Measles and rubella in Croatia

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Introduction

In Croatia, measles vaccination was first introduced in the national childhood vaccination schedule in 1968 and was replaced by the combined measles, mumps and rubella (MMR) vaccine in 1976. Vaccine coverage rates for the first MMR dose are more than 94% since 2004, and for the second dose more than 97%.

In the pre-vaccinal period, 5.000-20.000 cases of measles and rubella were notified each year in Croatia. In the last two decades, less than 10 measles cases have been reported annually, with the exception of three import-related outbreaks (2003/2004, 2008 and 2014/2015). In 2002, four SSPE cases were notified. Regarding rubella, only sporadic cases were reported with an outbreak in 2007 (Fig. 1). There was no reported congenital rubella syndrome. A seroepidemiological study conducted from 2005-2009 showed that 94.6% of the Croatian childbearing-aged women are immune to rubella. However, vaccination coverage has been decreasing since 2012.

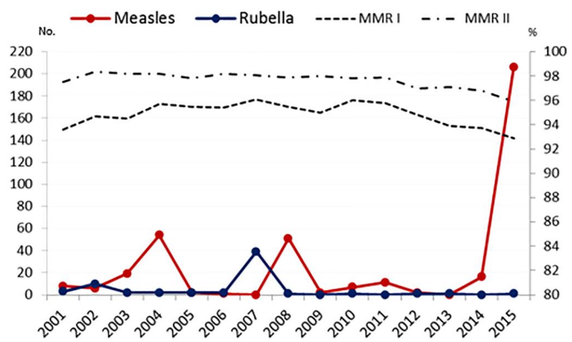


Fig. 1. Number of measles/rubella cases and vaccination rates in Croatia

Laboratory performance in 2015-2016

- **National Measles/Rubella Laboratory, Croatian National Institute of Public Health**
  Measles: virus isolation (B95a; Vero/hSLAM); RT-PCR; Serology (ELISA IgM/IgG; IFA IgM/IgG; IgG avidity)
  Rubella: virus isolation (Vero/hSLAM; Vero); RT-PCR; Serology (ELISA IgM/IgG; IgG avidity)

	NP swab Tested/Positive	Throat swab Tested/Positive	Urine Tested/Positive	Blood Tested/Positive	Serum Tested/Positive	Total Tested/Positive
Measles RT-PCR	83/50	8/8	72/47	1/0	-	164/105
Measles IgM	-	-	-	-	50/30	50/30
Rubella IgM	-	-	-	-	50*/0	50/0
Measles isolation	7/1	-	-	-	-	7/1

*Samples from suspected measles cases were tested for rubella

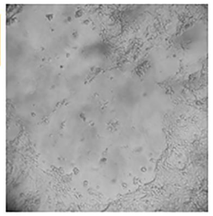


Fig. 5. Measles virus (syncytia) in Vero/hSLAM cells
6294/2015

2014-2015 measles outbreak

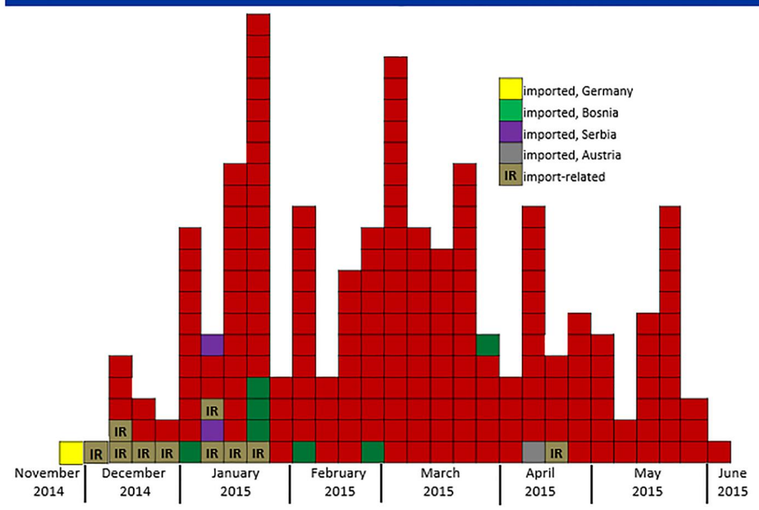


Fig. 2. Number of measles cases by month and country of origin

On 1 December 2014, measles was clinically diagnosed in a 6-year old boy (probably imported from Berlin). His brother developed symptoms on 11 December. Two additional family members with measles represent the first family cluster (4 patients). Until March 2015, 17 clusters (2-15 cases) of measles were identified. Cases were mainly members of Roma community with very low vaccination coverage (<50%) who had numerous contacts with family members from Bosnia and Herzegovina as well as autochthonous cases among members of Roma population. Sporadic cases in non-Roma community also occurred. Six healthcare workers acquired infection at work. Viruses from 30 cases were partially sequenced and all possessed identical or highly similar sequences indicating that the outbreak was caused by a single strain belonging to genotype D8.

