Acta virologica **57**: 347 – 351, 2013 doi:10.4149/av_2013_03_347

Increased incidence of mumps in the Czech Republic in the years 2011 and 2012

P. LEXOVÁ[1], R. LIMBERKOVÁ[2], J. ČÁSTKOVÁ[1], J. KYNČL[1,3]

[1]Department of Infectious Diseases Epidemiology, National Institute of Public Health, Šrobárova 48, Prague 10, Czech Republic; [2]National Reference Laboratory for Rubella, Measles, Mumps and Parvovirus B19, National Institute of Public Health, Prague 10, Czech Republic; [3]Department of Epidemiology, Third Faculty of Medicine, Charles University in Prague, Prague 10, Czech Republic

Received November 15, 2012; accepted July 3, 2013

Summary. – A nation-wide vaccination against mumps that had been launched in the Czech Republic in 1987 eliminated great outbreaks (up to 100,000 cases per year) of this disease in 1955–1988, but did not prevent small outbreaks (a few thousand cases per year) in 1995–1996, 2005–2007, and 2010–2012. The extent of these small outbreaks shows an increasing trend. The article describes mumps outbreaks in the Czech Republic in 2011 and 2012 with the aim to bring additional data contributing to the clarification of repeated outbreak triggers. In the years 2011 and 2012 there have been reported 2885 and 3902 mumps cases, respectively, in the Czech Republic. Similarly to other countries, a shift in the age-specific incidence of the disease towards higher age has been found, with the highest occurrence seen in the age group of 15–19 years. Men were slightly more affected than women. Clinical complications and vaccination status of patients were also observed.

Keywords: mumps; vaccination; outbreak; genotyping; waning immunity

Introduction

Mumps outbreaks have been reported even in countries where routine immunization against this disease has long been in place (Whelan *et al*., 2010; Walker *et al*., 2011). Increase in the number of mumps cases is often observed after several consecutive years with lower incidence of the disease (Kuzmanovska *et al*., 2010; Hukic *et al*., 2011; Walker *et al*., 2011).

Mumps outbreaks have occurred in both non-vaccinated individuals and populations with a high vaccination coverage (Whelan *et al*., 2010; Walker *et al*., 2011). There is a shift in mumps morbidity towards older age groups (Kuzmanovska *et al*., 2010; Otto *et al*., 2010; Walker *et al*., 2011; Whelan *et al*., 2010). Age distribution in EU/ EEA countries is shown in Fig. 1.

E-mail: plexova@szu.cz; phone: +420-26708-2717.

Abbreviations: EU = European Union; MMR = measles, mumps, rubella; WHO = World Health Organization

Efforts are made to map the situation in different countries, to understand recent mumps outbreaks, and to identify preventive strategies.

In the Czech Republic, mumps has been a reportable disease since 1955. Case-based data have been collected since 1993 (Boxall *et al*., 2008). The EU case definition is used in the mumps surveillance (Decision No 2008/426/EC).

The mass childhood immunization against mumps was implemented in the Czech Republic in 1987. Since 1995 a trivalent vaccine against measles, mumps and rubella (MMR) has been used (Mrazova *et al*., 2003; Boxall *et al*., 2008). MMR vaccine is given in a two-doses scheme – the dose 1 at 15 months of age or later is followed by the dose 2 after 6 to 10 months from dose 1.

Administrative surveys of MMR vaccinations performed annually in all regions in children of the appropriate age show high level of two-dose vaccination coverage (about 98% in 2010 and 2011).

Mumps incidence rates in the Czech Republic before and after mass vaccination are shown in Fig. 2.

