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MEASLES SITUATION IN SERBIA IN AN ERA OF MEASLES ELIMINATION (2007-2009)

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Abstract - Following the introduction of measles immunization in Serbia in 1971, measles outbreaks were recorded every 3 to 5 years until 1997. The outbreak in 1997 with 4000 cases was the last large outbreak in Serbia. In 2007, an outbreak with 191 laboratory confirmed or epidemiologically linked cases was reported in Vojvodina. In 2008 and 2009, only 3 cases were confirmed. From 2007-2009, measles infections were most frequently detected in the Roma population but also in non-immunized or partially immunized persons from the general population.

Key words: Measles virus, outbreak, molecular epidemiology

INTRODUCTION

The measles virus, a member of the Paramyxoviruses family, causes a common, acute infectious disease which is characterized by fever, cough, conjunctivitis and a generalized, maculopapular rash (Griffin, 2001; Rima and Duprex, 2006). Despite the availability of effective live vaccines for more than 40 years, measles is still responsible for 4% of deaths in children younger than 5 years of age worldwide (Bryce et al., 2005).

In Serbia, measles immunization with a monovalent vaccine was started in 1971. The bivalent measles/mumps immunization program was introduced in 1981. Since 1994, a two-dose schedule with trivalent MMR vaccine is used. Additionally, a supplementary immunization program of Roma population groups was organized from 2002-2004 by the Institute of Public Health (IPH) of Serbia and a network of 23 IPH and health centers and with the financial support of UNICEF.

Measles, rubella and CRS have been notifiable diseases in Serbia for decades. Cases are classified according to the WHO case definition. The National Commission for the Protection of the Population from Communicable Diseases adopted an action plan for the elimination of measles and prevention of CRS in the Republic of Serbia by the end of 2015 (WHO, 2010a and b). The present manuscript describes the measles epidemiology in Serbia between 2007 and 2009.

MATERIALS AND METHODS

Measles and rubella surveillance in Serbia is organized by the Institute of Public Health of Serbia and Institutes of Public Health throughout the country (epidemiological surveillance) and the WHO Measles/Rubella National Reference Laboratory (M/R NRL) at the Institute of Virology, Vaccines and Sera "TORLAK" Belgrade (laboratory surveillance). Together, they investigate each suspected case and outbreaks. The aim is early detection of disease, estimation of the extent of an outbreak, and to establish the possible source of infection and transmission route. Laboratory confirmation in the M/R NRL is done by detection of specific IgM and IgG antibodies using Enzygnost® kits (Siemens Healthcare Diagnostics Products GmbH, Marburg/Germany) in blood samples, and/or virus detection using nose or throat swabs (Real-time PCR in house test with primers and probes from the Statens Institute, Denmark, unpublished data) and/or isolation of virus in Vero/hSLAM cells. All measles virus positive swabs are sent to the WHO European Regional Reference Laboratory in Luxembourg (RRL) for confirmation and sequence analysis. In this paper, we analyze the epidemiological and virological surveillance data of measles infection in Serbia in the period 2007-2009.

RESULTS

Following the introduction of measles immunization in Serbia in 1971, measles outbreaks were recorded every 3 to 5 years (Fig. 1). The incidence rate was 90-350 cases per 100,000 between 1971 and 1985 and 90-150 cases per 100,000 in the period 1986 to 1993. The outbreak in 1997 with 4000 cases was the last big outbreak in Serbia (Fig. 1), and an incidence rate of 43/100,000 and 7 fatal outcomes. During the following nine years, decreasing case numbers were observed and an ever-low incidence of 0.02 cases per 100,000 was reached in 2005 and 2006.

In 2007, however, an outbreak with 191 laboratory confirmed or epidemiologically linked cases occurred in Vojvodina. The index case came from Bosnia and Herzegovina to attend a funeral. The index case and the majority of registered cases belonged to the Roma population. Out of 191 laboratory confirmed or epidemiologically linked cases, 45% were women. The most affected age groups were the 20-29 and 10-14 year olds (25.8% and 19.4%, respectively), followed by the 5-9 and 15-19 year olds (13.9% and 12.4%, respectively). In the population older than 30 years, 11.4% were affected, while in children from 1-4 the infection was detected in 10.4%.

The youngest patient was 8 days old and the oldest was 43 years. The large majority of the cases (166/191, 87%) were unvaccinated. A total of 47% of the patients were hospitalized and 12.9% had complications such as pneumonia.

Mop-up and urgent immunization campaigns were conducted in all municipalities in the affected high-risk Roma group. To prevent further spread and to wipe out the epidemic, the isolation of measles cases and vaccination of unvaccinated contacts were carried out in schools, hospitals, families, kindergartens, etc. according to the national regulations.

Sequence analysis confirmed the measles virus genotype D4, with the main outbreak strain being identical to the Romania variant. The same variant circulated in 2007 in Bosnia and Herzegovina (Fig. 2). Molecular analysis of later cases showed that this variant stopped circulating in Serbia after the outbreak.