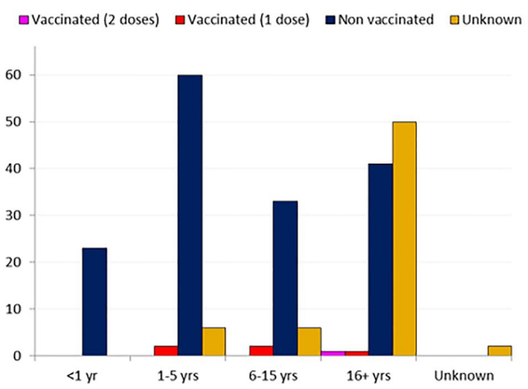


Fig. 3. Number of measles cases by age/vaccinal status

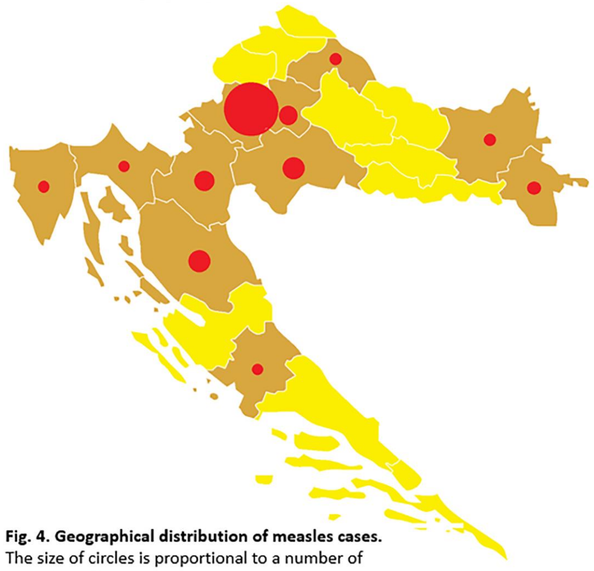
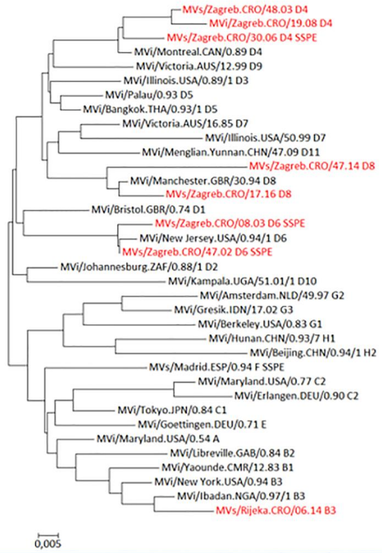


Fig. 4. Geographical distribution of measles cases. The size of circles is proportional to a number of cases (2-122).

Molecular epidemiology



- **University of Zagreb, Centre for research and knowledge transfer in biotechnology**

Genetic characterisation of wild type and SSPE strains detected in Croatia is performed since 2003. In-house RT-PCR methods are established for amplification and sequencing of complete measles genome. Sequencing of N450 (450 nucleotides encoding for the last 150 amino acids of the N protein) and genotyping is routinely performed and sequences are submitted to PubMed and MeaNS databases. Similar to contemporaneous epidemiological data from other European countries, strains detected in Croatia belong to genotypes D4 (epidemics in 2003 and 2008), B3 (single imported case in 2014) and D8 (epidemics in 2014/2015, single case in 2016).

Fig. 6. Measles virus phylogenetic tree based on N450 genomic segment. Wild type and SSPE strains detected in Croatia are shown in red. Scale bar indicates the number of base differences per site. As genotype references, strains defined by WHO were used (WHO, Wkly Epidemiol Rec 87 (2012) 73).

Conclusions and future challenges

Due to high vaccination coverage in the past decades, Croatia has interrupted measles and rubella circulation in the population. Only sporadic imported cases of measles occur, with three import-related outbreaks of limited magnitude in the last 15 years. Except one geographically limited outbreak of rubella in 2007, only sporadic imported cases of rubella without secondary cases are noted. The main challenge is to interrupt the decreasing trend in vaccination coverage, observed in the last four years, which represents a threat to population immunity level and can lead to reintroduction of measles or rubella circulation.

Publications

• Forcic D, *et al.* Genetic characterization of wild type measles virus isolated in Croatia during the 2003-2004 outbreak. J Med Virol 2005; 75(2):307-12. • Kaic B, *et al.* A measles outbreak in Croatia, 2008. Euro Surveill 2009;14(1). pii: 19083. • Ivić-Hofman I, *et al.* Simultaneous chickenpox and measles infection among migrant children who stayed in Italy during the second half of June 2011. Clin Pract 2011; 1(4):e113. • Vilibic-Cavlek T, *et al.* Subacute sclerosing panencephalitis in Croatia (1994-2004). Acta Microbiol Immunol Hung 2007; 54(1):57-63. • Ivancic-Jelecki J, *et al.* The first genetic characterization of a D4 measles virus strain derived from a patient with subacute sclerosing panencephalitis. Infect Genet Evol 2013;17:71-8. • Vilibic-Cavlek T, *et al.* Seroprevalence of TORCH infections in women of childbearing age in Croatia. J Matern Fetal Neonatal Med 2011; 24(2):280-3.

Acknowledgments

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