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# Measles elimination in Italy: data from laboratory activity, 2011–2013

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ABSTRACT

*Background:* The European Regional Office of the World Health Organization developed a strategic approach to halt the indigenous transmission of measles in its 53 Member States by 2015, World Health Organization [1]. Many European countries, including Italy began the implementation of national programs to reach this goal.
*Objectives:* To describe and discuss the results of laboratory activity in measles surveillance, performed from January 2011 to December 2013 by the Italian National Reference Laboratory for Measles and Rubella.
*Study design:* Samples of suspected measles cases were collected from different Italian regions to confirm clinical diagnosis. Anti-measles IgM antibodies detection by Enzyme-Linked Immunosorbent Assay and/or molecular detection by Reverse Transcriptase-Polymerase Chain Reaction assay were performed. Positive samples were sequenced for viral characterization.
*Results and conclusions:* According to results from the National Reference Laboratory's activity urine and blood seem to be the best specimens for measles laboratory surveillance. Phylogenetic analysis revealed a co-circulation of the genotypes D4 and D8 during the reviewed period, a cluster of B3 and sporadic cases of D9 and H1.



## 1. Background

Globally, measles morbidity and mortality have been dramatically reduced since the implementation of enhanced vaccination strategies [2,3] and the interruption of the indigenous transmission of measles virus (MV) has been reported from several countries [4]. Nevertheless, large outbreaks continue to occur in countries with high vaccination coverage after importation of the virus from endemic countries [5,6].

In September 2010, the World Health Organization (WHO) Regional Committee for Europe renewed commitment to the elimination of measles and rubella, and prevention of congenital rubella syndrome by 2015 [1].

In February 2011, Italy launched the "Piano Nazionale per l'Eliminazione del Morbillo e della Rosolia congenita (PNEMoRc)" following WHO indications to reach the goal of measles and rubella elimination by 2015 [7]. One of the PNEMoRc target is to reach a vaccination coverage of at least 95%, with a two-dose vaccination schedule for measles–mumps–rubella (MMR) free of charge. The first dose is generally given at 12–15 months of age, the second dose at 4–6 years of age. In Italy, measles vaccination is not mandatory but highly recommended. As a consequence, coverage levels for measles vaccine are still below the target in most regions. In 2012 the national immunization coverage for the first dose of MMR in children under two years of age was 90.0% of the 2010 birth cohort [8], and several outbreaks have occurred since the beginning of 2010 [9].

*Abbreviations:* MV, measles virus; WHO, World Health Organization; PNEMoRc, Piano Nazionale per l'Eliminazione del Morbillo e della Rosolia congenita; MMR, measles-mumps-rubella vaccine; LHA, Local Health Authorities; RRL, Regional Reference Laboratories; NRL, National Reference Laboratory; OF, oral fluid; ELISA, enzyme-linked immunosorbent assay; PCR, polymerase chain reaction; CSF, cerebrospinal fluid; BL, border-line.

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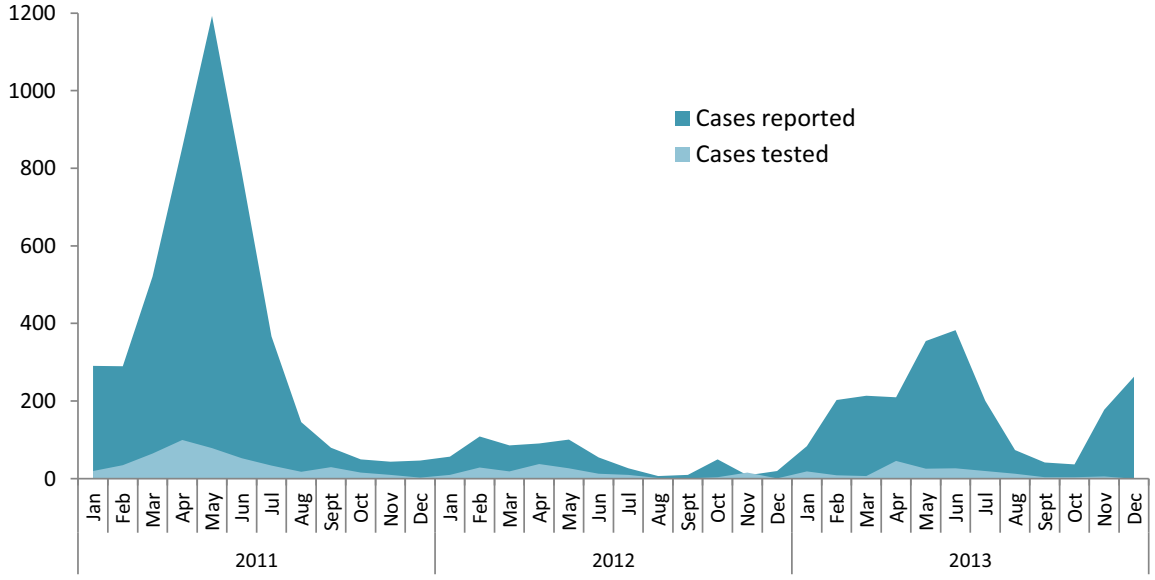


**Fig. 1.** Measles cases reported to the enhanced measles surveillance system (data from the Infectious Diseases Epidemiology Unit of the National Institute of Health)and cases tested by NRL.