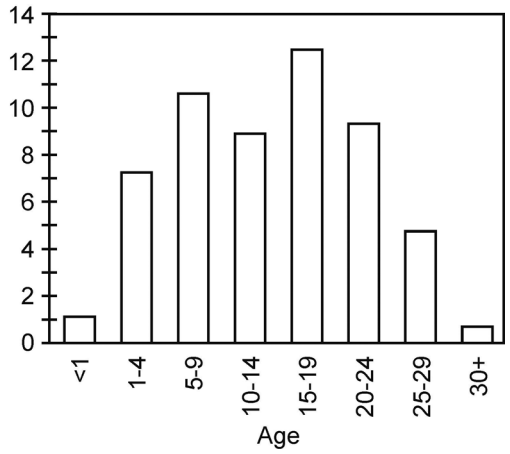

Fig. 1

Cumulative incidence of reported Mumps cases in EU/EEA countries by age group in 2011

Source: ECDC-TESSY (European Centre for Disease Prevention and Control – The European Surveillance System).

The number of mumps cases shows an increasing trend in the Czech Republic similarly to other European countries (Kuzmanovska *et al*., 2010; Otto *et al*., 2010; Whelan *et al*., 2010; Walker *et al*., 2011). The preceding mumps wave was observed in the Czech Republic in 2005–2007. The decreasing incidence in 2008 and 2009 was followed by an increasing incidence since 2010.

Materials and Methods

Patients. A uniform nationwide system of reporting communicable diseases (EPIDAT) laid down by the law has been used in the Czech Republic (Act. No. 258/2000 Coll. on Protection of Public Health). Case-based data are collected including information about age, gender, clinical course of illness, complications, laboratory results, vaccination status.

Mumps diagnostics. Mumps cases were diagnosed mainly from the clinical symptoms and epidemiological data. There were 1272 and 1656 cases laboratory tested in the regional laboratories in the years 2011 and 2012, respectively. Laboratory diagnosis was particularly based on serology (ELISA). The National Reference Laboratory (NRL) for Rubella, Measles, Mumps and Parvovirus 19 of the National Institute of Public Health in Prague recommends to support the diagnosis with the direct detection of mumps virus by isolation in the tissue culture and detection of viral RNA by RT-PCR techniques.

From February to December 2012 NRL analyzed clinical samples from 78 suspected cases collected in five regions of the Czech Republic with high mumps incidence: 47 buccal swabs, 9 paired sera, and 22 acute sera. All sera samples were tested with Siemens Enzygnost anti-parotitis virus kit for mumps-specific IgG and IgM antibodies, paired sera samples were tested also with hemagglutination inhibition test. Buccal swabs were first inoculated on continuous monolayers of Vero cell lines. Negative isolates and/or bacterially contaminated ones and isolates with atypical cytopathic effect were tested by RT-PCR (Mumps Virus RT-PCR kit Shanghai ZJ BioTech).

