

Measles outbreak in Apulia, southern Italy

To the Editor,

Recently, a serological study conducted in the province of Bari (Apulia, southern Italy) revealed a high level of susceptibility to measles virus (MV) in that area.¹ In our paper we describe the recent outbreak occurred in the province of Lecce (Apulia), where a high level of susceptibility can be hypothesized same as the province of Bari, with regard to the molecular epidemiology of MV.

From 2016 to 2018, more than 7000 measles cases were reported to the Italian National Integrated Measles and Rubella Surveillance System and more than 1900 cases during the year 2019.^{2,3}

In the Region Apulia, 25 cases have been reported in 2017, 58 in 2018, and 64 in 2019. In the short period from December 2019 to March 2020, 49 suspected cases were notified to the National Integrated Measles and Rubella Surveillance System. After epidemiological and laboratory investigation, 39 cases were laboratory confirmed, seven were defined as probable cases, and three discarded. All these cases occurred in the Province of Lecce (Figure 1), causing the outbreak described in this paper.

Of the 46 out of 49 cases classified as measles 8.7% ($n = 4$) were ≤ 1 year of age, 4.3% ($n = 2$) were 2 to 14, 65.2% ($n = 30$) were between 15% to 39%, and 21.7% ($n = 10$) were >39 years. The median age was 32 years (range: 3 months–55 years). Vaccination status was known for all the 46 cases: 97.8% ($n = 45$) were not vaccinated and 2.2% ($n = 1$) was vaccinated with one dose of measles-mumps-rubella vaccine.

According to the epidemiological data, 10 were sporadic cases and 36 were related to five separate chains of transmissions. Moreover, of the cases reported, 45 were autochthonous and one was imported from Bulgaria.

A rapid laboratory surveillance was set up by the Subnational Reference Laboratory of the Region Apulia, part of the measles and rubella surveillance network MoRoNet.⁴ A total of 39 cases were laboratory confirmed, by serology on blood ($n = 14$) and by both serology and reverse transcription-polymerase chain reaction (RT-PCR) on throat swabs ($n = 25$).

Of 25 samples that had a positive result by RT-PCR, 19 have been sequenced on the highly variable region of nucleoprotein gene (N-450) for genotyping. Of these cases, five were sporadic and the remaining 14 were related to the four following chains of transmission: focolaio_3_Puglia2019 (seven cases), focolaio_1_Puglia2020 (three cases), focolaio_2_Puglia2020 (three cases), and focolaio_3_Puglia2020 (one case). Thus, four out of the five chains of transmissions identified have been genetically characterized. For the fifth chain of transmission no samples have been collected for genotyping.

Phylogenetic analysis reveals that all the MV strains that co-circulated in the period considered belong to the genotype B3 and cluster in two different groups, called *Dublin* ($n = 13$) and *Lecce* ($n = 3$) variants (Figure 2). Within each group, sequences are 100% identical to each other. The variant *Dublin* had been already reported in Apulia during 2018 and in April 2019, in the provinces of Bari and Taranto. No sequences identical to the variant *Lecce* have been never reported to date.

Eliminating measles and rubella is a core goal of the World Health Organization and a sensitive laboratory-supported surveillance is an important tool in monitoring the success of the elimination program.⁵ Timely identifying and confirmation of suspected cases allow the early detection of outbreaks and the analysis of ongoing transmission to set more effective vaccination measures. In Apulia, measles vaccination coverage was 94.2% for the first dose and 91.9% for the second dose in 2019 (data from Ministry of Health), but age groups of young adults and adults have still a low vaccination coverage (far from the expected 95%) due to both vaccine hesitancy and anti-vaccination positions that affect most of Italy.^{6,7}

An increase in the number of measles cases started in December 2019 in the city of Lecce and surrounding areas. Our data show the co-circulation of two different MV strains (B3 *Dublin* and B3 *Lecce*) between December 2019 and March 2020. Most cases occurred among no vaccinated adults between 23 and 50 years of age, confirming that this age group has a low vaccination coverage, as stated by Marchi et al.¹

The Italian government, concerned by falling vaccine uptake rates and an apparent increase in antivaccine sentiment, introduced compulsory vaccination for measles and nine other diseases, in 2017.⁸ Vaccines are mandatory for Italian schoolchildren up to 16. However,

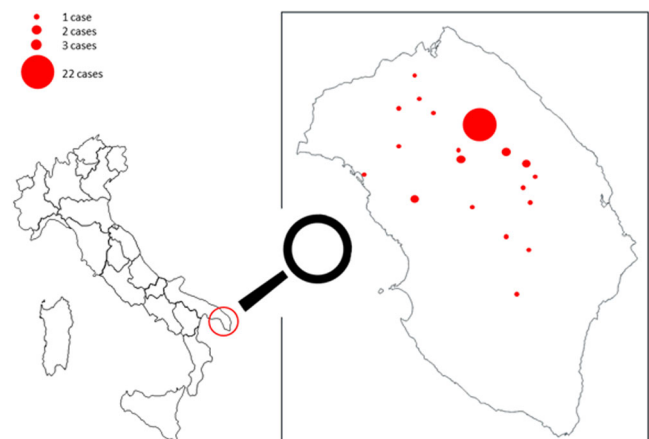


FIGURE 1 Geographical distribution of the measles cases notified from the province of Lecce (Apulia, South of Italy)

