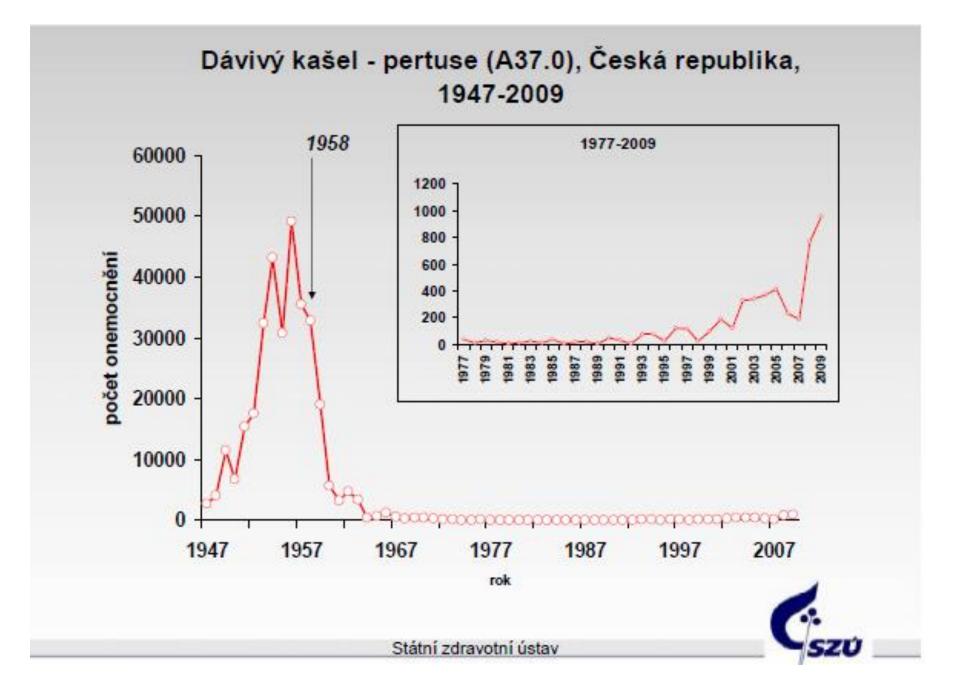
Affected children are also exposed to complications such as pneumonia, atelectasia, weight loss, hernia, seizures, encephalopathy (probably due to hypoxia). Antibiotics may reduce the duration of the disease, especially if administered in its early stages.

This graph illustrates the number of pertussis cases reported to CDC from 1922 to 2014. Following the introduction of pertussis vaccines in the 1940s when case counts frequently exceeded 100,000 cases per year, reports declined dramatically to fewer than 10,000 by 1965. During the 1980s pertussis reports began increasing gradually, and by 2014 more than 32,000 cases were reported nationwide.



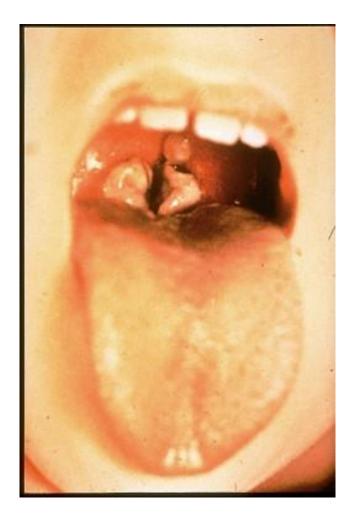
This graph shows reported pertussis incidence (per 100,000 persons) by age group in the <u>United States from 1990–2014</u>. Infants aged <1 year, who are at greatest risk for serious disease and death, continue to have the highest reported rate of pertussis. School-aged children 7 to 10 years continue to contribute a significant proportion of reported pertussis cases.