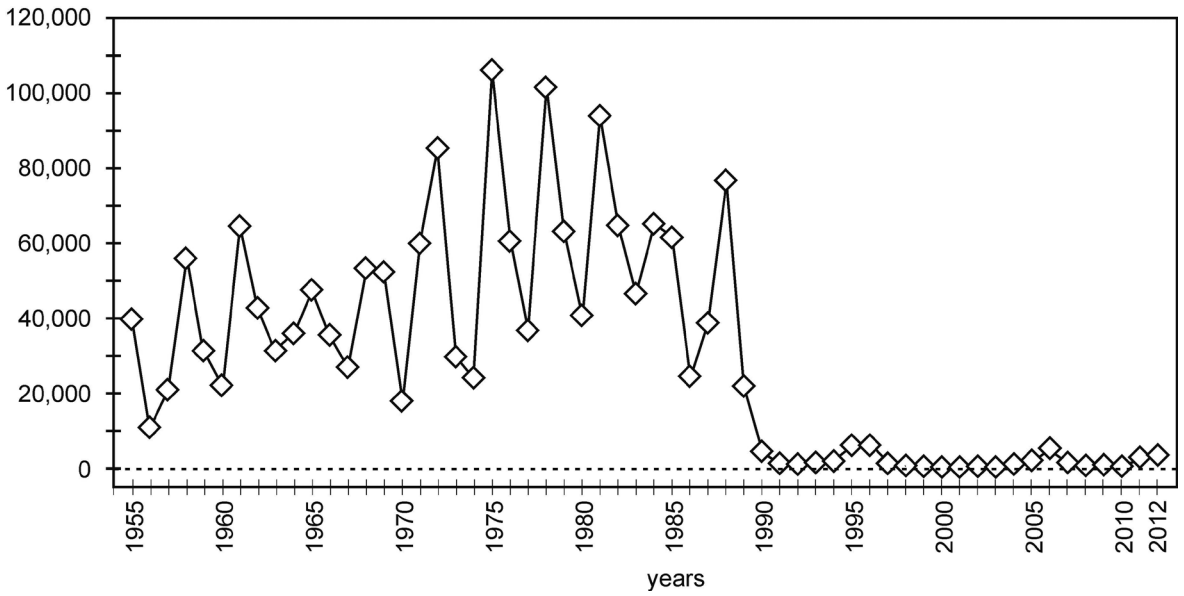

Fig. 2

Mumps, reported cases in the Czech Republic (1955–2012)

Source: EPIDAT.

The Regional Reference Laboratory for Measles, Mumps and Rubella virus in the Robert Koch Institute, Germany performed genotyping analyses from nineteen mumps isolates spotted on FTA cards.

Results and Discussion

In 2011, 2885 mumps cases were reported in the Czech Republic (27.5 cases per 100,000 population), of which 1041 were laboratory confirmed. Men were slightly more affected (1,653 cases – 57.3%) than women (1,232 cases – 42.7%). Over one third of mumps cases (1,128) occurred in the age group 15 to 19 years. Altogether 259 (9%) patients developed complications. Orchitis was recorded in 10.5% of male patients. Coverage with two doses of MMR vaccine was reported in 2,312 (80.1%) patients.

In the year 2012, 3902 mumps cases were reported in the Czech Republic (37.0 cases per 100,000 population). Similarly as in the previous year, 56% of patients were men and 44% women. The most affected age group was 15–19 years, accounting for 38 % of mumps cases reported. No epidemiological link was traced in more than half of mumps cases.

There were 3,302 patients (84.6%) vaccinated against mumps in the year 2012. 3,108 patients (79.7%) received two doses and 38 patients received a single dose of MMR vaccine. The data on the number of vaccine doses were not available for 156 vaccinated patients. The two-dose MMR vaccine-coverage rate in patients of the age group 15–19 years was 98.8% (1,479 cases).

Complications were reported in 10.1% of all mumps cases, with orchitis being the most common one and affecting 12.8% of male patients. Seven percent of vaccinated individuals developed complications in comparison with 27% of non-vaccinated patients. For instance, meningitis was reported in 1.3% vaccinated patients and 3.5% of non-vaccinated patients. Orchitis was reported in 8.6% of vaccinated male patients but in almost 35% of non-vaccinated male patients. The absolute numbers of different complications are summarized in Table 1.

Table 1. Clinical complications in mumps cases in the Czech Republic in 2012

Complications	No. of patients		
	Vaccinated	Non-vaccinated	Total
None	3068	440	3508
Encephalitis	1	8	9
Mastitis	1	0	1
Meningitis	42	21	63
Oophoritis	1	0	1
Orchitis	158	122	280
Pancreatitis	9	3	12
Other	22	6	28
Total	3302	600	3902

Virus specificity was confirmed in regional laboratories for 1406 cases. Forty of 78 cases analysed by NRL were positive. Six acute sera samples were IgM positive (6/22; 27%), other two acute samples were IgG high positive (2/22; 9%). Five paired sera samples were positive in hemagglutination inhibition test (5/9; 55%) and four of them were IgG-positive in ELISA as well (4/9; 44%). Twenty buccal swabs were positive in cultivation on Vero cells (20/47; 43%).

