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Measles, Mumps, Rubella and Chickenpox epidemic and vaccination in Eastern Sicily: an epidemiologic study on seroconversion

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ABSTRACT:

Objective: Measles, Mumps, Rubella, and Chickenpox are diffusive airborne viral infections. Especially measles can present high morbidity and mortality in the absence of adequate immunization. This study aimed to evaluate the epidemiological trend of the reported cases and relative vaccination coverage of Measles, Rubella, Mumps and Varicella in the northern-eastern Sicilian.

Materials and Methods: We conducted an epidemiological survey evaluating the trend of all the measles, rubella, mumps and varicella notifications reported in the entire territory of Messina province from 1997 to 2018. We also evaluated the MMRV vaccination coverage from 2007 to 2018.

Results: The recent 2017-2018 measles epidemic deserves a special mention. In particular, Sicily notified 425 (8.5%) in 2017 and 1,118 (44.2%) of the cases of the entire national territory with an incidence in the two years of 242 and 222 cases per million inhabitants, respectively. The trend of notifications related to mumps peaked in 1999, with 59 cases reported, followed by a major epidemic outbreak in 2000 with 163 cases, and a general decrease in subsequent years. The trend of the rubella notifications concerned four major outbreaks in the years 1997, 1998, 2002 and 2008 in which they were notified 118, 65, 38 and 122 cases, respectively. Chickenpox was the most notified disease with a very high number of cases throughout the considered twenty years. In particular, large outbreaks occurred in the period 1999-2007.

Conclusions: These results are the expression of an attitude of a certain part of parents that do not respect the suggested calendar delaying the administration of the first dose and avoiding the administration of the second dose to complete the recommended vaccine schedule. In order to improve the situation, parents should always be formed about the importance of vaccinate in the correct way their children and advised to administer the four vaccinations in a single session.

Keywords: Measles, Mumps, Rubeola, Chickenpox, Epidemiology, Vaccination coverage.

INTRODUCTION

Measles, Mumps, Rubella, and Chickenpox are diffusive airborne viral infections caused by viruses belonging to different families, against which we possess extremely effective and safe preventive weapons represented by the respective vaccines. Especially measles can present high morbidity and mortality in absence of adequate immunization, and it is able to cause more or less serious complications such as diarrhea, otitis, pneumonia, thrombocytopenia, encephalitis, epileptic seizures and death in 0.2% of cases[1]. Moreover, Rubella infection can determine serious

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complications when the virus is contracted during pregnancy, especially during the first three months, resulting in a severe syndrome known as Congenital Rubella Syndrome (CRS) characterized by miscarriage, stillbirth or physical malformations including deafness, blindness, cataracts, heart defects and mental retardation[2].

Worldwide, before the introduction of vaccine in 1963 and widespread vaccination, major measles epidemics occurred approximately every 2-3 years causing an estimated 2.6 million deaths each year. Although global measles deaths have decreased by 84% worldwide in recent years (from 550,100 deaths in 2000 to 89,780 in 2016), the infection is still common in many parts of the world both in developed and developing countries, the latter particularly in some parts of Africa and Asia. An estimated 7 million people were affected by measles in 2016. In 2017, there have been 145,356 confirmed cases of measles worldwide with 110,000 deaths, particularly among children <5 years. The vast majority (> 95%) of measles deaths occurred in low-middle income countries characterized by weak health systems and policies[3]. Since January 2016, a measles epidemic is taking place in all the countries of the European Union (EU) and the European Economic Area (SEE). Between 1 January 2016 and 31 March 2019, a very high number of cases (44,074 cases) were reported to the European Center for Disease Prevention and Control (ECDC), compared to the previous three years (2012-2015). In summary, the regional European Commission for the verification of the elimination of measles and rubella (RVC, Regional Verification Commission) on the basis of an evaluation of the annual status updates relative to 2018, presented by the 53 Member States of the Region stated that within the WHO European Region at the end of 2018, 35 countries have reached or maintained the elimination of measles (compared to 37 in 2017), 2 (Austria and Switzerland) have stopped endemic transmission (for 12-35 months), 12 remain endemic and 4 (Albany, Czech Republic, Greece and United Kingdom) who had previously eliminated the disease re-established transmission[4].

