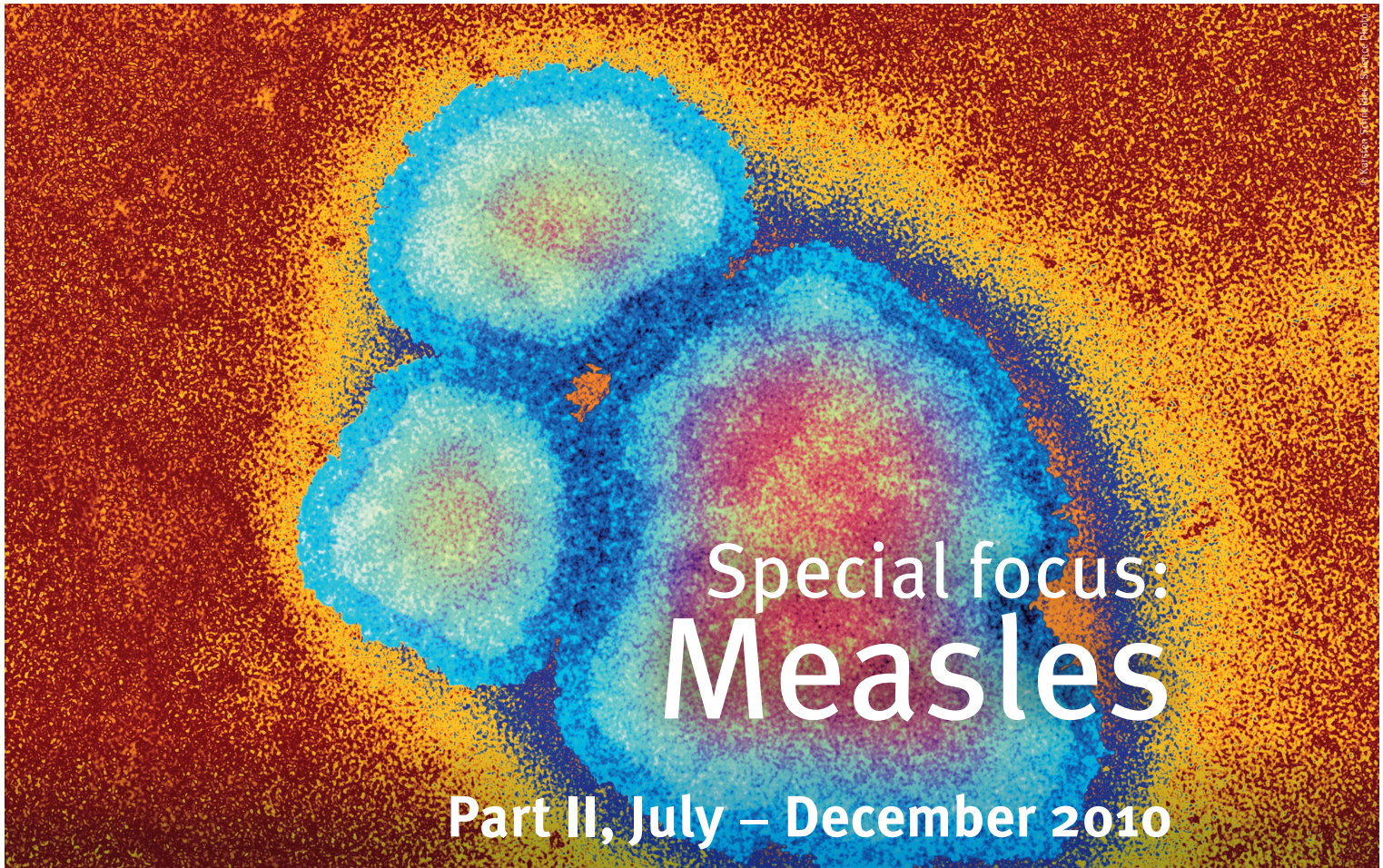




Eurosurveillance

Europe's journal on infectious disease epidemiology, prevention and control



Special focus: Measles

Part II, July – December 2010

- This second part of the 2010 Eurosurveillance 'Spotlight on measles' features ten articles from eight countries

Focus:

- Outbreaks of measles still occur regularly in many European countries
- Continued need for targeting unvaccinated subpopulations

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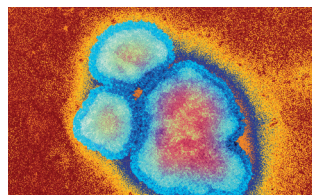
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Measles virus particles. Coloured transmission electron micrograph (TEM) of a virus that causes measles (from the morbillivirus group of viruses). Measles is highly infectious and mainly affects children, producing fever and rash. One attack usually gives life-long immunity. Magnification: $\times 144,000$ when printed 10 centimetres high.

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Spotlight on measles 2010: Measles elimination in Europe – a new commitment to meet the goal by 2015

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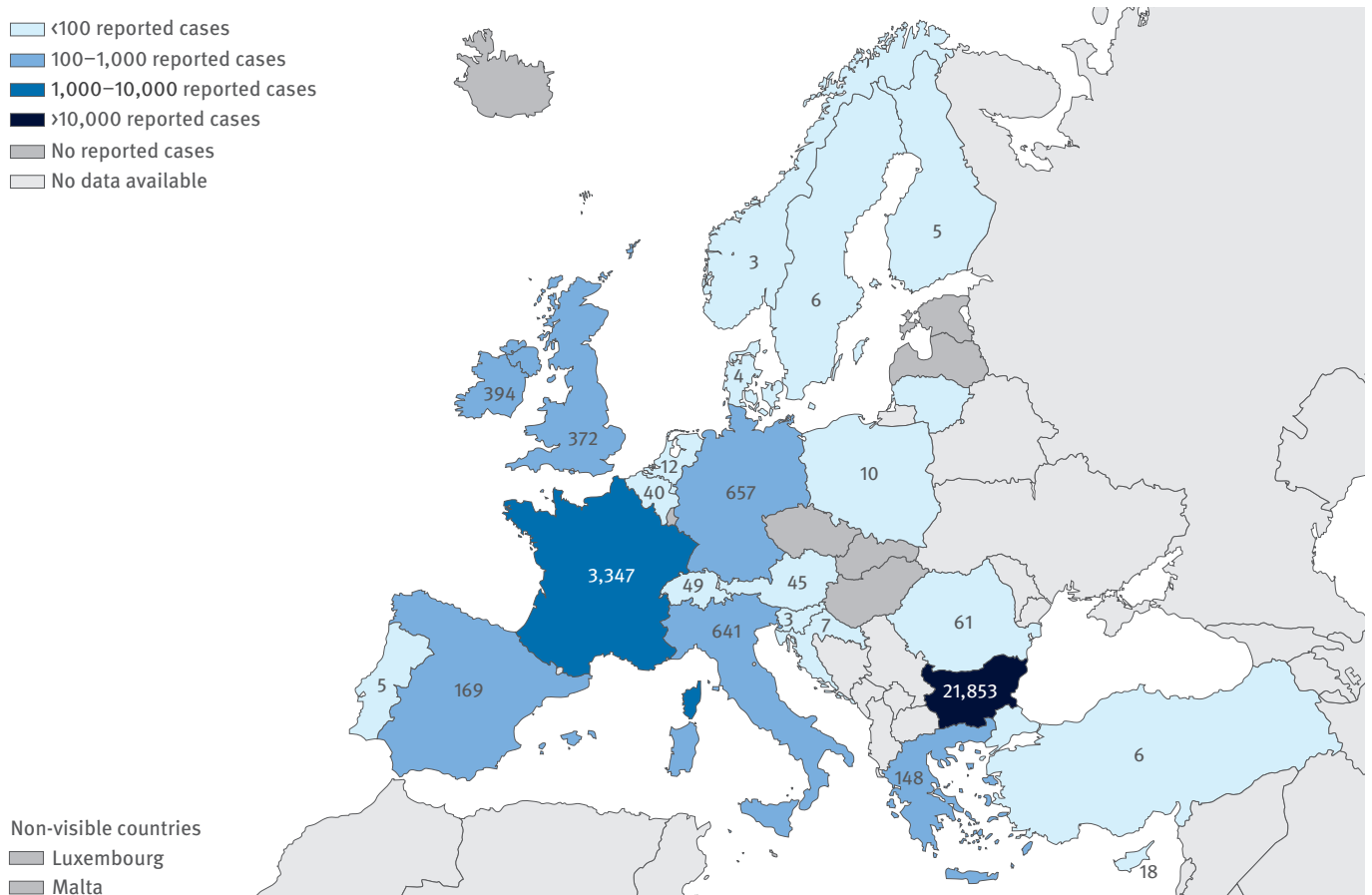
In September 2010, the 53 member states of the World Health Organization (WHO) European Region met in Moscow, Russia, and adopted a resolution to renew their commitment to the elimination of measles and rubella and the prevention of congenital rubella syndrome by 2015 [1]. While great progress has been made towards measles and rubella elimination in the Region, with some countries interrupting endemic transmission of one or both of the diseases, the public health community had to come to terms with the fact that 2010 will not be the year when measles and rubella elimination

is achieved in the European Region. As experience from the Americas shows, it is technically feasible to eliminate measles with a defined strategy [2]. So why has the goal not yet been reached in Europe?

