

A MEASLES OUTBREAK IN CROATIA, 2008

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We report an outbreak of measles in Croatia, involving 49 cases with onset of symptoms between end of April and June 2008. Cases occurred in Zagreb and Slavonski Brod but investigations indicated a common epidemiological link between these two geographically separate regions.

Introduction

Following an almost four-year period with zero indigenous measles cases notified in Croatia the disease reappeared during the second quarter of 2008. With the exception of an import-related outbreak in winter 2003-4, less than 10 measles cases have been reported annually since 2000, although none of them had been laboratory confirmed. Measles is a statutorily notifiable disease in Croatia since 1949.

In Croatia, all vaccinations offered to children within the universal immunisation schedule are mandatory and free of charge. Measles vaccination was first introduced in the national childhood vaccination schedule in 1968 at 12 months of age and was replaced by the combined measles, mumps and rubella vaccine (MMR) in 1976. A second dose was given at seven years of age as monovalent measles vaccine since 1968, and was replaced by MMR in 1994. During the period 1997-99, the second dose was recommended at 12 years of age. Vaccine coverage rates for the first MMR dose at two years of age in Croatia are estimated to have been above 90% since the mid-1980s, and more than 95% since 2004. Vaccination coverage estimates are done by administrative method based on data submitted annually by immunisation providers and verified by competent epidemiologists.

Sequence of events

The first notified case was a 27-year-old man who fell ill on 26 April 2008. He was hospitalized initially as a case of staphylococcal sepsis based on clinical suspicion, and identified as measles case only after his brother was hospitalized ten days later as a case of measles. Both patients are from the greater Zagreb area. Until 15 May, further five cases were notified from the same municipality as the index case, and included three community acquired cases and two visitors to the hospital where the index case was admitted (Figure 1). In the following weeks, the outbreak spread further in other municipalities of Zagreb area (community and nosocomial transmission), reaching a total of 29 cases (37 suspected), the last one with onset of symptoms on 20 June 2008.

In May, a measles outbreak was also reported in the province of Slavonski Brod, affecting 20 persons (32 suspected cases) of a

migrant Roma community (Figure 1). Members of this community had recently returned from abroad, most of them from Italy. Mistakenly, the Slavonski Brod outbreak was initially believed to be due to erythema infectiosum. The last case in Slavonski Brod fell ill on 30 May.

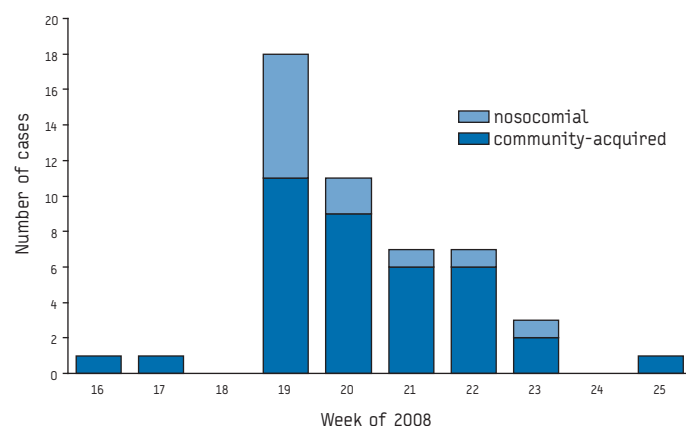
An additional case of measles was notified in a German tourist who stayed in Split and fell ill on 21 May, seven days after arrival to Croatia. However, there were no cases reported in connection with this case, so it was excluded from the analysis of the outbreak.

Laboratory and epidemiological investigations

Since the outbreak was first identified, 69 suspected cases of measles were notified. Of these, 40 (58%) were laboratory-confirmed using ELISA techniques on serum samples and/or polymerase-chain-reaction (PCR) analysis. Further four cases were epidemiologically linked and five were classified as clinical cases. The remaining 20 cases (35%) were discarded and excluded from further analysis.

Case classification was based on the European Commission case definition of measles [1]. In our classification a laboratory confirmed case corresponded to a confirmed case in the EC definition, an epidemiologically linked case corresponded to a probable case in the EC definition, and a clinical case corresponded to a possible case in the EC definition for which no laboratory information is

FIGURE 1
Cases reported in an outbreak of measles in Croatia, in 2008, by the week of onset of symptoms (n=49)



available. Discarded cases were clinical cases (possible cases in the EC definition) with negative serology and/or negative detection of measles virus/antigen from a clinical specimen.

Genotype D4 was identified in six PCR-positive cases all from cases reported in Zagreb area. There was no sequence diversity (unpublished data). Comparison of the isolated genotype with strains circulating in Europe is underway.

This outbreak was limited to greater Zagreb area (n=29, 59%) and the Slavonski Brod province (n=20, 41%). The mean age of all cases was 21 years (range 7 months - 50 years). The mean age of the cases from Zagreb was 27 years and that of the cases from the Slavonski Brod province was 12 years (Figure 2).