A sensitive and specific surveillance system, able to promptly detect measles cases, is essential to monitor the effectiveness of vaccination programs, and laboratory measles surveillance is an important tool in measles elimination. WHO established that the adequate specimens for detecting acute measles infection should be collected, and tested in a proficient laboratory, from at least 80% of suspected measles cases. In addition, WHO stated that the integration of measles and rubella surveillance is convenient since the symptoms of these diseases are similar, and both the diseases commonly affect the same age groups. Thus, the analysis of specimens from suspected cases of measles or rubella for both the diseases is clinically and epidemiologically relevant, as it allows to confirm or rule out each of the two diseases [10].

According to the Italian reporting surveillance system, physicians are required to report all the suspected measles cases to Local Health Authorities (LHA) within 12 h. For each suspected case, LHA are required to carry out an epidemiological investigation, to fill and send a standard measles notification form to Regional Health Authorities. The Regional Authorities forward the forms to the Ministry of Health and to the Infectious Diseases Epidemiology Unit of the National Institute of Health. Local Health Authorities (LHA) are also required to obtain specimens from the suspected measles cases, and to send them to the Regional Reference Laboratories (RRL) (if existing) or to the National Reference Laboratory (NRL) at the Italian National Institute of Health (Istituto Superiore di Sanità, Rome). RRLs confirm cases with serological and/or molecular tests, genotype and send data about sequences to the NRL. Hence, the role of NRL is to confirm and genotype measles cases/outbreaks collected from the LHA, and to collect data about MV sequences provided from those regions with a RRL.

In February 2013, the Italian Minister of Health published a document which regulates the integrated surveillance for measles and rubella (MR), recommending to test all negative suspected measles cases for rubella, and vice versa, as per WHO Guidelines [11].

Measles lab data are key elements for MR surveillance and elimination from WHO European Region. To successfully achieve MR elimination goal and to improve both MR lab and surveillance data quality, WHO European Region has developed and rolled out a web based Measles and Rubella Laboratory Data Management System (MRLDMS). It will support MR labs in recording, managing, linking, reporting and sharing measles data [12].

In 2011, 35,768 measles cases were reported in the WHO European region according to the WHO epidemiological brief [13]. Five countries (France, Italy, Romania, Spain and Germany) accounted for more than 90% of all measles cases. Outbreaks of measles in Europe were still observed in 2012 with 23,871 measles reported cases. Of the total, 88% of cases ($n$ = 20,891) were reported from Ukraine, Romania, the Russian Federation and the United Kingdom [14]. In 2013, 31,685 measles cases were reported with 81% ($n$ = 25,596) from Georgia, Italy, the Netherlands, Turkey, Ukraine and the Russian Federation [15].

In Italy the number of reported cases increased in 2011 compared to the year before [16], and a decrease was observed in 2012 and 2013 (Fig. 1) following the European trend.

## 2. Objective

According to the 2008 European Commission (EC) case definition a measles case is defined by clinical criteria as an association of fever, a generalized maculopapular rash and one of the following symptoms: cough, choryza, conjunctivitis, or Koplik spots [17]. EC's classification also provides the following case definition: possible case (any person meeting the clinical criteria), probable case (any person meeting the clinical criteria and with an epidemiological link) and confirmed case (any person not recently vaccinated and meeting the clinical and laboratory criteria). From January 2011 to December 2013 a total of 7538 cases, including confirmed, possible and probable cases, were reported in Italy. A notification rate of 7.7 cases per 100,000 population was observed in 2011, 1.0 per 100,000 in 2012 and 3.8 per 100,000 in 2013 (personal communication from the Infectious Diseases Epidemiology Unit of the National Institute of Health).

The aim of this article is to describe results from the laboratory activity on measles surveillance performed by the Italian NRL, between January 2011 and December 2013.

## 3. Study design

For measles confirmation urine, oral fluid (OF) and dried blood spots are required to be collected from patients meeting the EC measles case definition regardless of the age at time of sample collection.