The reasons are manifold. In 2010, *Eurosurveillance* has put a spotlight on measles to mark this, tracked measles outbreaks in Europe, and highlighted the associated challenges. In 19 papers, mostly rapid communications, ongoing outbreaks have been described and their implications discussed. Together with earlier

FIGURE

Number of measles cases reported by European Union and European Economic Area countries, January – October 2010 (n=27,795)*



Source: [3].

reports in this journal from recent years, the comprehensive compilation of reports on measles shows that measles virus is freely circulating in Europe and is not confined to specific populations or countries. According to preliminary data from EUVAC.net, the European surveillance community network for vaccine preventable infectious diseases, covering January to October 2010 [3], measles outbreaks of various sizes occurred in a majority of European Union (EU) countries, Iceland and Norway, with 27,795 notified cases (Figure). Only eight EU countries reported zero cases in 2010. In addition, five countries (Bosnia and Herzegovina, Israel, Russia, Switzerland, Uzbekistan) among the WHO European Region countries experienced outbreaks between 2007 and 2010.

The Region will not achieve the initial goal of eliminating measles by 2010 because not all children are immunised on time, and some are never immunised. Many member states from the eastern part of the Region have conducted national supplementary immunisation activities to vaccinate population cohorts that were susceptible to measles and rubella viruses. Over 57 million persons have been immunised through these activities between 2000 and 2010.

This is, however, not enough. The compilation of *Eurosurveillance* papers provides further evidence of the known fact that there are areas or pockets of individuals not protected against the measles virus where coverage for two doses of a measles virus-containing vaccine is often below the 95% minimum needed for the elimination of the disease. These pockets are present throughout Europe and disease can propagate and spread within them, but the virus can also spread across country and regional borders with the movement of individuals. Therefore it is important to identify specific groups at risk for measles at local and national levels and to tailor health information and preventive measures specifically for these groups. In addition, one needs to be aware that it is not always possible to identify a specific group at risk [4,5]. While we see many outbreaks reported among Roma populations [6,7], Irish travellers [7] and anthroposophical [9,10] or religious communities [11,12], these populations are from different social backgrounds and there are different reasons why they are not vaccinated. Moreover, clustering in space of highly educated individuals who do not immunise their children put them at increased risk of disease if the virus is introduced into such a community. While immunisation has led to a considerable reduction in disease over the years, there has been a shift in public perception from the risk, implications and severity of the disease to the safety of the vaccines.

Consequently, how do we increase measles vaccine coverage in the general population as well as among known risk groups? More information is needed in Europe on the severity of measles and secondary infections, including pneumonia and encephalitis, and the

healthcare costs associated with the disease. In addition, information about the benefits of vaccination should be shared with politicians, healthcare professionals and parents.

If Europe is to meet the new measles elimination target of 2015, accelerated actions and innovative approaches need to be implemented by countries and the described challenges should be addressed so as not to jeopardise the goal. Besides targeted supplementary immunisation activities, which are not common practice in western Europe, catch-up vaccination campaigns among identified groups and individuals who are not immunised can dramatically close immunity gaps. Health professionals – such as doctors, nurses and midwives – play a critical role in achieving and maintaining high vaccination coverage. They need to be partners in strategies to promote vaccination and aid in closing immunisation gaps at any possible occasion, including reminding their clients and recalling children for vaccination. Ensuring that these healthcare providers have an appreciation of the benefits of vaccination against measles and a sound scientific knowledge of vaccinology, including information about the relatively few contraindications, is imperative. Lastly, renewing high-level political and societal commitment and ensuring appropriate resources are needed to reach the elimination goal by 2015. The Region cannot afford to lose ground on the substantial gains made to date.

* Erratum: The colour for France was changed in the Figure on 11 February 2011.

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Spotlight on measles 2010: Measles outbreak in a mainly unvaccinated community in Essen, Germany, March – June 2010

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On 15 March 2010, a case of measles was reported to the District Health Office in Essen. In total 71 cases occurred from 15 March to 19 May (four cases hospitalised), with the majority linked to a Waldorf school. Only one case had been vaccinated twice, two cases had been vaccinated once. Immediate and consequent exclusion of non-immune children from classes for two weeks as well as the adjacent spring break prevented the wider spread of the virus.

Introduction

Measles outbreaks occurred in Germany in recent years [1,2] despite the recommendation of the German Standing Committee on Vaccination (STIKO) to vaccinate all children with two doses of the measles-mumps-rubella (MMR) vaccine, according to the vaccination schedule. Vaccinations are not mandatory in any of the German *laender* but vaccination cards are routinely checked at a medical examination at school entry.

The last major measles outbreak in Germany in 2006 [2] involved 2,300 cases. During this outbreak, 414 (18%) of the infected children in the town of Duisburg (North Rhine Westphalia) were hospitalised and two died with severe encephalitis. Since then, information and vaccination programmes were enforced in Germany and the number of reported cases declined to 574 in 2009 [3]. In 2008, countrywide vaccination coverage for measles (with two doses) in six-year-olds was 89% [4] whereas in Essen, vaccination coverage was 92% in the age group 11–13 years (unpublished data).

Outbreak description

On 15 March 2010 one serologically confirmed measles infection in a 13-year-old student and four clinical suspected cases from a Waldorf school in Essen were reported to the District Health Office.

By 19 May 2010, a total number of 71 cases (68 children and three adults) were reported to the District Health Office. Up to nine cases were reported on a single day but after the spring break from 29 March to 9 April

only a maximum of two cases were reported per day. Twenty-eight pupils (39%) infected in this outbreak are aged from 11 to 15 years, followed by 19 pupils (27%) aged between 0 and 5 years, four of whom were not eligible for vaccination. Eighteen children (25%) are aged between 6 and 10 years and two students between 16 and 20 years. All cases had epidemiological links apart from the three adults (4%), who were aged over 20 years. For one case the age was not known.

Sixteen of 71 reported cases were serologically confirmed. Genotyping of two isolates by the National Reference Centre revealed Genotype D8. A number of parents refused to have their children tested and this limited the outcome of our investigation.

Three children and one adult were hospitalised with fever and severe rash but they did not develop any major complications.

According to the information received from parents of the 71 cases, 30 could be identified as members of the Waldorf school or kindergarten, 18 as siblings of these members and 20 as visiting doctors who do not recommend vaccination. However, the members of the Waldorf school and their siblings might also visit doctors who do not recommend vaccination. The three adults did not have any link to any of these groups.

Seven siblings have not been seen by a doctor and therefore, have not been reported but they were included in the analysis with the date of onset of symptoms. Another seven cases attended different schools or kindergartens or were too young to attend one. Therefore 25 secondary cases occurred in other schools and kindergartens in unvaccinated children, whose parents refused vaccination. The number of infections through household contacts was 30. One case contracted the disease after vaccination with one dose and another one after vaccination during the incubation period. One of the adults (aged 28 years) had received two vaccinations against measles at the age of two years. All the other 68 cases had not been

vaccinated at all. Only three cases could not be allocated to one of the groups (Waldorf school, sibling or attending doctor who did not recommend vaccination) indicating that this outbreak was mainly restricted to the above-described groups.

In addition to the 71 cases reported in Essen, five cases reported in neighbouring cities could be traced back to contacts with children from the Waldorf school in Essen. Furthermore, one case reported to the District Health Office in Sonthofen (southern Germany) is linked to a child from Essen who spent his holidays there. Another case from Zwickau (eastern Germany) could have been exposed while visiting a paediatric practice in Essen that did not recommend vaccination but was seeing measles patients at this period.

Public health intervention

In order to stop this outbreak and to protect the non-immune children, and since this outbreak involves a school with low vaccination coverage against measles, measures to prevent the spread of the infection according to the national Protection Against Infection Act (Infektionsschutzgesetz) were immediately enforced [6]. This included obligatory control of vaccination certificates and exclusion of non-immune students from classes for 14 days. A firm recommendation for vaccination with a first or second dose against measles was given.

The measures started on 15 March 2010, when the school administration was advised by the District Health Office to hand out leaflets in order to inform the parents about the measles outbreak and the measures planned and recommending that children stay at home if they develop symptoms. Parents were asked to have their children vaccinated if they had not received two doses of MMR; in case of non-compliance, the children were excluded from classes for two weeks. On the following day, staff from the District Health Office (two paediatricians, two health supervisors and two assistants) checked the vaccination certificates of all the pupils attending school on that day, before the beginning of lessons. The control of the vaccination certificates showed that 311 of 762 children (41%) attending the Waldorf school were not vaccinated against the disease or had not had measles before. None of the susceptible students attended classes. However, of the 311 non-vaccinated pupils, 30 (10%) contracted the disease in the following four weeks. Some children had already contracted the disease before the index case but had not been reported earlier. The investigations revealed that the first patient had shown symptoms on 3 March and another six cases followed until the first serologically confirmed case was reported.