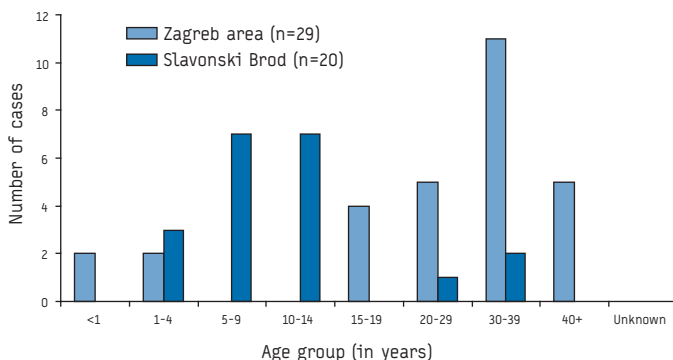
The vaccination status of cases was determined by interview and review of personal medical records. Overall, 32 cases had not been vaccinated against measles, three had received only one measles-containing vaccine (MCV), two cases had been vaccinated with two MCV doses and two had been vaccinated but the number of MCV doses was unspecified. In 10 cases the vaccination status was unknown. Of those with a known vaccination status there was a significant difference in the number of unvaccinated cases in the two affected areas: 16 out of 23 (70%) in Zagreb and all 16 (100%) in Slavonski Brod ($p<0.05$)

Of the 49 cases included in the outbreak, 11 (22%) were hospitalised and five (10%) had an unknown hospitalisation status. In two cases complications with pneumonia occurred. Nosocomial transmission was reported in 12 (24%) cases, all from Zagreb area.

Further investigations

Upon further enquiry to identify a possible source of infection and reveal further contacts, it transpired that a Roma girl developed a rash whilst visiting the family of the 27-year-old man in Zagreb whom we had identified as the outbreak index case. The paediatrician who suspected rubella referred the child for laboratory testing to the University Hospital for the Infectious Disease in Zagreb. However, the child never attended the clinic, because she and her mother left Croatia. They were both Italian citizens who were visiting Serbia and Croatia on their way to Germany.

FIGURE 2
Number of reported measles cases by area of notification and age group, Croatia, 2008 (n=49)



It was later revealed that this child and her mother had travelled from Italy to visit family members in the Slavonski Brod province before they visited the family in Zagreb. This led to the hypothesis that this child with an undiagnosed rash was the source of infection in both geographically separate areas of Croatia.

Control measures

After notification of this first generation of cases, a circular letter was sent to all health-care institutions notifying them of the outbreak and providing guidelines on reporting and investigating suspected measles cases.

To control the outbreak, the Department of Infectious Disease Epidemiology performed contact tracing, vaccinated susceptible contacts and recommended voluntary quarantine of susceptible contacts to those who could not be vaccinated due to contraindications to vaccination or because it was too late to vaccinate them because their exposure had occurred more than 72 hours before. Paediatricians were instructed to invite parents to vaccinate all previously unvaccinated children above 12 months of age. Recommendations for vaccination were also issued to healthcare workers without evidence of immunity. It is not known, however, how many people were vaccinated as a result of these outbreak control measures.

Discussion

With the outbreak described in this paper, Croatia joins some other European countries that have recently experienced a resurgence of measles [2]. The presence of pools of individuals in the general population and amongst members of the Roma community susceptible to measles infection still exists in Croatia and is brought to light when the measles virus is imported from abroad. A serological survey carried out on samples collected in 1999-2000 showed a high susceptibility to acquire measles in those aged 16-40 years [3]. This conclusion is compatible with our findings, as the proportion of cases in this age group (particularly in Zagreb) was high. It is believed that the vaccination coverage amongst members of the Roma community living in Croatia, i.e. non-migrating Roma, does not differ largely from the coverage of the rest of the population, since they are well integrated into the primary health care system, which provides immunisation. However, migratory members of the Roma community, who spend a substantial time abroad do not benefit from the immunisation system, although the services are free of charge and available to everyone regardless of insurance status and citizenship. There is, therefore, a need to improve vaccination coverage using innovative ways in such groups that are hard to reach by normal vaccination programmes. In doing so, the herd immunity would be maintained at level conducive of measles elimination from Croatia.

The outbreak clearly demonstrates the role of nosocomial transmission in the spread of infection. Nosocomial transmission of measles virus has also recently been described elsewhere [4,5]. In the import-related outbreak in winter 2003-4, nosocomial transmission had also played a significant role (unpublished data). This shows the importance for health-care workers to be fully vaccinated against measles if they have no history of the disease. This investigation also demonstrates the potential of measles to be misdiagnosed as other infectious diseases presenting with a rash and fever. It is also evident that at least in some healthcare settings, health personnel's awareness of measles should be increased, in order to suspect measles in a timely manner. This also stresses the

importance of laboratory testing of suspected measles cases and to identify the circulating measles virus genotype.

As part of the measles and rubella elimination plan by 2010 from the WHO European Region [6], the Croatian Ministry of Health has on several occasions sent circular letters to all healthcare workers urging all suspected cases of measles and rubella to be notified immediately, emphasizing the need for enhanced surveillance, and providing instructions on sampling and transportation of specimens to the national measles and rubella reference laboratories affiliated to the National Institute of Public Health.

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