Twenty-three problematic samples (bacterially contaminated, with atypical cytopathic effect or with negative results in cell culture cultivation) were in addition tested by RT-PCR; seven of them were positive. Regardless of the method used, mumps virus-specific antibody response was positive in 13/31 cases (42%) and virus isolation and/or detection of mumps virus nucleic acid were positive in 27/47 cases (57%). Genetic characterization of mumps virus detected in the clinical material of nineteen cases revealed presence of the genotype G (in four local variants).

The mumps incidence rates in our country follow those reported in some other European countries, but with a delay that can be explained by high vaccination coverage of the Czech population. Similar to other countries, mumps cases tend to shift to higher age groups and are slightly more frequent in males (Kuzmanovska *et al*., 2010; Whelan *et al*., 2010; Hukic *et al*., 2011; Walker *et al*., 2011). Considerable rates of complications, e.g. orchitis, in more than 10% of male patients, are also in line with the data from other countries (Otto *et al*., 2010; Whelan *et al*., 2010). A significant difference was observed in the rates of complications between vaccinated and non-vaccinated patients.

In the Czech Republic, administrative survey of vaccine coverage is conducted on an annual basis, using medical records of a random sample of children of specific age groups (i.e. those who should have been vaccinated according to the childhood immunization schedule). The vaccination coverage rates from administrative surveys have long been above the herd immunity threshold. In 2001, a nationwide serological survey for mumps virus antibodies was conducted in the Czech Republic in 3010 sera from persons of both genders aged 1–64 years (Mrazova *et al*., 2003). Sera were collected from a randomly selected representative sample of the population. The antibody prevalence rates revealed in the survey (70–86%) did not correspond with the vaccination coverage rates in children under 15 years of age (97–100%) as found by the administrative survey. Natural immunity levels in the population above 15 years of age were higher than post-vaccination immunity levels. It was concluded that the herd immunity achieved is not high enough to prevent epidemic spread of the mumps virus (Mrazova *et al*., 2003). The reported outcome of the serological survey corresponds

to the high proportion of mumps patients vaccinated with two doses of MMR vaccine in the Czech Republic (about 80% in the past years).

The decrease in the antibody titers with the time elapsed from the vaccination results in the waning of the protective effect. Furthermore, the immunity of a population with high vaccination coverage is not boosted by the naturally circulating mumps virus, thus the protective effect of the vaccination can also be reduced (Date *et al.*, 2008; Domínguez *et al.*, 2010; Whelan *et al.*, 2010; Trmal *et al.*, 2011). An extra third dose of MMR vaccine is considered in adolescents or young adults, particularly in collectives whose members come from geographically distant areas or different social groups (boarding schools, student residences, etc.). An extra dose of MMR vaccine can play a positive role in the onset of mumps outbreaks (Trmal *et al.*, 2011).

The currently used vaccine is derived from the Jeryl Lynn vaccine strain of mumps virus (genotype A) that differs phylogenetically from the circulating genotypes. The antigenic differences between genotypes are responsible for incomplete cross neutralization. At present, there is no clinical evidence that the difference in the genotype might be the cause of primary vaccine failure or that it might be of considerable epidemiological importance. Even when the vaccine strains were not matched with circulating strains, the ongoing outbreak stopped (Domínguez *et al.*, 2010; Trmal *et al.*, 2011).

Nevertheless, the genotype-related vaccine efficacy as well as the possible role of the waning immunity in mumps outbreaks remains an open question that needs to be answered.

To draw a more comprehensive picture of the current situation, it is crucial to change the laboratory diagnosis strategy. A considerable proportion of vaccinated persons do not develop IgM antibodies detectable in the acute serum sample and often do not show seroconversion or significant increase in the IgG antibody titer in paired sera, as IgG antibodies increase rapidly in these persons soon after infection.