Only children who had been immunised against the disease or who had a history of previous disease were allowed to attend lessons. All the others were sent home and the parents were recommended to have their children vaccinated. Following this recommendation,

four children were vaccinated. Information on teachers' and other school staff's immunisation status was also available and it was communicated to the District Health Office: all were immune.

The school administration and the teachers were very cooperative in the organisation of the vaccination certificates control. However, the majority of parents indicated clearly that they disagreed with having their children vaccinated against measles.

All the paediatricians in the area were informed by email about the outbreak. The population of Essen was informed via newspapers, Internet and local television. Staff from the District Health Office had several discussions as well as conversations via email with parents who were concerned about the exclusion of their children from school. In the end, the necessity of these measures was agreed upon at a meeting with parents' representatives and staff from the District Health Office held on 25 March 2010.

Discussion and conclusions

Of the 71 cases in this outbreak, only one had received two doses of MMR and a further two cases had received only one dose. Given the high rate of second-dose MMR vaccination coverage (92%) in six-year-old pupils during the school entry examination of 2009, as well as in 12-year-olds by annual control of vaccination certificates [7], we hope that the outbreak will stop soon and not extend far beyond the Essen Waldorf community, which has a critical attitude towards vaccination. However, seven new cases were reported in late June in Essen, who have no epidemiological link to the outbreak in the Waldorf community.

Immediate temporary exclusion of children without measles vaccination or naturally acquired immunity from classes has helped to prevent the spread of the virus to a larger number of children. The cases that occurred during spring break had had the incubation period before the break, and the spring break might have contributed to the decrease in the number of newly reported cases.

The virus detected in this outbreak is very similar to a virus imported from India, which caused an outbreak at a Waldorf school in Berlin at the beginning of 2010 [8], but it is not identical (one sequence variation). Therefore, a link to the current outbreak is possible but could not be confirmed.

The goals of the World Health Organization (WHO) to eliminate measles [9,10] cannot be achieved as long as doctors do not recommend vaccination or parents refuse to have their children vaccinated against measles. More efforts and a 95% coverage with two doses of MMR vaccine in children are needed for measles eradication in Germany, in order to meet the WHO goals [11].

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Spotlight on measles 2010: Ongoing measles outbreak in Greece, January–July 2010

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A measles outbreak (126 reported cases to date) has been ongoing in Greece, since January 2010, originally related to the recent outbreak in Bulgaria. Cases are mostly unvaccinated, and mainly belong to three groups: Roma population of Bulgarian nationality, Greek Roma population, and Greek non-minority population. In these population groups, 67%, 95%, and 25% of cases respectively were children aged 0-14 years. Measures were taken to raise clinical awareness, and vaccination of specific population groups was undertaken. Policies are necessary to increase routine vaccination uptake of hard-to-reach groups.

Background

Measles is still present in Europe, causing severe complications and deaths in children [1,2]. Despite a large decline in measles incidence in the past decade in Europe, the World Health Organization (WHO) target

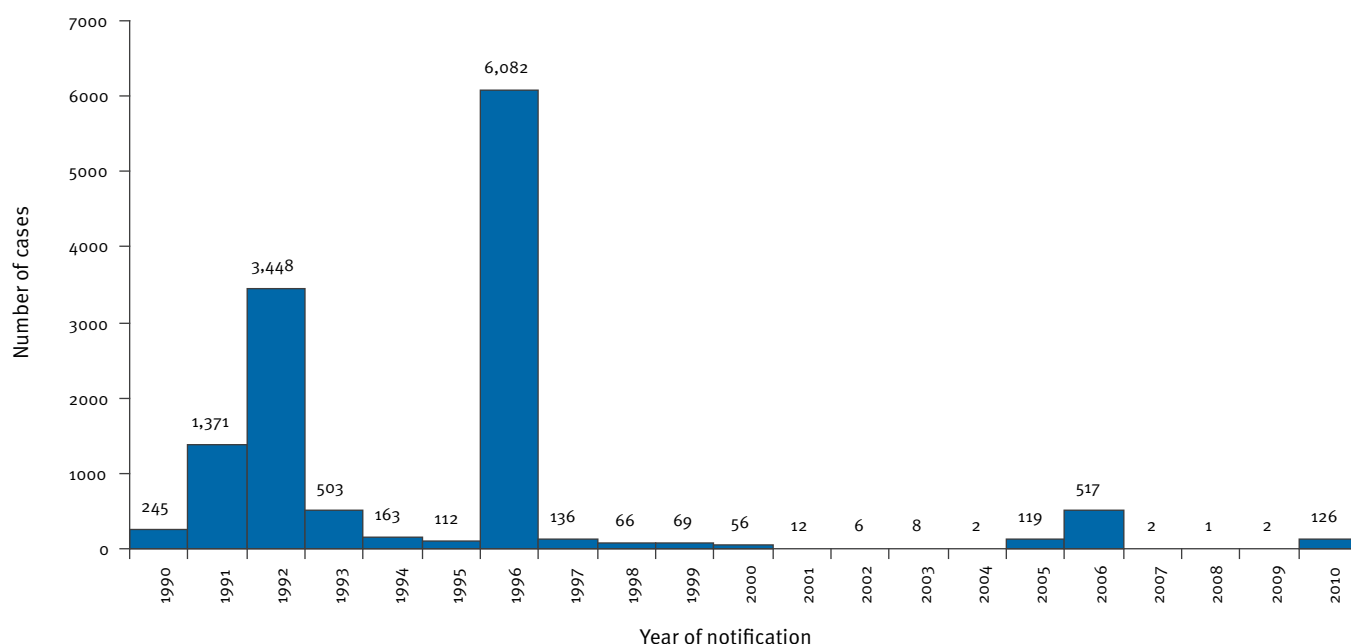
to eliminate measles in Europe by 2010 does not seem feasible [2]. A measles outbreak with more than 20,000 reported cases has been taking place in Bulgaria since April 2009 [3,4], and clusters of cases have been reported from several countries in Europe in 2009 and 2010 [5-9].

Measles is a notifiable disease in Greece; the European Union (EU) case definition of 2008 is used [10]. Overall, measles incidence has been steadily declining in Greece during the past 25 years. The last measles outbreaks occurred in Greece in 1996 and in 2005 and 2006 (Figure 1).

The 2-5-year measles epidemic cycles previously observed ended after the 1996 measles outbreak. The last outbreak, in 2005-2006, had mainly affected unvaccinated Roma children aged 0-14 years, older

FIGURE 1

Reported measles cases by year of notification, Greece, 1 January 1990–25 July 2010



teenagers and young adults from the non-minority general population who were either unvaccinated or had had one dose of measles-containing vaccine, and unvaccinated or incompletely vaccinated immigrants [11].

Ongoing measles outbreak in Greece

A total of 126 measles cases have been reported to the Hellenic Centre for Disease Control and Prevention through the mandatory notification system by 25 July 2010 (rate 1.1 cases per 100,000 population). The first case was notified on 29 January 2010.

Case classification

Seventy-seven (61%) of 126 reported cases were laboratory-confirmed (by serology and/or by PCR). Thirty-one cases (25%) were classified as probable (cases meeting the clinical criteria with an epidemiological link). Eighteen cases (14%) were classified as possible (cases meeting the clinical criteria).

Laboratory investigation

So far, measles virus genotype D4 was identified in all 19 cases genotyped by the National Measles Reference Laboratory (Hellenic Pasteur Institute). Nine of these cases are of Bulgarian nationality (Roma), nine are of Greek nationality (six of them are Roma) and one case is of Albanian nationality. Genotyping is in process for more cases.

Nationality / high-risk populations

Thirty-six (29%) of 126 reported cases belonged to Roma communities of Bulgarian nationality, mostly families of seasonal workers in Greece (usually living in poor conditions). Eighty-seven cases (69%) were persons of

Greek nationality, 43 (34%) of whom belonged to the Greek Roma community. Seven cases (6%) were health-care workers. Three (2%) cases were persons of other nationalities (one immigrant from Albania, one tourist from Denmark and one from France).

Progress of the outbreak over time

As indicated in the epidemic curve (Figure 2), during the first seven weeks of the outbreak, the majority of cases were of Bulgarian nationality. In the following weeks cases of Greek nationality were reported as well, and after week 21/2010 the majority of cases belonged to Greek Roma communities.

Age distribution

Seventy-eight (62%) of 126 reported cases were children aged 0-14 years, with the largest number of cases (n=34, 27%) in the age group of 1-4 years. Ten cases (8%) were younger than 1 year.

