Measles is a serious and highly contagious infectious disease caused by a paramyxovirus (measles virus, MV) that can easily spread through airborne respiratory droplets or by direct contact with upper respiratory tract secretions of infected individuals (1,2). Following an incubation period of 10-14 days, infected patients experience a fever, coryza or conjunctivitis, cough, and a generalized rash that lasts 5-6 days and spreads in cranio-caudal direction. The disease in the vast majority of patients terminates with pathogen elimination and results in lifelong specific immunity that prevents reinfection (1,3). Although the majority of patients recover without any complication, approximately 30% of cases are complicated by diarrhea, pneumonia, acute otitis media, encephalitis, and even death. Infants and preschool aged children, as well as adults older than 20 years, are more prone to an unfavorable disease course (3). In 0.01% of patients who acquired natural measles infection, MV remains in a dormant form within the neural tissues and progresses, usually after a latency period of 5-10 years, into subacute sclerosing panencephalitis (SSPE) (4-6). SSPE is a chronic devastating encephalitis most commonly affecting children in whom wild MV infection occurred before the age of 2 years (4-7). Although partial and temporary remission could occur, the disease is invariably fatal. Progressive mental and motor deterioration leads to a vegetative state and fatal outcome usually 1-3 years after the occurrence of the first symptoms (4-7). Currently, there is no effective antiviral treatment either for the acute disease or SSPE. Active immunization thus remains the only way for disease burden reduction.

In the pre-vaccination era, more than 90% of children in the world under the age of 15 years were infected with MV, resulting in more than 2 million deaths annually (8). With the introduction of active immunization, the global number of measles cases decreased significantly. During 2000–2011 period, annual measles incidence decreased by 65% worldwide, from 146 to 52 cases per 1 million population, and the estimated number of measles deaths decreased by 71%, from 548 000 to 158 000 (9).

The European Vaccination Action Plan for 2015-2020, based on the World Health Organization (WHO) Global Vaccination Action Plan, anticipates the elimination of measles in the WHO European Region (10). According to this Plan, the interruption of indigenous measles transmission should have been achieved by 2015 and elimination in the WHO European Region should have been declared in 2018. However, continuous transmission with occasional measles outbreaks in the European region still occurs. In the first six months of 2019, approximately 90 000 measles cases were reported in the European Region, which is more than the number reported during the entire 2018 (11). The question arises as to the reasons for the failure to eliminate the disease. From the medical point of view, the prerequisites for elimination and eventual eradication of measles have been met:

• humans are the only natural reservoir of MV,
• long-term carriage and shedding of MV does not occur,
• there is no antigenic diversity among strains and genotypes, so the available vaccines provide protection against all circulating strains of MV,
• the low price of vaccine allows it to be universally available, and
• the vaccine provides long-term protection in a high percentage of vaccinated persons.

Therefore, elimination goals have been unmet not because of the suboptimal characteristics of the avail-
able vaccines or disease features, but because of the “lo-
gistical” failure of the health systems to achieve optimal
vaccination coverage of the European population for a suf-
ficiently long period.

Within the Region, reasons for low vaccination coverage
vary. Some countries, in the past two to three decades
have faced immunization coverage gaps created by mas-
Sive migrations, difficulties in vaccine supply, inequitable
access to vaccine of particular population subgroups, and
breaches in the cold chain affecting vaccine quality. Nev-
evertheless, countries without vaccine supply problems and
with good access to vaccination for the majority of the
population have also faced inadequate coverage, largely
due to the lack of awareness of the need for vaccination,
fear of adverse events, which results in delayed or missed
vaccinations, or refusal of vaccination by anti-science vac-
cine opponents (12-14).

Since the introduction of measles vaccination into the Cro-
atian Immunization Program in 1968, Croatia has never ex-
perienced a shortage of measles-containing vaccine that
would affect vaccine coverage. In the last fifty years, vac-
cination rates in Croatia have been high enough to ensure
a level of population immunity sufficient to interrupt in-
digenous circulation of the MV in the population and to
eliminate measles.

Individual cases of measles are regularly imported to Croa-
tia by Croatian citizens returning from abroad or by for-
eigners. In the last two decades, the majority of measles
importations have not resulted in transmission to con-
tacts due to a high level of population immunity. For ex-
ample, in 2018 there were eight imported measles cas-
es across Croatia. Only one of these imported cases led
to disease transmission to contacts, resulting in a small
outbreak in Dubrovnik and the surrounding area (15 di-
rectly linked cases). However, as the last year’s outbreak
in Dubrovnik and this year’s clusters of measles in Split,
Slavonski Brod, and Zagreb demonstrate, vaccination cov-
earage achieved in the previous decades is not sufficient
to completely prevent the circulation of the introduced
MV and the occurrence of measles clusters in adults. It is
important to emphasize, however, that each of the clus-
ters could have grown to larger outbreaks if timely and
extensive outbreak response activities had not been car-
ried out. Nevertheless, the measles outbreaks witnessed
in Croatia in the last ten years have been less intensive
than the outbreaks in other European countries, such
as North Macedonia, Serbia, Italy, France, Romania,
or Ukraine, indicating a relatively high level of population
immunity in Croatia.