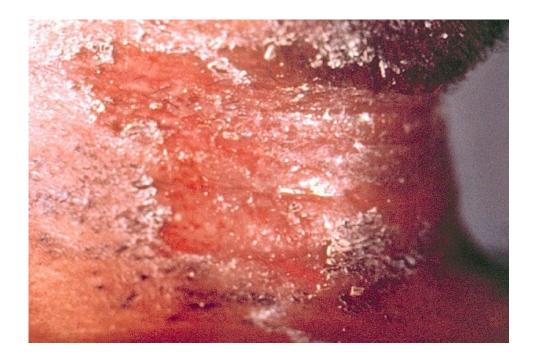




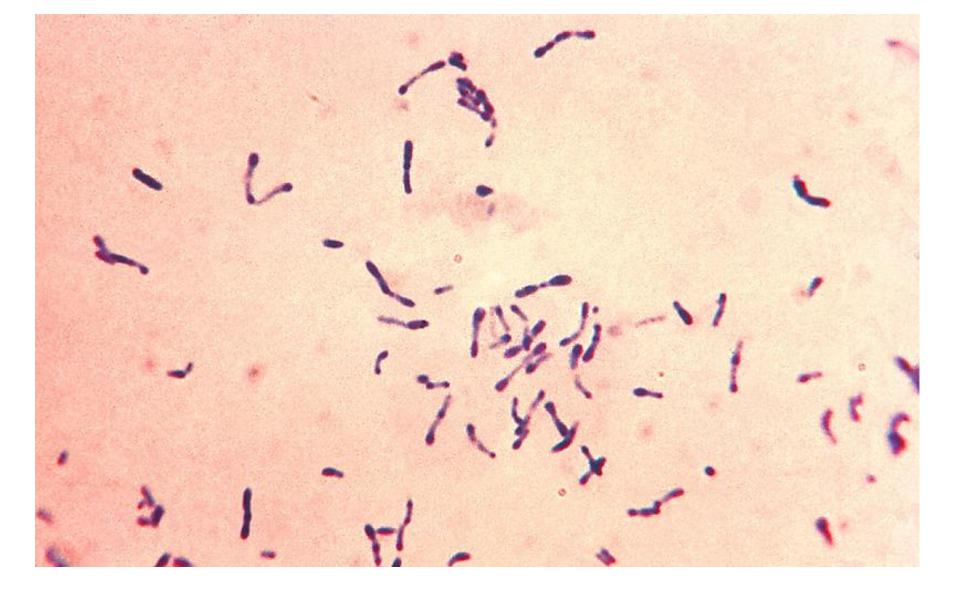
 Recommendation for vaccination against pertussis for of women in pregnancy.

Diphtheria:









PHIL Photo ID#7323

Causes and Transmission

Diphtheria is an infection caused by the toxic *Corynebacterium diphtheriae* bacterium.

Diphtheria is spread (transmitted)

from person to person,

usually through respiratory droplets, like from coughing or sneezing.

Rarely, people can get sick from touching open sores (skin lesions) or clothes that touched open sores of someone sick with diphtheria.

A person also can get diphtheria by coming in contact with an object, like a toy, that has the

Symptoms

When the bacteria get into and attach to the lining of the respiratory system, they produce a poison (toxin) that can cause:

- Weakness
- Sore throat
- Fever
- Swollen glands in the neck (sometimes referred to as "bull neck")



The poison destroys healthy tissues in the respiratory system. PHIL Photo ID#5325

Within two to three days, the dead tissue forms a thick, gray coating that can build up in the throat or nose. This thick gray coating is called a "**pseudomembrane**."

It can cover tissues in the nose, tonsils, voice box, and throat, making it very hard to breathe and swallow.

The poison may also get into the blood stream and cause damage to the heart, kidneys, and nerves.

The incubation period of diphtheria is 2–5 days (range: 1–10 days).

After:

✓ the provisional clinical diagnosis is made
 ✓ and appropriate cultures are obtained,
 persons with suspected diphtheria should be given:

1.	 antitoxin and
2.	- antibiotics in adequate dosage
and	
3	 placed in isolation

Diphtheria once was a major cause of illness and death among children. This upper airway infection often results in a grayish, thick membrane that grows in the throat and obstructs breathing. Other symptoms include fever, hoarseness, and coughing.

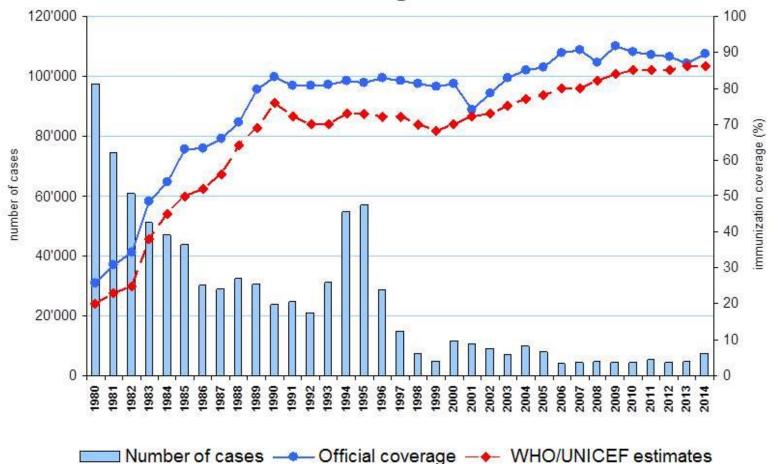
Most diphtheria deaths resulted not from <u>blocked airways</u> but from the paralyzing **toxin** the bacterium secretes, which can cause the heart or other organs to fail.

For clinical purposes, it is convenient to classify diphtheria into a number of manifestations, depending on the site of disease:

- Respiratory diphtheria
 - Nasal diphtheria
 - Pharyngeal and tonsillar diphtheria
 - Laryngeal diphtheria
- Cutaneous diphtheria



Diphtheria global annual reported cases and DTP3 coverage, 1980-2014





In 2014, 7,321 cases of diphtheria were reported worldwide to the World Health Organization, but many more cases likely go unreported.

The case-fatality rate for diphtheria

has changed very little during the last 50 years.

The overall case-fatality rate for diphtheria is 5%–10%,

with higher death rates (up to 20%) among persons younger than 5 and older than 40 years of age.

Before there was treatment for diphtheria, the disease was fatal in up to half of cases.

Some strains are toxin-producing and can cause fatal illness.

In the EU/EEA.

The reported number of cases of diphtheria remains low.