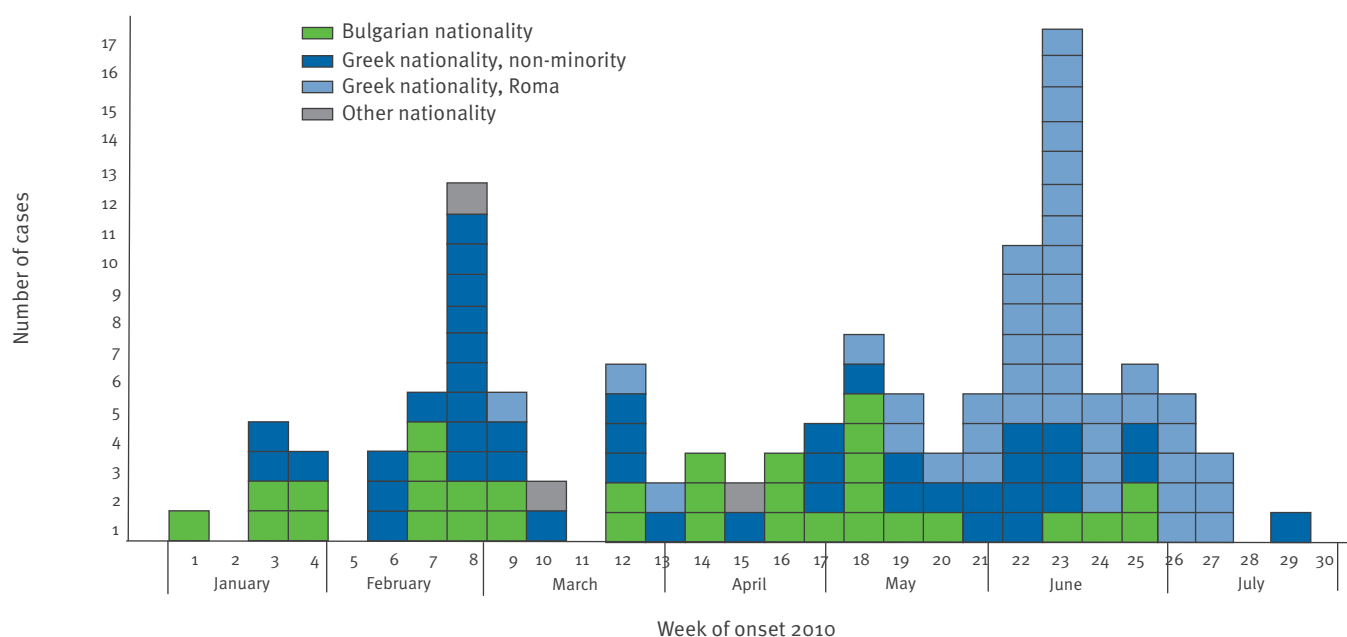
As indicated in the Table, the majority of measles cases of Bulgarian nationality were children 0-14 years (67%), mainly children aged 0-4 years (42%). Almost all cases in the Greek Roma population were children aged 0-14 years (95%), half of whom were 0-4 years-old. The majority of cases from the non-minority Greek population were young adults older than 20 years (66%).

Vaccination status

Information on vaccination status was reported by physicians who got this information from children's health booklets, or by parents or patients themselves. Of the 106 measles cases with known vaccination status, 93 cases (88%) were reported as unvaccinated. Thirteen cases (12%) were vaccinated for measles, all of them

FIGURE 2

Reported measles cases by week of symptoms' onset and by population group, Greece, 1 January–25 July 2010 (n=122^a)



^a Date of onset of symptoms was known only for 122 cases.

of Greek nationality (12 cases from the non-minority general population and one from the Roma community). Nine cases were reported to have had one dose of measles vaccine (the case from the Roma community was vaccinated seven days before disease onset) and four cases were vaccinated with an unspecified number of doses.

History of recent travel abroad

Information on recent travel abroad (within three weeks before onset of symptoms) was available for 114 of the 126 cases. One hundred and four cases (91%) had no history of recent travel abroad, including 22 cases of Bulgarian nationality. Ten cases (9%) had a history of recent travel: eight cases had recently travelled to Bulgaria (six persons of Bulgarian nationality, one Roma person of Greek nationality and one of Danish nationality), one case to France (person of French nationality) and another one had an unknown travel itinerary.

Hospitalisation, complications and outcome

Of the 125 cases with known hospitalisation status, 83 (66%) were hospitalised. Of 125 measles cases with known complication status, complications were reported in 31 (25%) of the cases. Complications included pneumonia (18 cases), otitis media (seven cases), laryngitis and/or bronchitis (six cases). Measles was complicated by meningitis in one male aged 29 years, whose vaccination status was unknown. No death has been reported.

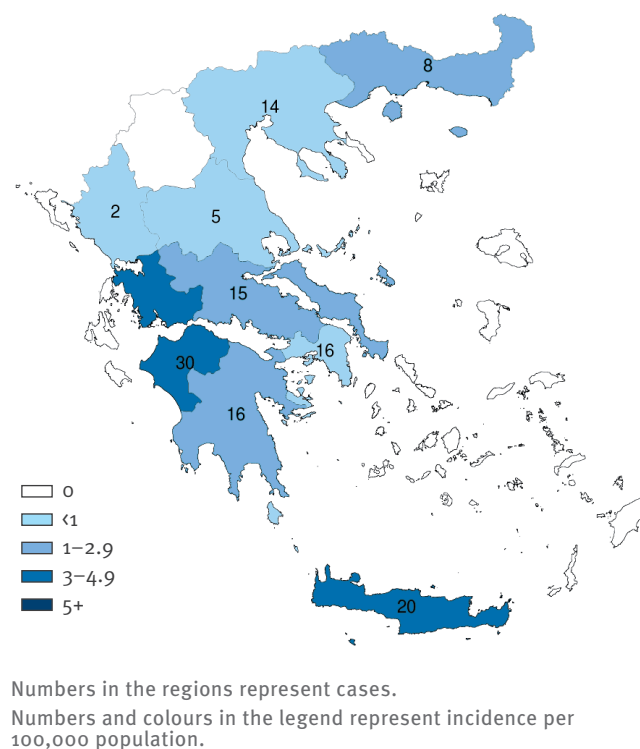
Geographical distribution

The first measles clusters were reported from the district of Ilia in southwestern Greece (a total of 30 cases, most of them in three villages) and from the island of Crete (six cases from the district of Chania and 13 cases from the district of Heraklion, 10 of them from one village). No connection was identified between the clusters in Ilia, Chania and Heraklion.

As of 25 July 2010 measles cases have been reported from 21 of the 52 districts of the country, without any

apparent geographical pattern. Clusters have been reported in Greek Roma camps (33 cases from eight clusters in Greek Roma camps) and in villages where Roma of Bulgarian nationality stay (26 cases from five villages). The largest reported cluster had thirteen cases (12 cases from one village, most of them relatives, and one healthcare worker) all belonging to the Greek non-minority population. Only two of the clusters were directly related to imported cases with recent travel history abroad. Of infants under 1 year, half (5/10) were part of family clusters, and one was part of a community cluster.

FIGURE 3
Notified measles cases and incidence rate per 100,000 population in the 13 administrative regions, Greece, 1 January–25 July 2010



TABLE

Reported measles cases by age group and nationality/population group, Greece, 1 January–25 July 2010 (N=126)

Age group (years)	Bulgarian nationality, Roma	Greek nationality, non-minority	Greek nationality, Roma	Other nationality	Total
<1	4	1	5	0	10
1-4	11	5	16	2	34
5-9	4	3	9	0	16
10-14	5	2	11	0	18
15-19	3	4	0	0	7
20-24	3	8	1	0	12
25-29	2	7	1	0	10
≥30	4	14	0	1	19
Total	36	44	43	3	126

Control measures

The following public health measures were implemented. All regional and local public health authorities, physicians and other healthcare workers in the public and private sector in Greece were informed about this outbreak and the outbreak in Bulgaria, and about the appropriate investigation and management of measles cases and their contacts (isolation of cases, contact tracing and vaccination of susceptible contacts). Guidelines for measles control were distributed to healthcare staff and are available on the website of the Hellenic Centre for Disease Control and Prevention (www.keelpno.gr). Furthermore, physicians were alerted to increase their awareness for measles cases and to strengthen surveillance and to complete routine immunisation of children, adolescents and young adults in the wider community, according to the national immunisation schedule. In addition, vaccination campaigns of population groups with low vaccine coverage were organised in the country, with priority to high risk communities (mainly Roma) in affected areas.

Discussion and conclusions

This is a preliminary report of an ongoing measles outbreak in Greece, based on national surveillance data. The first cases and clusters were among persons of Bulgarian nationality, probably related to the measles outbreak in Bulgaria which started in April 2009 [3]. However, the high proportion of Greek nationals, mainly from Roma communities, underlines that despite the high national immunisation coverage with measles-mumps-rubella (MMR) vaccine, pockets of unvaccinated populations still exist.