In Italy, many cases of measles have been consistently reported since 2013 with a severe outbreak; in 2017 were reported 4,991 cases of measles (3.4% of all cases worldwide), of which 79% were laboratory confirmed, with 4 deaths. 88% of the cases occurred in unvaccinated subjects while 6% received only a dose of vaccine, the median age of cases was 27 years but most cases (74%) were reported in people ≥15 years, with the highest incidence occurring in children under one year of age. Three hundred fifteen cases were reported among health professionals. Of all Italian cases, Sicily notified 425 cases (8,5%)[5]. Moreover, from 1 January to 31 August 2019, 1,571 measles cases were reported with a median age of 30 years (range: 0 - 89 years). Over 80% of the cases occurred in people between 15 and 64 years of age. However, the highest incidence occurred in the range of 0-4 years, in which 161 cases were reported (10.2% of total cases). More than 30% of patients (n = 484) reported at least one complication and, in February 2019, a measles-induced death due to respiratory complications was reported in an unvaccinated adult (45 years) with concomitant diseases. Sicily notified 4% (63) of all the Italian cases with an incidence of 18.8/1.000.000[6].

According to the last WHO Global Measles and Rubella Update (September 2019), 14,621 rubella cases were notified in 2018 and 37,787 in the first nine months of 2019 worldwide[7]. In Italy, rubella cases have decreased after early 2013. Since the beginning of 2013, 252 cases of rubella have been reported (possible, probable and confirmed) of which 65 in 2013, 26 in 2014, 27 in 2015, 30 in 2016, 68 in 2017, 20 in 2018 and 16 in 2019[6]. However, between January 2005 and February 2018, 88 cases of congenital rubella were reported, 80 of which were deemed as confirmed and 8 as probable cases. Moreover, from January 2005 to February 2018, 173 cases of rubella in pregnancy were notified, of which 160 confirmed, 9 probable and 4 possible. In the same period, among the infected women, one death, a miscarriage and 32 voluntary interruptions of pregnancy were reported.

This study aimed to evaluate the epidemiological trend of the reported cases and relative vaccination coverage of Measles, Rubella, Mumps and Varicella in the northern-eastern Sicilian territory in a twenty-year period even in order to evaluate the provision of our territory in the large measles outbreak occurred in Italy during the last two-year 2017-2018.

MATERIALS AND METHODS

We conducted an epidemiological survey evaluating the trend of all the measles, rubella, mumps and varicella notifications reported in the entire territory of Messina province from 1997 to 2018. We also evaluated the MMRV vaccination coverage from 2007 to 2018.

For the collection of the epidemiological data about the incidence of the considered infectious diseases, all the notifications regarding the considered period were evaluated by analyzing the computerized and paper records of the Epidemiology Unit belonging to the Prevention Department of the Messina Provincial Health Agency. In addition to the local registers, the Infectious Diseases Information System (SIMIWEB) of the Italian Higher Health Institute (in Italian ISS), where all mandatory notifications of the national territory converge and, as far as measles and rubella are concerned, the System Integrated Measurement Survey of Measles and Rubella of the same Institution were consulted.

For the collection of data concerning vaccination coverage, the computerized vaccination registry, to which converge all the information about the vaccination coverage from all the 19 vaccination centers present in the 8 districts in which the entire provincial territory is divided, was used.