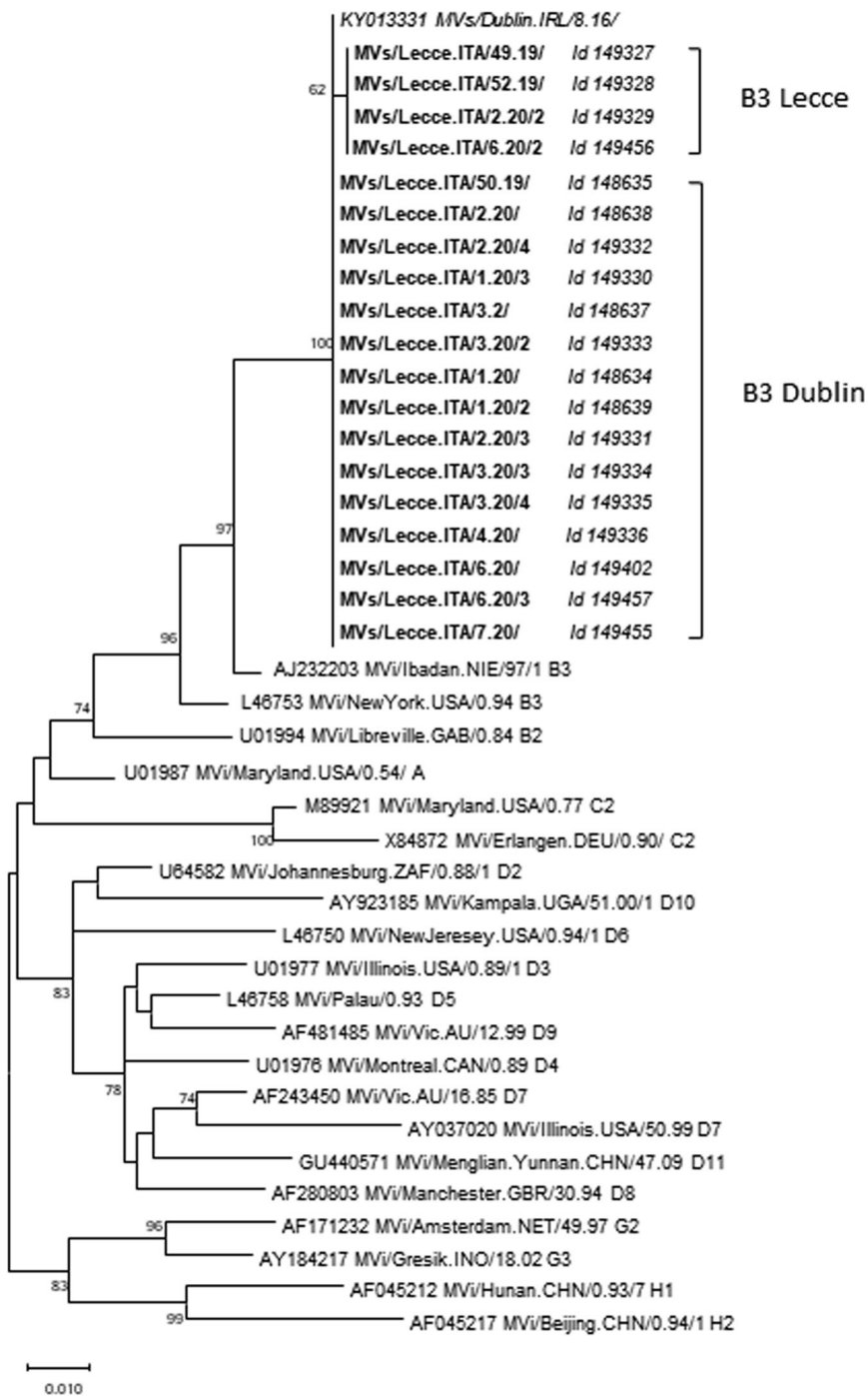


FIGURE 2 Phylogenetic tree constructed with sequences of the N-450 region of MV strains identified in Apulia from December 2019 to March 2020. The evolutionary history was inferred by using the Maximum Likelihood method and Kimura 2-parameter model. The percentage of trees in which the associated taxa clustered together is shown next to the branches. Initial tree(s) for the heuristic search were obtained automatically by applying Neighbor-Join and BioNJ algorithms to a matrix of pairwise distances estimated using the maximum composite likelihood (MCL) approach, and then selecting the topology with superior log likelihood value. A discrete Gamma distribution was used to model evolutionary rate differences among sites. All the sequences have been submitted in the World Health Organization's measles nucleotide surveillance (MeaNS) database (IDs numbers for nucleotide sequences are reported in figure)

measles transmission can be interrupted only by achieving high population immunity in all age groups and seroprevalence studies and laboratory surveillance are fundamental tools to promote supplementary immunization activities and sustain measles elimination.

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CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.


ETHICS STATEMENT

The local ethics committee consent was not required as the investigation was conducted according to the National Integrated Surveillance Plan to eliminate measles, rubella and congenital rubella syndrome (Italian Ministry of Health, DGPRES 0033189-12/11/2018).


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