Vaccination with two doses of MMR vaccine has been included in the national immunisation schedule in Greece since 1991. According to the national immunisation schedule, vaccination with the first dose of MMR is recommended at the age of 12-15 months and with the second dose at the age of 4-6 years. Immunisation coverage with MMR is high in children in Greece, but less than optimal in adolescents and young adults. In some population groups (e.g. Greek Roma) vaccination coverage is low. According to the last national study on vaccination coverage, carried out in 2006, about 99% of first grade school children (about 6 years-old) were immunised with one dose of a measles-containing vaccine, and 77% with two doses. In Roma children, coverage was 82% and 45% respectively, but this refers to Roma children going to school and may represent an overestimation of the coverage of all Roma children. In ninth grade school children (about 14 years-old), coverage with one dose of a measles-containing vaccine was 92%, and 80% with two doses [12].

It is of concern that the age distribution of cases in the Greek Roma population (95% of cases under 15 years) is similar to the one observed in many countries in the pre-vaccination era [13]. Children under the age of one year represented 8% of all cases (rate 9.1 per 100,000 population). In some recent outbreaks, the incidence of

measles in this age group was found increased compared to previous years [14]. The hospitalisation rate we found (66%) is similar to that reported in some recent outbreaks in Europe [3,5] but higher than in others [6,14], possibly reflecting a greater extent of under-reporting of mild cases.

The occurrence of this outbreak highlights the need to achieve high vaccination coverage with two doses of MMR vaccine through routine immunisation in the general population (not only among children, but also among adolescents and young adults) and the need to increase immunisation coverage in hard-to-reach populations. It is equally important to have systematic policies that ensure good access to vaccination services for children in Roma communities in Greece.

Acknowledgements

We wish to sincerely thank clinicians and local public health authorities who contributed to measles surveillance in Greece.

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Spotlight on measles 2010: Excretion of vaccine strain measles virus in urine and pharyngeal secretions of a child with vaccine-associated febrile rash illness, Croatia, March 2010

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We describe excretion of measles vaccine strain Schwarz in a child who developed a febrile rash illness eight days after primary immunisation against measles, mumps and rubella. Throat swabs and urine specimens were collected on the fifth and sixth day of illness, respectively. Genotyping demonstrated measles vaccine strain Schwarz (genotype A). If measles and rubella were not under enhanced surveillance in Croatia, the case would have been either misreported as rubella or not recognised at all.

Introduction

Vaccination against measles was introduced into the Croatian vaccination schedule in 1968 for all children at the age of 12 months and at first grade of elementary school. The vaccine containing the Edmonston-Zagreb measles virus strain was produced by the Institute of Immunology, Zagreb. In 1976, the monovalent measles vaccine was replaced by a trivalent measles, -mumps, -rubella (MMR) vaccine, containing the same Edmonston-Zagreb strain of the same producer. In 2008, 18 cases of vaccine-associated mumps were reported that has resulted from transmission of the mumps component (L-Zagreb) to close contacts of children who had received primary vaccination with this trivalent vaccine [3,4,11]. This vaccine was thereafter replaced by Priorix (GSK; containing the RIT 4385 mumps virus strain and the Schwarz measles virus strain) for the first MMR vaccination in January 2009. The MMR vaccine produced by the Croatian Institute of Immunology is still used for the second dose of MMR. Since the MMR vaccine used for primary vaccination was changed in January 2009, vaccine-associated mumps in contacts of vaccinees have no longer been reported [5].

No suspected measles or rubella cases were reported in Croatia during 2010. In the last five-year period, one local outbreak of rubella occurred in Croatia in 2007, affecting 39 adolescents and one outbreak of measles

in 2008, affecting 51 people. The illness in the index cases of both outbreaks was imported. Independently of these two outbreaks, only five cases of measles and another five cases of rubella were reported in Croatia from 2005 to 2009, which were eventually discarded by serology or classified as imported. After receiving information on a measles outbreak in Roma children in Bulgaria in 2009 [6,7] and media reports on rubella cases in neighbouring Bosnia and Herzegovina, the Croatian Institute of Public Health sent a circular letter to healthcare workers in Croatia on 15 March 2010 to raise awareness of possible importations of measles and rubella.

Four suspected rubella cases were notified in Croatia in the second half of March 2010. Three cases were discarded based on negative serology for measles and rubella and lack of epidemiological link to a possible source. One case may have had a chance to be exposed to rubella but also had a history of MMR vaccination and is described here.

Case description

A healthy child (14 months-old) was vaccinated on 9 March 2010 with Priorix MMR vaccine according to the Croatian childhood vaccination schedule. The child had facial erythema without fever on 14 March and developed a macular rash and fever on 17 March. It was examined on 21 March at the county hospital and reported as a possible case of rubella to the epidemiology department at the County Institute of Public Health on 23 March.

Since rubella and measles are under enhanced surveillance according to the national action plan for measles and rubella elimination, an epidemiological investigation was initiated, and serum, urine and throat swab specimens for laboratory testing were obtained. The investigation found no similar cases among contacts of the patient. A source of rubella infection was not

identified, however, possible exposure to rubella or measles virus could not be completely excluded, because the child had travelled abroad during the two weeks preceding the illness.

A serum sample and throat swabs were taken on 23 March and a urine specimen on 24 March. On 26 March, the rash was still present. Serum was obtained again from the convalescent child on 11 April. In addition, a serum sample from the asymptomatic pregnant mother was obtained on 24 March.

Laboratory investigation

Serologic tests of the patient and mother were performed at the World Health Organization (WHO) national measles laboratory, Virology Department, Croatian Institute of Public Health. For the detection of specific measles and rubella IgM and IgG antibodies we used commercial ELISA (Rubella IgM/IgG: Dia Sorin; Measles IgM/IgG: Genzyme Virotech GmbH). For detection of specific mumps IgM and IgG antibodies, a commercial immunofluorescence test was used (Euroimmun). Throat swab and urine were initially tested for measles virus at the Department of Molecular Diagnostics, Croatian Institute of Public Health using real-time RT-PCR (Applied Biosystems), using the primer/probe set for the measles virus nucleoprotein (N) gene [2].

The child's paired sera were tested in parallel. The first serum tested negative for IgM and IgG antibodies against rubella virus and mumps virus, while measles antibodies were equivocal for IgM and negative for IgG. The child's second serum obtained on 11 April also tested negative for both IgM and IgG rubella antibodies, while measles antibodies were negative for IgM, but IgG-positive, and mumps antibodies were positive for IgM as well as for IgG. The mother was negative for IgM and positive for IgG antibodies against both measles and rubella virus (the mother's vaccination status could not be determined with certainty). The child's throat swab was negative in RT-PCR for measles RNA, while the urine tested positive.

An additional RT-PCR was performed, targeting the 3'-end of the N gene [1]. PCR products were obtained from throat swab and urine, sequenced and compared using the BLAST algorithm, and finally identified as Schwarz vaccine strain (genotype A).

Discussion

We demonstrated excretion of the Schwarz measles vaccine virus in a child with a vaccine-associated febrile rash illness in urine and in pharyngeal excretions.

Virus excretion in vaccinees has been reported before [8-10], but to our knowledge, this is documented for the first time for the Schwarz vaccine strain. Interestingly, although the blood for serology testing was obtained 14 and 32 days after vaccination, the child still had no antibodies to rubella virus in either serum sample. It is unclear why there was no seroconversion to rubella 32 days after vaccination, although this is not an unusual finding. The dynamics of measles and mumps

antibodies were as expected for someone who had either been vaccinated or had natural infection, indicating that the child did not have impaired antibody production kinetics in general.

According to WHO guidelines for measles and rubella elimination, routine discrimination between aetiologies of febrile rash disease is done by antibody assays, not necessarily by virus detection [12]. However, in a patient recently MMR-vaccinated, only molecular techniques can differentiate between wildtype measles or rubella infection or vaccine-associated disease.

This case report demonstrates that excretion of Schwarz measles virus occurs in vaccinees. Also, it demonstrates a need to strengthen surveillance of measles and rubella cases continuously, also in countries that are currently approaching elimination of measles and rubella.

Competing interests:

Maja Santak is an employee of the Institute of Immunology, Zagreb, the national vaccine producer.

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Spotlight on measles 2010: Update on the ongoing measles outbreak in France, 2008-2010

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Since early 2008, France has been experiencing a measles outbreak with almost 5,000 notified cases as of 30 June 2010, including three measles-related deaths. The proportion of cases 20 years or older reached 38% during the first half of 2010. This situation is the consequence of insufficient vaccine coverage (90% at age 24 months in 2007) that led to the accumulation of susceptibles over the last years. It underlines the need for additional measures targeting susceptible children and young adults.

The current measles outbreak in France was first noticed in early 2008 [1] when a preliminary number of 579 notified measles cases contrasted sharply with the low number of notified cases in 2006 and 2007 (44 and 40 cases, respectively). The outbreak intensified and continued to spread throughout the country during 2009 and 2010 with a total number of notified cases that has reached almost 5,000 by 30 June 2010.