RESULTS

Measles

The trend of measles notifications suffered a drastic decline from the two-year period 1997-1998, in which two important epidemic outbreaks occurred with 444 and 181 cases, respectively, to following years with a new slight increase in the three-year period 2009-2011 in which 38,

98 and 23 cases were notified respectively. In recent years, only very few cases have been reported until the new 2017-2018 outbreak in which 65 and 42 cases were reported (Figure 1A). The most affected age group was 0-14 with 82.3% of notifications; the other age groups were affected with a percentage, respectively, of 9.9%, 7.8% and 0%. The highest number of notifications occurred, as for all other pathologies, in the district comprising the metropolitan area of Messina city with a percentage of 79.9%.

The recent 2017-2018 measles epidemic deserves a special mention. In particular, Sicily notified 425 (8.5%) in 2017 and 1,118 (44.2%) of the cases of the entire national territory with an incidence in the two years of 242 and 222 cases per million inhabitants, respectively[4,8]. The province of Messina, in particular, reported 107 cases in the two-year period (7.6% of the entire Region), with a similar percentage in the two sexes (46.4% M, 53.6% W). The average age was 19.5 years, the pediatric age group (0-14 years) was affected with a percentage of 50.4% while the 15-64 years range was interested in the remaining 49.6%. No cases were recorded in the >65 years. Almost all the cases (96.3%) were not vaccinated (3.7% were vaccinated only with a single dose). The hospitalization rate was 67.6% and 15.2% of cases developed some clinical complications mainly represented by diarrhea, kerato-conjunctivitis and pneumonia. No death occurred. The hospitalization involved children (0-14) for 51.0%, the remaining percentage (49.0%) involved people >14 years old.

Mumps

The trend of notifications related to mumps peaked in 1999, with 59 cases reported, followed by a major epidemic outbreak in 2000 with 163 cases, and a general decrease in subsequent years. Very few cases have been reported in recent years (Figure 1B). The most affected age class was 0-14, with a percentage equal to 80.0%; the 15-64 age group was affected with a percentage of 20.4%. No case was recorded among people aged >65 years. The largest number of notifications occurred in the metropolitan area of Messina with a percentage of 77.1%.

Rubella

The trend of the rubella notifications has interested by four major outbreaks in the years 1997, 1998, 2002 and 2008 in which they were notified 118, 65, 38 and 122 cases, respectively. In recent years, only few cases have been reported (Figure 1C). The most interested age class was 0-14 but with a lower percentage (47.5%) compared to measles and mumps. A high percentage (52%) interested the class 15-64 years. In particular, the 15-44 age group, which includes women of childbearing age, was affected with a percentage of 48%. Only 0.5% of cases occurred in the people ≥ 65 years. The most affected district was Messina with a percentage of 66%. As regards the 2008 epidemic, 75% of cases occurred in the four-month period February/May with 92 total notified cases. The female sex was affected for 52.2%, while the most affected age groups were those 15-24 and 25-64 with a percentage, respectively, of 50% and 27.2%. Only 1% of those affected were vaccinated. In the same year, four cases of rubella in pregnancy were also verified but all of them contracted the virus in the 2nd trimester of pregnancy. In all four cases there was laboratory confirmation of rubella infection. Furthermore, all the women involved were unvaccinated and three newborns tested negative for the virus