Additionally, we are worried about a negative trend in vac-
cine coverage in children that occurred over the last eight
years. From 2011 to 2017, childhood vaccination rates in
Croatia declined steadily. So far, we have been lucky not to
have measles introduced into a poorly vaccinated popula-
tion of preschool children, but in the near future this sce-
nario cannot be ruled out. If vaccination rates continue to
decline, even if we are spared the outbreaks in preschool
children, the proportion of the susceptible individuals in
the population will increase and we can expect major
measles outbreaks among children and adolescents.

Measles is not the only potential problem caused by de-
clining vaccination rates. When vaccine coverage deces-
es, measles is the first disease to resurge only because it is
the most contagious of all vaccine-preventable diseases.
Although measles can cause serious morbidity with se-
vere complications, including death, as vaccination rates
decline, more serious vaccine-preventable diseases may
find their way into the population. Therefore, measles out-
breaks are a warning sign that we might expect the out-
breaks of serious illnesses, such as whooping cough, diph-
theria, or polio.

In order to prevent future outbreaks of measles and other
vaccine-preventable diseases, we should remove obstacles
to vaccination. As noted earlier, barriers to vaccination in
Croatia are not the lack of vaccines and inadequate storage
and transportation conditions, but a lack of interest in vac-
cination, fear of vaccinations, and anti-scientific attitudes.
These barriers are not only present among lay people,
who perpetuate unscientific attitudes through social net-
works, but also among health care professionals, who, due
to lack of confidence, attribute false contraindications to
vaccination and unnecessarily delay vaccinations, further
contributing to parents’ skepticism. In Croatia, as in most
European countries, research has shown that, despite the
abundance of information available on the internet and
social networks, health care workers are the major source
of information and have the greatest influence on the at-
titudes of young parents toward childhood vaccinations
(15-19). Therefore, vaccine coverage can be considerably
increased by empowering the attitudes, skills, and knowl-
ergie of primary care physicians through better, science-
based, education of physicians about the benefits, risks,
purpose, and procedures of vaccination. Of course, there
will always be a small number of individuals who refuse to
accept global scientific consensus. However, many parents who hesitate to vaccinate their children might overcome their fear or lack of recognition of the need for vaccination if they see the primary care physician’s positive attitude toward vaccination based on a thorough understanding of the benefits and risks of vaccination.

The medical profession can contribute to the ongoing debate on compulsory vaccination in Croatia with three evidence-based pieces of information:

1. It is in the interest of the protection of individuals, public health, and economic prosperity of the population, to continuously maintain high vaccine coverage in the population, as this will eliminate some vaccine-preventable diseases and curb the spread of the diseases that cannot be eliminated, reducing the suffering, treatment expenditure, and loss of life.

2. In European countries, no correlation has been established between the legal status of vaccination and coverage rates (2021). Some countries where childhood vaccinations are strongly recommended but not mandatory, such as the Scandinavian countries, have higher vaccination coverage than countries with statutory vaccination. Countries that mandate vaccination against some diseases and only recommend it against others achieve higher coverage for mandatory vaccinations. For example, in France a higher coverage was achieved for the compulsory polio vaccine than for the recommended measles vaccine. Measles vaccination in France became mandatory in 2018, but it is still too early to assess the impact of this legislative change on vaccination coverage.

3. A correlation has been observed between vaccination rates and the involvement of the attending physicians and the availability of services. Countries where physicians are more diligent in calling and reminding parents about scheduled and missed childhood vaccinations achieve higher coverage rates (22, 23).