In France, a combined measles-mumps-rubella (MMR) vaccine has been recommended since 1986. The first dose is currently recommended at the age of 12 months and the second dose during the second year of life. A catch-up measles vaccination programme with two doses is recommended for children born in 1992 or later. For those born between 1980 and 1991, a single MMR vaccine dose is recommended [2].

Measles has been a mandatory notifiable disease in France since mid-2005. Clinicians and microbiologists are requested to report suspected measles cases immediately to the regional public health authorities. Notifications are collected and analysed at national level by the French Institute for Public Health Surveillance (InVS).

We included in our analysis the notified clinical and confirmed cases with a date of rash onset between January 2008 and June 2010 (preliminary data). A confirmed case can be i) laboratory-confirmed, by detecting either measles IgM antibodies or measles virus

nucleic acid using RT-PCR in serum or oral fluid, or ii) epidemiologically confirmed, when a link with a laboratory-confirmed case is proven. Case definitions for measles are detailed on the InVS website [3].

Outbreak description

The outbreak started during early spring 2008 among students attending traditionalist catholic private schools for whom a low immunisation coverage was identified retrospectively [1]. It then spread first into other schools including public ones, and by the end of 2008 into the general population. The outbreak also affected socially vulnerable communities such as France's nomadic minorities ('gens du voyage') and Roma communities.

A total of 4,753 cases were notified as of 30 June 2010: 604 cases in 2008, 1,544 in 2009 and 2,605 in the first half of 2010 (Figure 1).

After excluding 99 cases (2%) who had returned from abroad within 7–18 days before the rash onset, the incidence of indigenous measles was highest, four cases per 100,000 population, in the first half of 2010, compared with 2.3 in 2009 and 0.9 in 2008 ($p < 0.0001$). In 2010, the crude incidence was higher than 5.0 per 100,000 population in seven of the 22 regions in mainland France (Figure 2). Only three cases were reported from the French overseas regions but for two of these cases, the transmission has most likely occurred in mainland France.

The proportion of laboratory-confirmed cases increased from 50% ($n=306$) in 2008, to 54% ($n=832$) in 2009 and to 56% ($n=1,410$) in the first half of 2010.

The National Reference Centre for Measles in France identified the main measles virus genotypes in 2009 as D4 and D5. They accounted for 75% and 20% respectively of 284 genotyped cases. Genotypes D8, H2 and B3 accounted for the remaining 5%. Genotype D4 became predominant in 2010 (99% of the 467

genotyped cases). A great majority of the strains are linked to the last D4 variant identified in the United Kingdom in 2007, MVs/Enfield.GBR/14/07 (Gene Bank accession number EF600554).

Among the 4,753 cases, the sex ratio M/F was equal to 1.08. In 2010, the age distribution of measles cases has changed significantly compared with 2009 and 2008. The proportion of cases under one year of age has increased significantly from 4% (n=25) in 2008 to 8% (n=126) in 2009 ($p < 0.001$) and 9% (n=243) in 2010 ($p < 0.001$). The proportion of cases aged 20 years or older increased from 17% (n=100) in 2008 to 23% (n=360) in 2009 ($p = 0.002$) and 38% (n=992) in 2010 ($p < 0.001$). In the first half of 2010, the highest age-specific incidence rate was found in children under the

age of two years (Figure 3). Over this six-month period, 56% (n=135) of the cases under one year of age were younger than nine months.

In 2010, 82% of the 2,123 cases with a known vaccination status were unvaccinated, 13% had received one dose, 3% two doses and 2% had been vaccinated with an unspecified number of doses. A high proportion of unvaccinated cases (86%) was observed among the cases aged between 5 and 19 years, who should have been vaccinated with two MMR doses. The highest proportion of cases vaccinated with at least one dose of MMR was 32% (156/487) in 20-29-year-old adults (Figure 4).

FIGURE 1

Notified measles cases by month of rash onset, France, January 2008 – June 2010 (n=4,753)

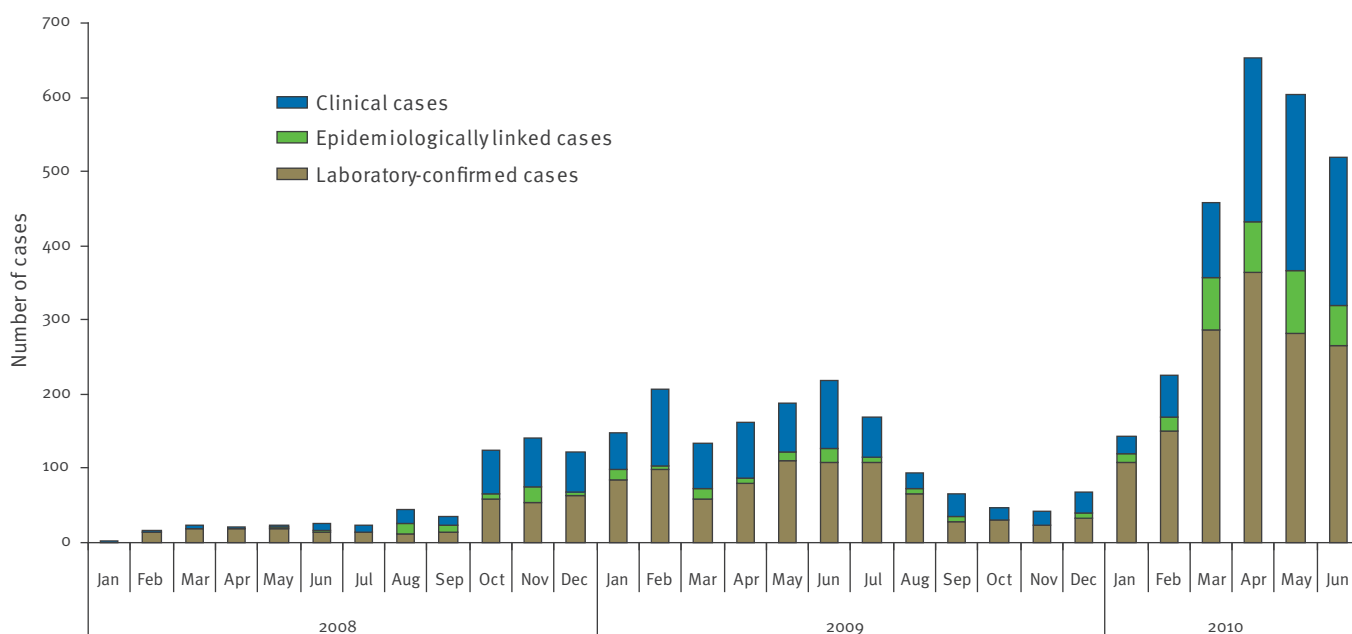
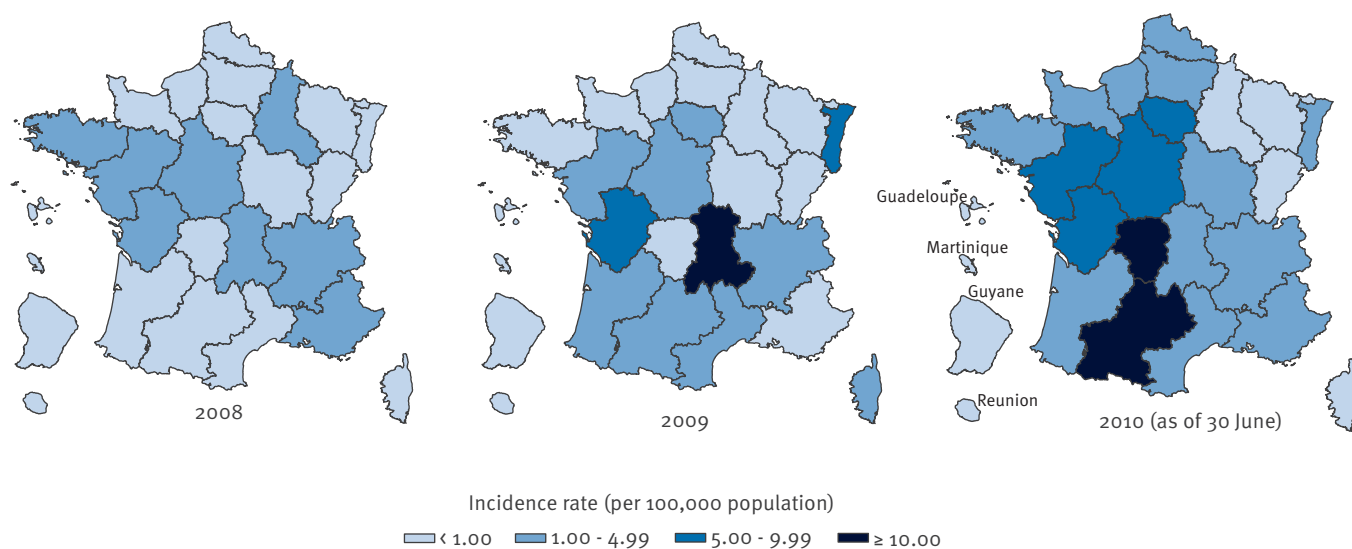