This immediate increase in the IgG antibodies is also responsible for the fact that the vaccinated patients shed smaller amount of the virus for a shorter period of time, thus making direct diagnosis of mumps virus more difficult (Narita *et al.*, 1998; Sanz *et al.*, 2006; Krause *et al.*, 2007; Bitsko *et al.*, 2008; Hatchette *et al.*, 2009; Rota *et al.*, 2009; Royuella *et al.*, 2011).

The results presented by the Czech National Reference Laboratory suggest the need for a switch from the commonly used serological tests to methods for the direct detection of the virus to be coupled with centrally performed genotyping. Molecular epidemiological studies including genotyping of recent strains should be part of the surveillance program as recommended by the World Health Organization (WHO) (WHO, 2005; Pandurang *et al.*, 2011).

Despite the existing uncertainty about the vaccine efficacy and protective effect duration, vaccination is still the most effective tool in reducing mumps morbidity and complications.

Acknowledgement. The authors thank the field epidemiologists and colleagues from clinical settings and collaborative laboratories for their contribution to the monitoring of the epidemiological situation, collection of biological specimens and laboratory investigation. The Regional Reference Laboratory of the Robert Koch Institute in Berlin is acknowledged for carrying out the genotyping. The authors also wish to thank Dr. Sarka Nemeckova from the Institute of Hematology and Blood Transfusion in Prague for valuable comments to the manuscript and Dr. Cestmir Benes from the National Institute of Public Health in Prague for providing historical data on mumps incidence.

References

Act. No. 258/2000 Coll. on Public Health Protection.

Bitsko RH, Cortese MM, Dayan GH, Rota PA, Lowe L, Iversen SC, Bellini WJ(2008): Detection of RNA of mumps virus during an outbreak in a population with a high level of measles, mumps, and rubella vaccine coverage. J. Clin. Microbiol. 46, 1101–1103. http://dx.doi.org/10.1128/JCM.01803-07

Boxall N, Kubinyiova M, Prikazsky V, Benes C, Castkova J (2008): An increase in the number of mumps cases in the Czech Republic 2005–2006. Euro Surveill. 13, 18842.

Date AA, Kyaw MH, Rue AM, Klahn J, Obrecht L, Krohn T et al. (2008): Long-term persistence of mumps antibody after receipt of 2 measles-mumps-rubella (MMR) vaccinations and antibody response after a third MMR vaccination among a university population. J. Infect. Dis. 197, 1662–1668. http://dx.doi.org/10.1086/588197

Decision No. 2008/426/EC amending Decision No. 2002/253/EC laying down case definitions for reporting communicable diseases to Community network under Decision No 2119/98/EC of European Parliament and of the Council.

Decree No. 473/2008 Coll. on Epidemiological Surveilance System for Selected Infections.

Dominguez A, Torner N, Castilla J, Batalla J, Godoy P, Guevara M *et al.* (2010): Mumps vaccine effectiveness in highly immunized populations. Vaccine 28, 3567–3570. http://dx.doi.org/10.1016/j.vaccine.2010.02.107

Hatchette T, Davidson R, Clay S, Pettipas J (2009): Laboratory diagnosis of mumps in a partially immunized population: The Nova Scotia experience. Can. J. Infect. Dis. Med. Microbiol. Winter 20, 157–162.

Hukic M, Ravlija J, Dedeic Ljubovic A, Moro A, Arapcic S, Muller CP, Hübschen JM (2011): Ongoing large mumps outbreak in the Federation of Bosnia and Herzegovina, Bosnia and Herzegovina, December 2010 to July 2011. Euro Surveill. 16, 19959.

Krause CH, Molyneaux PJ, Ho-Yen DO, McIntyre P, Carman WF, Templeton KE (2007): Comparison of mumps-IgM

ELISAs in acute infection. J. Clin. Virol. 38,153–156. http://dx.doi.org/10.1016/j.jcv.2006.10.010

Kuzmanovska G, Polozhani A, Mikik V, Stavridis K, Aleksoski B, Cvetanovska Z, Binnendijk R, Bosevska G (2010): Mumps outbreak in the former Yugoslav Republic of Macedonia, January 2008–June 2009: epidemiology and control measures. Euro Surveill. 15, 19586.