References

1. World Health Organization position on measles vaccines. Vaccine. 2009;27:7219-21. doi:10.1016/j.vaccine.2009.09.116
2. Atkinson W, Wolfe SJH. Centers for Disease Control and Prevention. Epidemiology and Prevention of Vaccine-Preventable Diseases. The Pink Book: Course Textbook - 12th Edition Washington DC: Public Health Foundation; 2012.
3. Measles: global update. Available from: http://www.phac-aspc.gc.ca/tmp-pmv/notices-avis/notices-avis-eng.php?id=98.
4. NINDS Subacute Sclerosing Panencephalitis Information Page. Available from: https://www.ninds.nih.gov/disorders/all-disorders/subacute-sclerosing-panencephalitis-information-page. Accessed: October 28, 2019.
5. Anlar B. Subacute sclerosing panencephalitis. Paediatr Croat. 2012;56:111-4.
6. Zubčević S, Ćatibušić F, Užičanin S. Subakutni sklerozirajući panencefalitis u djece – različitost kliničke slike. Paediatr Croat. 2008;52:165-9.
7. Ivančić-Jelečki J, Baričević M, Šantak M, Harcet M, Telović G, Marušić Della Marina B, 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. Medline:23542094 doi:10.1016/j.meegid.2013.03.032
8. World Health Organization (WHO). Global measles and rubella strategic plan 2012–2020. Available from: http://www.who.int/immunization_delivery/adc/measles/measles/en/index3.html or http://www.who.int/immunization/newsroom/Measles_Rubella_StrategicPlan_2012_2020.pdf. Accessed: October 24, 2019.
9. Report A. 2012. Measles and Rubella Initiative. Available from: http://www.who.int/immunization_delivery/adc/measles/MRI_2012_Annual_Report.pdf. Accessed: October 24, 2019.
10. World Health Organization Regional Office for Europe. European Vaccine Action Plan 2015-2020. Copenhagen: WHO; 2014. Available from: http://www.euro.who.int/__data/assets/pdf_file/0007/255679/WHO_EVAP_UK_v30_WEBx.pdf?ua=1. Accessed: October 24, 2019.
11. World Health Organization Regional Office for Europe. Measles in the WHO European Region Situation Report No. 2. Copenhagen: WHO; August 2019. Available from: https://www.euro.who.int/__data/assets/pdf_file/0001/410779/Measles-Sitrep-2-Aug-2019_.pdf?ua=1. Accessed: October 24, 2019.
12. Fournet N, Mollema L, Ruijs WL, Harmsen IA, Keck F, Durand JY, et al. Under-vaccinated groups in Europe and their beliefs, attitudes and reasons for non-vaccination; two systematic reviews. BMC Public Health. 2018;18:196. Medline:29378545 doi:10.1186/s12889-018-5103-8
13. European Parliament. Vaccine hesitancy and drop in vaccination rates in Europe. European Parliament resolution of 19 April 2018 on vaccine hesitancy and the drop in vaccination rates in Europe (2017/2951(RSP)). Available from: http://www.europarl.europa.eu/docms/document/TA-8-2018-0188_EN.pdf. Accessed: October 24, 2019.
14. European Commission. Vaccination: European Commission and World Health Organization join forces to promote the benefits of vaccines. Press release12 September 2019. Brussels. Available from: https://ec.europa.eu/commission/presscorner/detail/en/IP_19_5536. Accessed: October 24, 2019.
15. Gargano LM, Herbert NL, Painter JE, Sales JM, Morfaw C, Rask...
K, et al. Impact of a physician recommendation and parental immunization attitudes on receipt or intention to receive adolescent vaccines. Hum Vaccin Immunother. 2013;9:2627-33. Medline:23883781 doi:10.4161/hv.25823

16 Ames HM, Glenton C, Lewin S. Parents' and informal caregivers' views and experiences of communication about routine childhood vaccination: a synthesis of qualitative evidence. Cochrane Database Syst Rev. 2017;2:CD011787. Medline:28169420

17 Čulina T, Andelić Breš S, Kresina S, Sepčić M. Stavovi roditelja o cijepljenju u nekoliko škola PGŽ-a. Paediatr Croat. 2018;62:20-5.

18 Juren G. Stavovi roditelja o obveznom cijepljenju djece. Diplomski rad. Zagreb: Hrvatsko katoličko sveučilište; 2019. Available from: https://www.google.com/url?sa=t&rct=j&q=&esrc=s&source=web&cd=1&cad=rja&uact=8&ved=2ahUKEwjth6Wk66rlAhVqMEAHDOg1C1MQFjAAegQIARAC&url=http%3A%2F%2Fbib.irb.hr%2Fdatoteka%2F1014720.Glorija_Juren_-_diplomski_rad_konna_verzija.doc&usg=AOvVaw0IVvyuUJgfY7FqVvwoVSt. Accessed: October 24, 2019.

19 Lovrić Makarić Z, Kolarić B, Tomljenović M, Posavec M. Attitudes and beliefs related to childhood vaccinations among parents of 6 years old children in Zagreb, Croatia. Vaccine. 2018;36:7530-5. Medline:30366807 doi:10.1016/j.vaccine.2018.10.055

20 Haverkate M, D’Ancona F, Giambi C, Johansen K, Lopalco PL, Cozza V, et al. Mandatory and recommended vaccination in the EU, Iceland and Norway: results of the VENICE 2010 survey on the ways of implementing national vaccination programmes. Euro Surveill. 2012;17. Medline:22687916 doi:10.2807/ese.17.22.20183-en

21 MacDonald NE, Harmon S, Dube E, Steenbeek A, Crowcroft N, Opel DJ, et al. Mandatory infant & childhood immunization: Rationales, issues and knowledge gaps. Vaccine. 2018;36:5811-8. Medline:30143274 doi:10.1016/j.vaccine.2018.08.042

22 Sabin vaccine Institute. Legislative Landscape Review: Legislative Approaches to Immunization Across the European Region. December 2018. Available from: https://www.sabin.org/sites/sabin.org/files/legislative_approaches_to_immunization_europe_sabin_0.pdf. Accessed: October 28, 2019.

23 Suppli CH, Rasmussen M, Valentinier-Branth P, Milbak K, Krause TG. Written reminders increase vaccine coverage in Danish children - evaluation of a nationwide intervention using The Danish Vaccination Register, 2014 to 2015. Euro Surveill. 2017;22. Medline:28488995