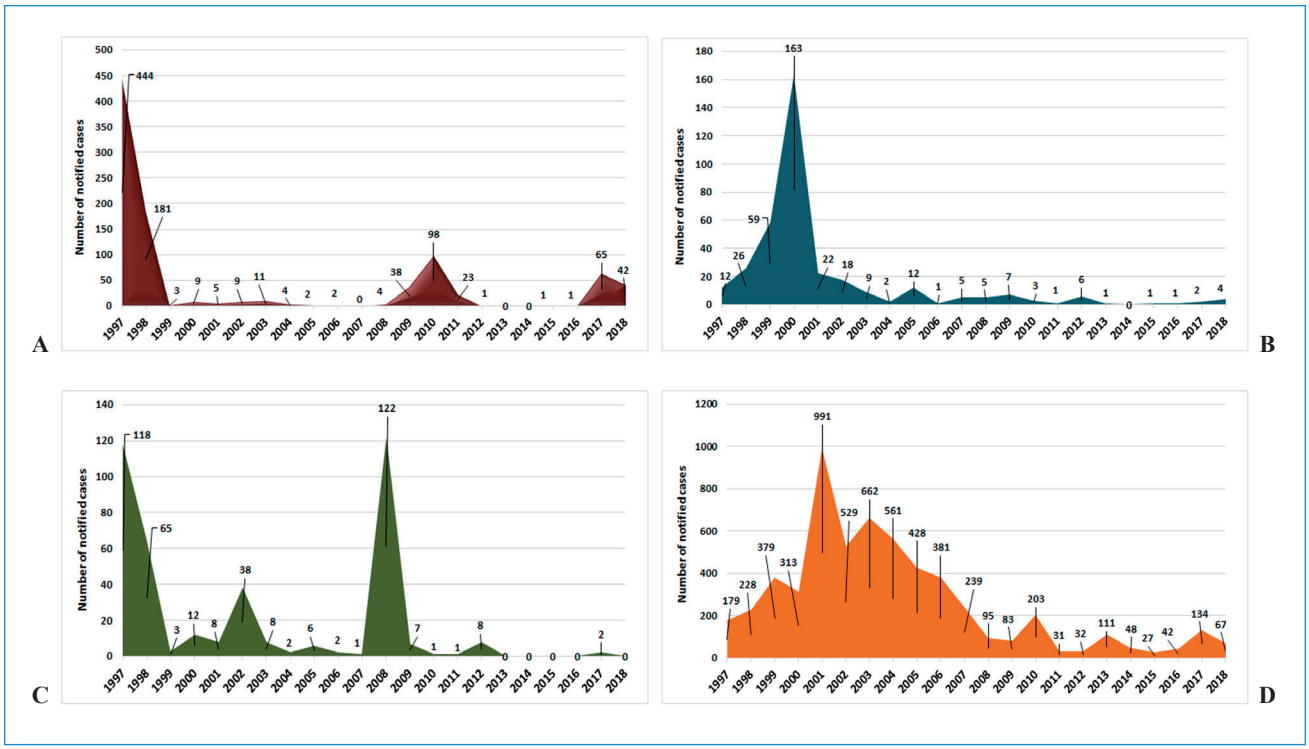

Figure 1. Epidemiological trend of Measles (A), Mumps (B), Rubella (C) and Chickenpox (D) notified cases in 1997-2018.

(IgM and PCR negative). Only one child was positive for IgM (negative PCR) without development, however, of signs and symptoms of the disease.

Chickenpox

Chickenpox was the most notified disease with a very high number of cases throughout the considered twenty years. In particular, large outbreaks occurred in the period 1999-2007 with a number of cases equal to 379, 313, 991, 529, 662, 561, 428 and 381, respectively. In recent years, the disease, despite a general decrease, was still very much notified (Figure 1D). The most affected age group was 0-14 with a percentage of 83%; the 15-64 group was affected by 17%. No case has occurred among people >65 years. The district most affected was Messina with a notification rate of 68.4%.

Vaccination coverage

The MMR vaccination coverage from 2007 to 2017 showed a quite stable trend except for 2017, in which the percentage was lower than previous years. However, the percentage values are constantly at a lower level compared to those suggested by the WHO as recommended (95%) to prevent the transmission of the infection. For Varicella vaccination, we observed coverage values lower compared MMR and always far below the recommended ones (Figure 2).