In 2008, only two measles cases were confirmed out of 16 suspected and laboratory investigated cases. The first case was a man who had travelled to Thailand while the second patient was epidemiologically linked to him. Sequence analysis identified genotype D9 and identical sequences were found in the same year in Thailand, supporting the epidemiological link to this country (Fig. 2).

In 2009, a single case of measles was confirmed in a person who came from Germany. Molecular analysis detected genotype D4, Enfield variant (Fig. 2).

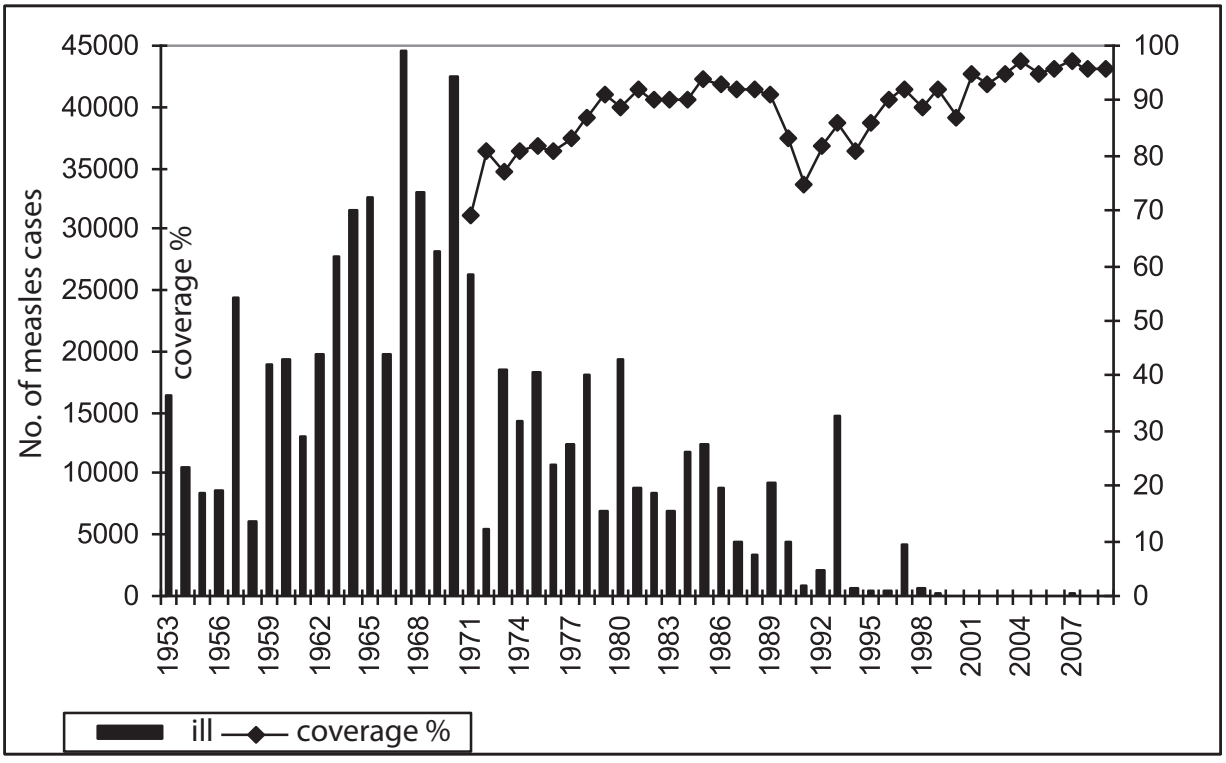

Fig. 1. Measles cases and immunization coverage in Serbia 1953-2009

DISCUSSION

In the pre-vaccination period, measles was a disease of childhood in Serbia. Recently mostly non-immunized adults in specific subpopulations, such as international travelers, healthcare workers and closed communities were affected. The analysis of epidemiological and virological surveillance data of measles infection in Serbia in the period 2007-2009 shows that all index cases were imported. In 2007, the infection spread rapidly in the very mobile Roma population, causing an outbreak. Most cases occurred in the Roma population but also in non-immunized or partially immunized persons from the general population. Out of 191 laboratory confirmed cases, 47 % were hospitalized. The majority of them were from the Roma population, who were hospitalized due to malnutrition and poor housing conditions. In recent years, several outbreaks of measles in Europe were started by traveler communities or they were the most affected population group (e.g. Marinova et al., 2009; Orlikova et al., 2010; Pervanidou et al., 2010). Pockets of susceptible persons are present throughout Europe and they may sustain transmission and spread the virus across borders (Steffens et al., 2010).