During 2009–2013, 102 cases of diphtheria were reported in the EU/EEA with 55 cases of C. diphtheriae (cca 0.01 per 100 000 population).

There has been an increase in the number of C. diphtheriae cases reported at EU level since 2011.

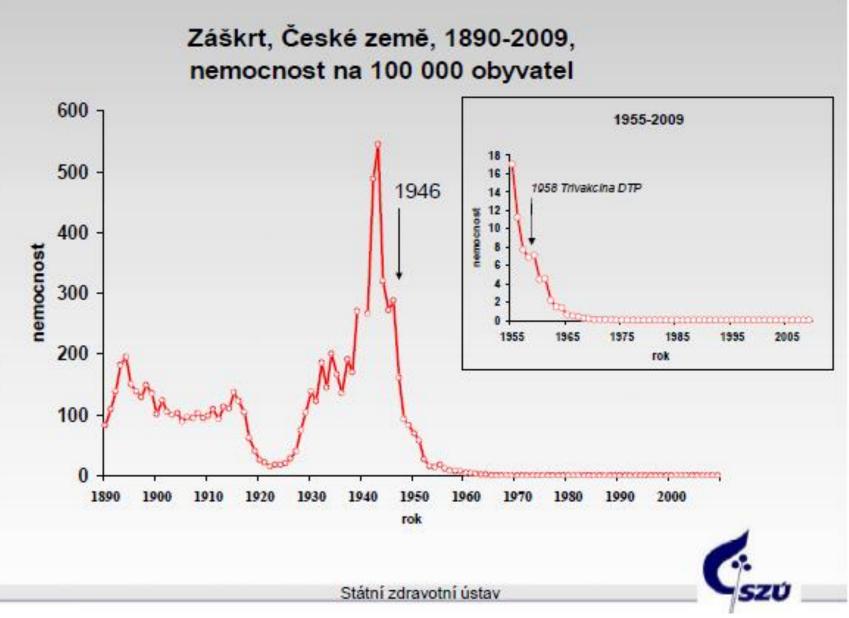
Latvia is the only EU Member State that reports indigenous transmission.

In a recent European study, ten European countries each screened between 968 and 8551 throat swabs from patients with upper respiratory tract infections for C. diphtheriae during 2007–2008.

Six toxigenic strains of C. diphtheriae were identified: two from symptomatic patients in Latvia and four from Lithuania (two cases, two carriers).

Among the toxigenic isolates, the Sankt Petersburg epidemic clone that caused large diphtheria outbreaks in Russia and the NIS* countries in the 1990s was still in circulation .

Carriage rates among household contacts of a laboratory-confirmed case may be as high as 25% .



22.10.2020

A case of diphtheria in Spain 15 June 2015

The detection, management and public health response to the first case of diphtheria in Spain in nearly 30 years has highlighted challenges for preparedness against diphtheria in the European Union.

The case is a 6-year-old <u>unvaccinated child.</u> A case of diphtheria in an unvaccinated individual within a highly protected population is not unexpected, because vaccinated people can be asymptomatic carriers of toxigenic C. diphtheriae.

The challenges for diphtheria case management, preparedness and public health response experienced in Spain are shared by many EU Member States. The most urgent critical issue is the shortage of diphtheria antitoxin (DAT) for immediate use when clinicians suspect diphtheria.

DAT must be given <u>as early as possible to be effective</u>, often on the suspicion of diphtheria before a laboratory confirmation.

EU Member States have for a number of years reported difficulties with sourcing and maintaining adequate stockpiles of DAT for emergency use, a problem they share with many countries around the world. EU Member States have on occasion been forced to arrange emergency deliveries of DAT for patients with diphtheria.

Úmrtí na záškrt v Belgii

24. březen 2016 | MUDr. Jana Košťálová

17. března 2016 zemřelo v Belgii, v Antverpách, na záškrt <u>neočkované 3leté dítě</u> čečenského původu, narozené v Belgii (dívka). Dítě nikde necestovalo, rodiče zřejmě ano.

První příznaky onemocnění se objevily 6. března, na jednotce intenzivní péče byla dívka hospitalizována 11. března 2016, později se zdravotní stav dítěte zhoršoval.

Diagnóza záškrtu byla potvrzena 15. března Národním referenčním centrem v Belgii a konfirmována WHO spolupracujícím centrem pro difterii ve Velké Británii.

Protože Belgie nemá difterický antitoxin, nabídlo ECDC zprostředkovat jeho zajištění. Národní institut pro veřejné zdraví a životní prostředí (RIVM) Nizozemska dodal antitoxin 16. března 2016.

Přes veškerou snahu a podání antitoxinu dítě zemřelo 17. března, příčina úmrtí - srdeční selhání (fatální myokarditida) v souvislosti s progresivním průběhem onemocnění. Zdravotnické orgány Vlámského regionu nyní posuzují další případná rizika např.: vyšetření kontaktů (rodina, zdravotníci, ošetřující personál, zaměstnanci děti ze školky), preventivní profylaxe antibiotiky, očkování, aby se zavedla případná dodatečná opatření pro prevenci a kontrolu.



- 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.