DISCUSSION

Eliminating measles and rubella is one of the top immunization priorities of the European region, as outlined in the European Vaccine Action Plan 2015-2020. The WHO recommends immunization for all susceptible children and adults for whom vaccination is not contraindicated (WHO/Europe, 2014). To reach all children with two doses of MMR vaccine should be the standard for all national immunization programs[9]. In Italy, the last national vaccine program, summarized by the National Plan for Vaccine Prevention (NPVP) 2017-2019, includes the first dose of the trivalent MMR and Varicella vaccinations (or tetravalent MMRV) at 13th-15th month of life and the second at 4th-5th year of life. However, measles vaccination coverage is suboptimal in Italy with a percentage of 93.2% at 24 months for those born in 2016; in Sicily, the percentage was of 90.9%. For the same cohort, much lower coverage values were reported for Varicella vaccine. Particularly, the national percentage value was 74.2% while in Sicily there was a higher value of 86.1%[10]. For these reasons, the National Ministry of Health decided to turn mandatory these vaccinations through the emanation of the recent law 117/2019, whose effects will certainly be observed in the following years[11].

The wrong belief of a hypothetic association between MMR vaccine and autism has certainly played an important role in the measles vaccination coverage decrease worldwide, also because it represented one of the most widely used anti-vaccine movements thesis over the last decade that has contributed significantly to create alarmingness and fears about vaccines. However, many following studies and several data reviews by independent organizations have all concluded that there is no evidence to support a causal association between MMR and autism[12-15]. Nevertheless, this wrong idea had a remarkable echo by media resulting in failure to achieve adequate vaccine coverage (≥ 95%) with the spread of thousands of new cases (and related complications) of measles, mumps and rubella since the 2000s, as reported by the WHO Global Health Observatory Data Repository[16,17]. About 20 years later, there are still