Due to the conflicts in the 1990s in the ex-Yugoslav countries, it has been difficult to perform continuous monitoring of the migration of Roma refugees and of their immunization status. During a supplementary immunization program of Roma population groups in 17 districts between 2002 and 2004, 36,611 Roma children aged 0-14 years were registered and included in the Serbia healthcare system. The data showed that only 36.3% of these children were fully immunized against measles before the campaign. The supplementary vaccination program was initially planned to cover 23,339 Roma children. However, only 12,090 children were vaccinated with

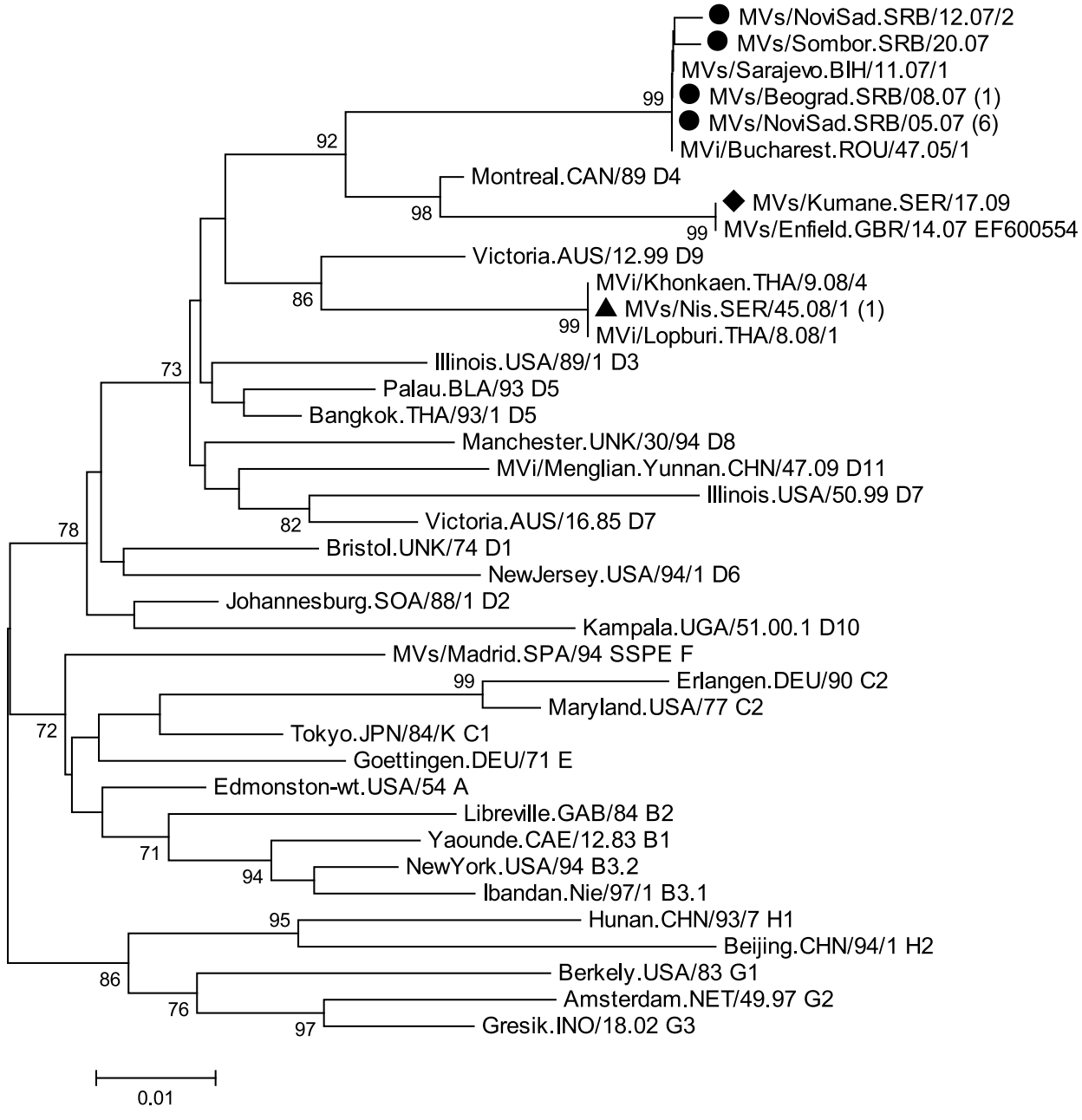

Fig. 2. Phylogenetic tree based on 450 nucleotides of the measles virus N gene and the Neighbor-Joining and Kimura 2-parameter methods of MEGA 4.0 (Tamura et al., 2007). Only bootstrap values (n=1000) above 70 are shown. Sequences from Serbia are marked with dots (year 2007), a triangle (2008) or a diamond (2009). Numbers in brackets behind the sequence names indicate the number of additional identical sequences from the same location and year.

MMR as some refused immunization and others had changed their place of residence.

CONCLUSION

To achieve measles elimination in Serbia by 2015, it is necessary to maintain vaccination coverage above 95% for both doses at the national and district levels. It is important to identify susceptible candidates among the Roma and the general population and to offer supplementary immunization opportunities to all non-immune people. Along with this, it is necessary to perform continuous surveillance of the disease, including case investigation and laboratory confirmation of clinical cases.

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