Mrazova M, Smelhausova M, Sestakova Z, Svandova E, Benes C (2003): The 2001 serological survey in the Czech Republic – mumps. Cent. Eur. J. Public Health 11 (Suppl.) 50–53.

Műhlermann K (2004): The molecular epidemiology of mumps virus. Infection, Genetics and Evolution 4, 215–219. http://dx.doi.org/10.1016/j.meegid.2004.02.003

Narita M, Matsuzono Y, Takekoshi Y, Yamada S, Itakura O, Kubota M, Kikuta H, Togashi T (1998): Analysis of mumps vaccine failure by means of avidity testing for mumps virus- specific immunoglobulin G. Clin. Diagn. Lab. Immunol. 5, 799–803.

Nöjd J, Tecle T, Samuelson A, Örvell C (2001): Mumps virus neutralizing antibodies do not protect against reinfection with a heterologous mumps virus genotype. Vaccine 19, 1727–1731. http://dx.doi.org/10.1016/S0264-410X(00)00392-3

Otto W, Mankertz A, Santibanez S, Saygili H, Wenzel J, Jilg W, Wieland WF, Borgmann S (2010): Ongoing outbreak of mumps affecting adolescents and young adults in Bavaria, Germany, August to October 2010. Euro Surveill. 15, 19748.

Örvell C, Tecle T, Johansson B, Saito H, Samuelson A (2002): Antigenic relationship between six genotype s of the small hydrophobic protein gene of mumps virus J. Gen. Virol. 83, 2489–2496.

Kolekar PS, Kale M, Kulkami-Kale U (2011): Genotyping of Mumps viruses based on SH gene: Development of a server using alignment-free and alignment-based methods. Immunome Res. 7, 1–7.

Rota JS, Turner JC, Yost-Daljev MK, Freeman M, Toney DM, Meisel E, Williams N, Sowers SB, Lowe L, Rota PA, Nicolai LA, Peake L, Bellini WJ (2009): Investigation of a mumps outbreak among university students with two measles-mumps-rubella (MMR) vaccinations, Virginia, September–December 2006. J. Med. Virol. 81, 1819–1825. http://dx.doi.org/10.1002/jmv.21557

Royuela E, Castellanos A, Sanches-Herrero C (2011): Mumps diagnosis and genotyping using a novel single RT-PCR. J. Clin. Virol. 52, 359–362. http://dx.doi.org/10.1016/j.jcv.2011.09.007

Sanz JC, Mosquera M del M, Echevarria JE (2006): Sensitivity and specificity of immunoglobulin titer for the diagnosis of mumps virus in infected patiens depending on vaccination status. APMIS 114, 788–794. http://dx.doi.org/10.1111/j.1600-0463.2006.apm_463.x

Trmal J, Koci J, Simunkova L, Storkanova O, Trmalova Z (2011): Mumps outbreak in Usti administrative region. Zpravy CEM (SZU Praha) 20, 219–223.

Walker J, Huc S, Sinka K, Tissington A, Oates K (2011): Ongoing outbreak of mumps infection in Oban, Scotland, November 2010 to January 2011. Euro Surveill. 16, 19803.

Whelan J, van Binnendijk R, Greenland K, Fanoy E, Khargi M, Yap K, Boot H, Veltman N, Swaan C, Van der Bij A, de Melker H, Hahne S. (2010): Ongoing mumps outbreak in student population with high vaccination coverage, Netherlands 2010. Euro Surveill. 15, 19554.

WHO (2005): Global status of mumps immunization and surveillance. Wkly Epidemiol. Rec. 80, 418–424.