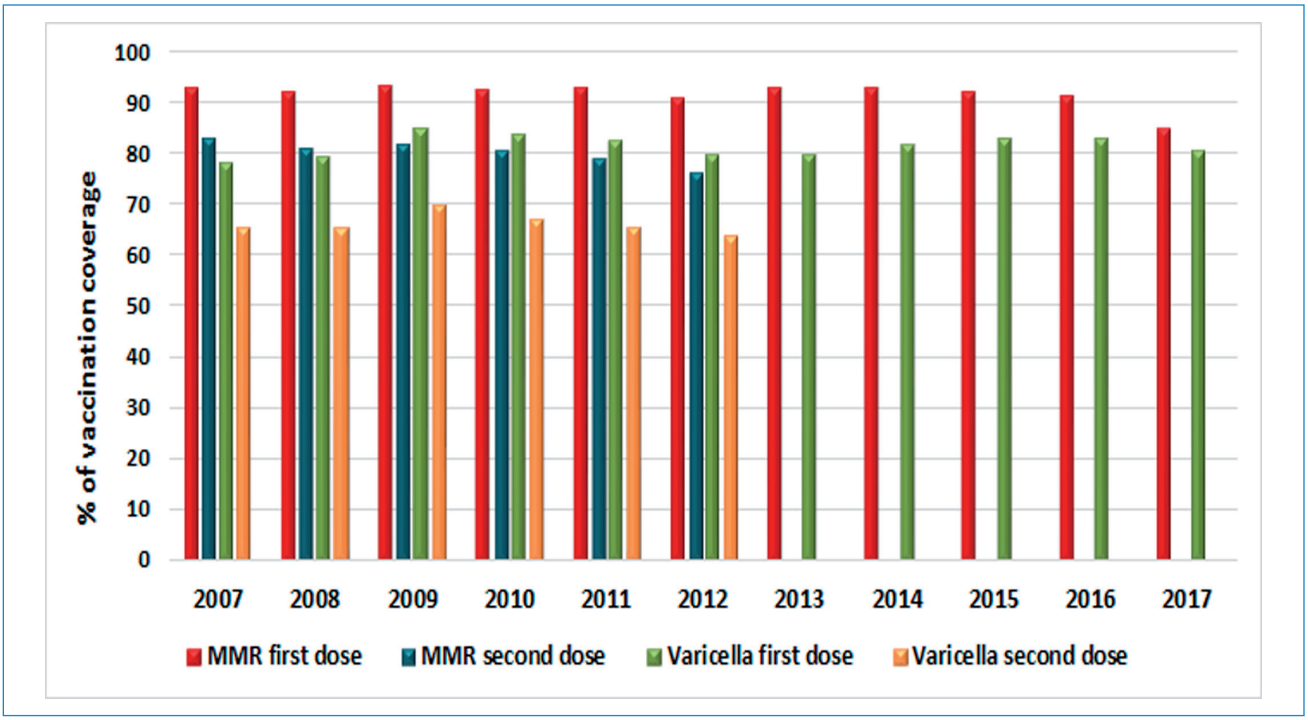

Figure 2. Trend of vaccination coverage of MMRV first and second doses 2007-2017.

doubts within the public opinion and the fear that MMR immunization could cause autism is still one of the most reported causes of missed vaccination[18,19]. Under the Global Vaccine Action Plan, measles and rubella are targeted for elimination in five WHO Regions by 2020[20].

Between 1 January 2016 and 31 March 2019, a very high number of measles cases (44,074 cases) were reported to the ECDC, compared to the previous three years (2012-2015). On 28 May 2019, the ECDC published the Risk Assessment "Who is at risk of measles in the EU/EEA? Identifying susceptible groups to close immunity gaps towards measles elimination", which also contains the epidemiological profiles of individual countries. Based on the ECDC evaluation, the risk of a continuous and widespread measles circulation persists in Europe. Three main risk factors were identified: the presence of a high number of people susceptible to measles (over 4.5 million children and adolescents born since 1999) due to the low vaccination coverage (in 2017 only 4 EU countries achieved a vaccination coverage of 95% for two doses of measles-containing vaccine, while in 2007 they were 14); the presence of a high number of cases of measles among newborns and adults representing the groups with the highest risk of complications; the persistence of the risk of importing the infection, which can aggravate ongoing outbreaks or start new ones in communities where the virus is not currently in circulation and where groups susceptible to infection persist (in the 2016-2019 period almost half of the imported cases of measles reported in the EU countries have been infected in another European country, especially in countries where measles is still endemic and/or where large epidemics were in progress).

In our territory, all the childhood diseases preventable by MMRV vaccination showed a declining trend over the considered period, with isolated epidemic peaks that, however, never reached the numbers of the past, a sign that vaccination coverage in the local population is present anyway. However, the recent measles outbreak denotes that there are groups of susceptible individuals on which we should act in order to avoid epidemics. Sicily was one of the most affected Italian regions, but Messina's territory has played a minimal role in this epidemiological picture. However, even in our territory, it was reported a very high hospitalization rate and number of complications. This picture was probably due to the high number of cases occurred in adults in which, as shown by previous studies, the disease is often characterized by a more serious clinical trend[21,22]. Therefore, it is necessary to act through campaigns to the general population, underlining not only that measles is not a trivial disease free of complications in all ages but even that in adults these complications could be serious or even fatal.

Concerning rubella, the danger must be emphasized especially to the women of childbearing age that represent the population more at risk of complications, in order to persuade them to carry out checks on their immune status against rubella and, if negative, to undergo vaccination. In two previous study, we demonstrated how far we are to the objectives of the "National Measles Elimination Plan and Congenital Rubella" (PNEMoRC) 2010-2015, especially that to eliminate congenital rubella within 15 years from its implementation. Indeed, we found a very high percentage of women declaring a negative serological status for this infection and, especially, the extremely low rate of preconception tests suggested a very little attention to the prevention of congenital rubella[23,24]. We highlight that the elimination of measles and congenital rubella are also two of the objectives set by the recent PNPV 2017-2019.