FIGURE 2

Incidence of notified measles cases, by regions, France, January 2008 – June 2010



Complications and deaths

Throughout the study period, 35% (n=137) of the cases under the age of one year, 18% (n=549) of the cases in the age group of 1-19-year-olds and 50% (n=725) of the cases aged 20 years or older were hospitalised. The percentage of hospitalised cases increased from 18% (n=110) in 2008 to 27% (n=422) in 2009 and to 34% (n=879) in 2010 ($p < 0.0001$) reflecting the change

FIGURE 3

Age-specific incidence rates of measles cases, France, January 2008 – June 2010

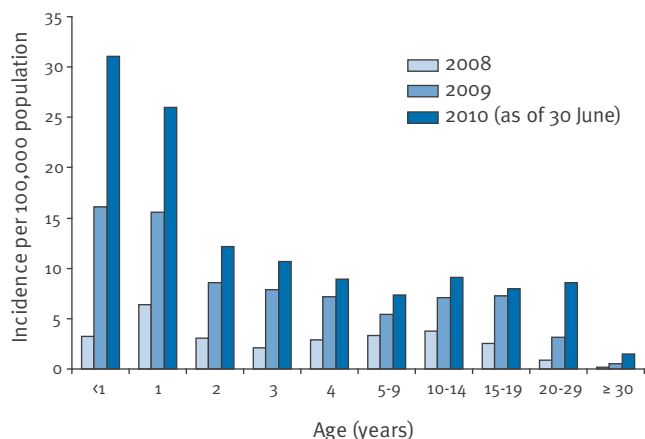
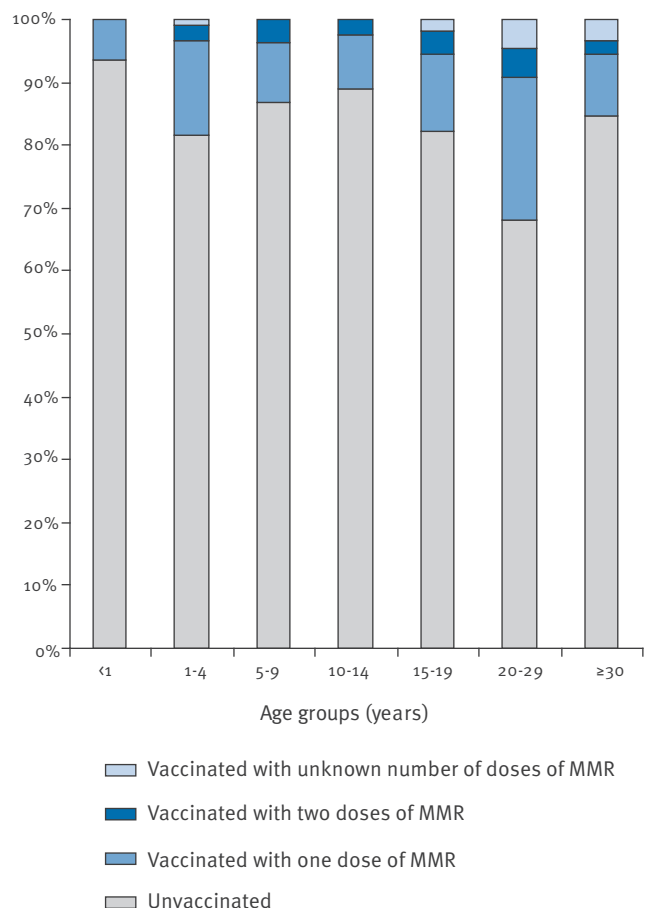


FIGURE 4

Vaccination status of measles cases by age groups, France, January–June 2010 (n=2,123)



MMR : measles-mumps-rubella.

in age distribution. In fact, the proportion of complications reported for the hospitalised cases was significantly higher among the cases aged 30 years or older (40%) than in the younger age groups (25%, $p < 0.001$), whereas it remained stable over time (25%, 26% and 29% in 2008, 2009 and 2010 respectively). Among the hospitalised cases, three cases of acute measles encephalitis and 253 cases of measles-related pneumonia were reported.

Three measles-related deaths occurred during the study period: two in 2009 and one in 2010, all among unvaccinated cases. One death was linked to acute encephalitis in a 12-year-old girl and the other two occurred in young men, aged 23 and 18 years, with underlying immunodeficiency disorders (Crohn and Hodgkin).

Control measures

Specific control measures including catch-up and post-exposure vaccinations were recommended by local health authorities, targeting affected populations according to national guidelines within the National Plan for Elimination of Measles [4]. In case of localised outbreaks or clusters, the catch-up recommendation is to reach two doses of MMR vaccine for the susceptible individuals (not vaccinated or without history of measles) aged between 12 months and 45 years in the affected area or community.

Communication to the general public (e.g. leaflets, newspapers) and health professionals (e.g. medical journals) has been strengthened with also specific emphasis to the religious community concerned and to the national 'gens du voyage' associations (a meeting between representatives from the Ministry of Health and from the affected groups). Advantage was taken of the European Immunisation Weeks (EIW) in April 2009 and 2010 to reinforce this communication, with a special focus on the vaccination recommendations [5].

Discussion

Our data show that France has emerged as another among several European countries (e.g. Bulgaria, Switzerland, Ireland) with more than one measles case per 100,000 population (i.e. having a high incidence according to the criteria set by the World Health Organization (WHO) for the elimination of measles), together with countries like Greece, and Germany which have recently experienced measles outbreaks [6-11].

Measles reporting rate has probably increased since early 2008 in France. However, several factors still argue for an underestimation of the current incidence of the disease. The high proportion of hospitalised cases probably reflects a higher compliance of hospital health professionals than of general practitioners with regard to the notification of measles cases. In some local outbreak investigations less than 50% of cases were notified, and once a case was diagnosed in a household, the secondary cases were less likely

to seek medical advice. The number of patients with measles-positive results in the data collected from the main laboratories testing for measles IgM in France was 1.5 higher than the number of positive cases that were notified. The spread of the disease among socially vulnerable communities is even more difficult to assess because the notification forms do not contain information on social conditions.

It had already been predicted in 1998 that countries like France or England and Wales, where vaccine coverage had remained around 80% to 85% for many years with insufficient catch-up programmes, have built up large cohorts of susceptible people, becoming prone to large outbreaks with an increase of the average age of cases [12].

Despite the current French recommendations, immunisation coverage for measles remains insufficient. At the age of two years, the vaccination coverage with one dose of MMR vaccine was estimated at 90% in 2007. Information on vaccination coverage in France is to be found on InVS website [3].

The vaccination coverage survey conducted in the school year 2005-6 among six-year-old school children, has shown a vaccination coverage of 93% for the first dose of an MMR containing vaccine and 44% for the second dose, and the one conducted in 2004-5 among 11-year-olds has shown a vaccination coverage of 96% and 74% respectively [13].

The proportions of vaccinated cases in different age groups have to be interpreted with caution. It is possible that cases being more severe in the age group of 20-29-year-olds are more likely to be hospitalised and notified. The proportion of vaccinated cases in this population born after MMR introduction could therefore reflect a more accurate picture of the virus circulation in a population with suboptimal vaccination coverage.

Both awareness of the disease and a commitment by the French health authorities and health professionals are essential to strengthen the vaccination programme. The current measles situation in France underlines the need for additional urgent measures, both in terms of communication and vaccination, targeting susceptible children and young adults.

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Spotlight on measles 2010: An ongoing measles outbreak in the district of Neamt, Romania, August – September 2010

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We report an outbreak of measles that has been ongoing in the district of Neamt, Romania, since 22 August 2010. As of 21 September, 17 of 21 suspected cases have been laboratory-confirmed and there was one measles-related fatality.

Introduction

An outbreak of measles was detected in late August 2010 in the Romanian north-eastern district of Neamt with an estimated population of 566,940 (2009) (Figure 1). Earlier in the year, between 1 January and 3 August, 15 cases of measles had been notified from different parts of the country. These included two family clusters among members of the Roma ethnic minority. The first cluster involving five family members

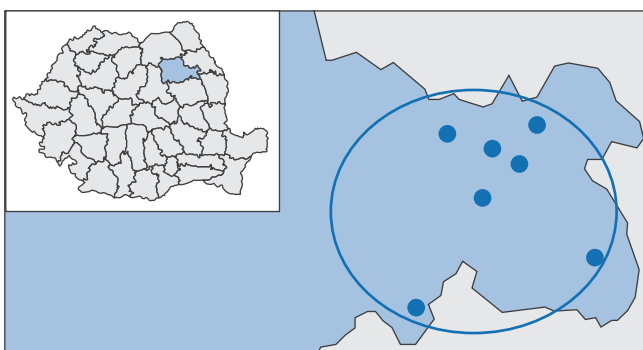
occurred between late February and mid-March (weeks 7 and 11). The index case had a history of travel to France. The second cluster involved three cases in Neamt and occurred in mid-June (week 24). We report on the outbreak that emerged in Neamt by analysing preliminary data from late August to late September (weeks 33 to 38).