The much higher number of notified cases of chickenpox compared to the other diseases and the more fewer percentages of vaccination coverage confirm that a lot needs still to be done in the promotion of vaccination against this disease, for example always suggesting parents to perform the tetravalent vaccine and not the trivalent. Chickenpox, in fact, can cause complications sometimes of a certain gravity (especially in pregnancy), also considering that the virus is a herpes and, after the primary infection, enters in a phase of latency in the nervous ganglia where it remains for the whole life, reactivating itself in conditions of immunodepression and giving the clinical picture of herpes zoster. Therefore, to improve the coverage of Varicella vaccination is able to modify not only the epidemiology of chickenpox but also of herpes zoster, against which we have a specific vaccine that, however, in Italy it is characterized by very low vaccination coverage[25].

Finally, concerning the vaccination coverage for the first and second dose of MMR and Varicella vaccination, a stable but always below the recommended values trend was observed. The 2017 values (84.7% for MMR and 80.3 for Varicella vaccines) of the first doses, which are lower compared to previous years, are probably consequent to the time of administration that, in Italy, is between the 13th and the 15th month of life. Certainly, we will assist to a catch up in the future years. Moreover, the remarkable difference between the values of the MMR first and second doses could explain the last measles outbreak occurred in our territory. It is well known, indeed, that only making the complete vaccination cycle (with both doses) it is possible to obtain a good protection level. The same consideration we can also make for Varicella vaccination. The period considered for this vaccination is the same considered for MMR vaccination, as it can be administered in the same periods of life. It should be noted, however, that the percentages for this vaccination are always much lower than the MMR one, far below the targets set by the PNPV 2017-2019. This explains the constant presence of this disease on our territory, with an exceptionally higher number of cases compared to the other three diseases, and the outbreaks of 2010 and 2013 in which 203 and 111 cases were notified, respectively.

CONCLUSIONS

These results are the expression of an attitude of a certain part of parents that do not respect the suggested calendar delaying the administration of the first dose and avoiding the administration of the second dose to complete the recommended vaccine schedule[19]. In order to improve the situation, parents should always be formed about the importance to vaccinate in the correct way

their children and advised to administer the four vaccinations in a single session using the tetravalent MMRV vaccine and not the trivalent MMR, avoiding in this way a further injection and/or vaccination session for the administration of varicella vaccine.

Conflict of Interest:
The authors declare that they have no conflict of interests.

REFERENCES

1. Battistella M, Carlino C, Dugo V, Ponzo P, Franco E. Vaccines and autism: a myth to debunk? Ig Sanita Pubbl 2013; 69: 585-596.
2. Duszak RS. Congenital rubella syndrome--major review. Optometry 2009; 80: 36-43.
3. World Health Organization (WHO). Measles. 2019. https://www.who.int/news-room/fact-sheets/detail/measles. Accessed: 20 October 2019
4. Epicentro. Morbillo. Ultimi aggiornamenti. 2019. https://www.epicentro.iss.it/morbillo/aggiornamenti. Accessed: 20 October 2019
5. Palamara MA, Visalli G, Picerno I, Di Pietro A, Puglisi G, Marano F, D'Andrea G, Facciolà A. Measles outbreak from February to August 2017 in Messina, Italy. J Prev Med Hyg 2018; 59: E8-E13.
6. Istituto Superiore di Sanità. Sorveglianza Integrata Morbillo e Rosolia. Rapporto N° 55- Settembre 2019. https://www.epicentro.iss.it/morbillo/bollettino/RM_News_2019_55.pdf. Accessed: 20 October 2019
7. World Health Organization (WHO). Measles and Rubella Surveillance Data. Global Measles and Rubella Monthly Update. 2019. https://www.who.int/immunization/monitoring_surveillance/burden/vpd/surveillance_type/active/measles_monthlydata/en/. Accessed: 20 October 2019
8. Epicentro. Le vaccinazioni in Italia, copertura vaccinale Morbillo – età pediatrica. 2017. Available from: http://www.epicentro.iss.it/temi/vaccinazioni/dati_Ita.asp#morbillo. Accessed: 20 October 2019
9. Centers for Disease Control and Prevention (CDC). Measles, Mumps, and Rubella (MMR) Vaccine Safety. 2017. Available at: http://www.cdc.gov/vaccinesafety/vaccines/mmr-vaccine.html Accessed: 20 October 2019
10. Epicentro. Rosolia Congenita e in Gravidanza. Rapporto Semestrale N. 8-Marzo 2018. https://www.epicentro.iss.it/rosolia/bollettino/Rosolia_congenita_news_numero%208%20IT.pdf. Accessed: 20 October 2019
11. Ministero della Salute. Piano Nazionale della Prevenzione Vaccinale 2017-2019. 2017. Available at: http://www.salute.gov.it/imgs/C_17_pubblicazioni_2571_allegato.pdf. Accessed: 20 October 2019
12. Taylor B, Miller E, Farrington CP, Petropoulos MC, Favot-Mayaud I, Li J, Waight PA. Autism and measles, mumps, and rubella vaccine: no epidemiological evidence for a causal association. Lancet 1999; 353: 2026-2029.
13. Mäkelä A, Nuorti JP, Peltola H. Neurologic disorders after measles-mumps-rubella vaccination. Pediatrics 2002; 110: 957-963.
14. Madsen KM, Hviid A, Vestergaard M, Schendel D, Wohlfahrt J, Thorsen P, Olsen J, Melbye M. A population-based study of measles, mumps, and rubella vaccination and autism. N Engl J Med 2002; 347: 1477-1482.
15. Wilson K, Mills E, Ross C, McGowan J, Jadad A. Association of autistic spectrum disorder and the measles, mumps, and rubella vaccine: a systematic review of current epidemiological evidence. Arch Pediatr Adolesc Med 2003; 157: 628-634.
16. MMWR. Measles Outbreak – Netherlands, April 1999 January 2000. April 14, 2000/49(14); 299-303.
17. MMRW. Measles Epidemic Attributed to Inadequate Vaccination Coverage - Campania, Italy, 2002. October 31, 2003/52(43);1044-47.
18. Di Pasquale A, Bonanni P, Garçon N, Stanberry LR, El-Hodhod M, Tavares Da Silva F. Vaccine safety evaluation: Practical aspects in assessing benefits and risks. Vaccine 2016; 34: 6672-6680.
19. Facciolà A, Visalli G, Orlando A, Bertuccio MP, Spataro P, Squeri R, Picerno I, Di Pietro A. Vaccine hesitancy: an overview on parents' opinions about vaccination and possible reasons of vaccine refusal. J Public Health Res 2019; 8: 1436.
20. World Health Organization (WHO). Global Measles and Rubella Strategic plan 2012–2020, WHO 2012. http://apps.who.int/iris/bitstream/10665/44855/1/9789241503396_eng.pdf.
21. Caseris M, Houhou N, Longuet P, Rioux C, Lepeule R, Choquet C, Yazdanpanah Y, Yeni P, Joly V. French 2010-2011 measles outbreak in adults: report from a Parisian teaching hospital. Clin Microbiol Infect 2014; 20: O242-244.
22. Casasoprana A, Honorat R, Grouteau E, Marchou B, Claudet I. A comparison of adult and pediatric measles patients admitted to emergency departments during the 2008-2011 outbreak in the Midi-Pyrénées region of France. Jpn J Infect Dis 2014; 67: 71-77.
23. Facciolà A, Squeri R, Genovese C, Alessi V, La Fauci V. Perception of rubella risk in pregnancy: an epidemiological survey on a sample of pregnant women. Ann Ig 2019; 31: 65-71.
24. La Fauci V, Squeri R, Genovese C, Alessi V, Facciolà A. The 'Dangerous Cocktail': an epidemiological survey on the attitude of a population of pregnant women towards some pregnancy risk factors. J Obstet Gynaecol 2019 Aug 2:1-6. doi: 10.1080/01443615.2019.1621818. [Epub ahead of print]
25. Di Pietro A, Facciolà A, Visalli G. Herpes zoster vaccine: a protection for the elderly. Ann Ig 2018; 30: 23-27.