Measles is a statutorily notifiable disease since 1978, obliging medical practitioners to immediately report suspected measles cases to the local Public Health Authorities. Notifications of measles cases are collected and analysed nationally at the National Centre for Communicable Diseases Surveillance and Control in Bucharest. National case-based notification was initiated in 1999 and the European Union (EU) case definition and case classification have been adopted since 2005 [1].

The measles vaccine was introduced in 1979 into the Romanian national immunisation programme for children 9-11 months of age. In 1994, the second measles vaccine dose was introduced for children six to seven years of age (first school grade). The combined measles-mumps-rubella (MMR) vaccine replaced the monovalent measles vaccine in 2004 and was recommended as a first dose for children at 12-15 months of age. The second MMR vaccine dose has been recommended since October 2005 for children at six to seven years of age. In the period from 2000 to 2008, the national measles vaccination coverage for children aged 18-24 months with the first dose of measles-containing vaccine was estimated at 97-98%. For children aged seven years, the measles vaccination coverage with the second dose was estimated at 96-98% [2].

FIGURE 1

Measles cases in the district of Neamt, Romania, August-September 2010



The blue spots indicate areas in Neamt affected where cases occurred. The blue circle indicates the containment area chosen for the vaccination campaign.

Outbreak description

Between 22 August and 21 September 2010, a total of 21 suspected cases were notified. In one case, the infection was fatal. The first measles cases of this outbreak were reported in two children and an infant. The close dates of onset of disease of these first cases suggest previous contact with an unreported case of measles.

Serum samples from all suspected cases were available for laboratory testing. Measles was confirmed in 17 of them (Figure 2), which corresponds to a crude incidence of three per 100,000 inhabitants in the district (95% confidence interval (CI): 1.9–4.9). Of the remaining four cases, three cases had a negative test result and were discarded and in one case the result is still pending.

Laboratory confirmation was performed by detecting measles IgM antibodies in serum samples. RT-PCR to detect measles virus nucleic acid was also used to confirm the first five cases. The National Reference Laboratory for Measles and Rubella ‘Cantacuzino’ identified measles virus genotype D4 in clinical specimens from these five cases.

The outbreak investigators reported that the laboratory-confirmed cases involved both the general population (n=11) and members of the Roma ethnic community (n=6). The median age was 11 months (range: four months to nine years). Ten of the 17 cases were infants (under the age of one year), six were one to four years-old and one was in the age group from five to nine years. The status of measles vaccination was known in all notified cases. Fifteen cases were unvaccinated (Table). These included 10 infants who were not eligible for vaccination because of their age and five cases who were eligible but for whom the indicated reason for non-vaccination was contraindications including underweight, hydrocephalus and Down syndrome. The remaining two cases had been vaccinated with one dose of MMR.

The death was reported in a seven month-old, unvaccinated infant who was admitted to a paediatric ward with gastrointestinal symptoms, anaemia and pharyngitis. The infant later developed a rash and acute pneumonia

which was the ultimate cause of death. Of the 17 notified cases, 14 were hospitalised as in-patients in a paediatric ward. Six of those were probably infected with measles through nosocomial transmission on the ward.

Control measures

Several control measures have been implemented by local health authorities. A supplementary MMR vaccination campaign was started on 6 September in the defined containment area including all affected communities and neighbourhoods in Neamt (Figure 1). It targeted all children from seven months to seven years of age who did not have documented evidence of vaccination. The MMR vaccine was supplied by the Ministry of Health and offered free of charge through the routine immunisation services (family doctors) and special outreach teams in the community. Of 1,345 eligible individuals, 956 (71%) have been vaccinated by 19 September 2010. In addition, existing MMR vaccination campaigns were reinforced in the border areas of four neighbouring districts close to the affected areas in Neamt.

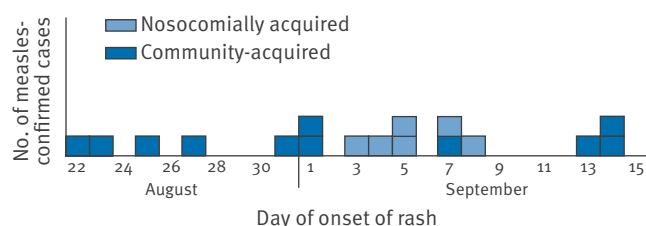
Moreover, active case finding by general practitioners has been instigated in the areas where cases were living, as well as tracing contacts of cases in hospitals and in the community. All children with fever and rash were referred to the infectious disease ward and were investigated. MMR vaccination was given to all contacts between seven months and seven years of age who did not have documented evidence of vaccination. To date, 29 close contacts of the hospitalised patients were identified, nine of whom acquired measles (secondary attack rate: 31%). Additional activities to increase awareness of the ongoing outbreak included sending medical bulletins with information to all physicians in the district and all public health authorities in the country.

Discussion

The source of this outbreak has not yet been identified. The earlier occurrence of measles in the same district in mid-June 2010, suggests that transmission may have continued unnoticed in the meantime. The local health

FIGURE 2

Number of measles cases by day of onset of rash, Neamt district, Romania, August–September 2010 (n=17)



TABLE

Number of measles cases by age group and vaccination status, Neamt district, Romania, August–September 2010 (n=17)

Age group	No. of measles cases	Vaccination status
<1 year	10	Not eligible for vaccination
1–4 years	6	1 had received one MMR dose, 5 had contraindications for vaccination
5–9 years	1	1 had received one MMR dose
Total	17	

MMR: measles, mumps, rubella vaccine.

authorities may not have been notified or the cases may not have sought medical attention. Nevertheless, any link between the earlier cluster and this outbreak remains speculative.

Despite the high national vaccination coverage with MMR vaccine, this outbreak highlights the presence of pockets of individuals vulnerable to measles, in the general population and among members of the Roma community. The vulnerability of Roma communities to acquire measles is well documented, most recently with the outbreak that occurred in Bulgaria [3]. In areas and communities where vaccination coverage remains sub-optimal, cohorts of susceptible individuals accumulate and represent a potential for outbreaks to occur. The current ongoing outbreak involves a large proportion of infants too young to be vaccinated according to the national childhood vaccination programme, which is indicative of widely circulating measles virus. A similar situation had been observed earlier in Romania in 2006 [4].

The five children with measles who were not vaccinated due to perceived contraindications may have been prevented. All of these children could have been vaccinated unless they also had a serious allergy to any of the ingredients of the MMR vaccine, an acute severe illness or severe immunodeficiency. Inadequate knowledge of the contraindications for MMR vaccination by general practitioners is a recognised problem that needs to be addressed.

In 2008 and 2009 the measles situation in Romania had improved dramatically compared with previous years, with reported incidences of less than 0.1 per 100,000 inhabitants [5,6]. However, the emergence of this outbreak highlights the need for urgent preventive and control measures to be taken once again. For the goal of measles elimination to be reached, awareness of the disease and a commitment by public health authorities in Romania are essential to strengthen vaccination programmes. The World Health Organization's strategic plan for the elimination of measles from the European region stipulates that vaccination programmes should achieve and sustain a minimum of 95% coverage with two doses of vaccine and should target susceptible individuals in the general population [7] as well as in vulnerable groups. Moreover, constant vigilance is needed to ensure that suspected measles cases are promptly investigated to identify outbreaks and instigate the control measures to curtail them.

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Spotlight on measles 2010: Ongoing measles outbreak in Northern Ireland following an imported case, September-October 2010

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We report an ongoing outbreak of measles with five laboratory-confirmed and four epidemiologically linked cases in Northern Ireland as at 26 October 2010. The index case was an unvaccinated non-Northern Ireland resident with subsequent genotyping suggesting that infection originated in the usual country of residence of this case. Confirmed cases include one patient with a history of two measles-mumps-rubella vaccine doses.

Measles is a statutorily notifiable disease on the basis of clinical suspicion in Northern Ireland under the Public Health Act [1]. Although measles vaccine was first introduced in Northern Ireland in 1968, it was not until the combined measles-mumps-rubella (MMR) vaccine was introduced in 1988 at the age of 15 months that transmission was significantly interrupted. In response to the United Kingdom (UK) seroprevalence surveys, a vaccination campaign with measles-rubella vaccine was implemented for all school age children in 1994. This campaign achieved high uptake. A second dose of MMR was introduced in 1996 at the age of 3-4 years. As elsewhere in the UK, MMR uptake in Northern Ireland declined as a result of the controversy surrounding the alleged link between the MMR vaccine and autism and inflammatory bowel disease. However, uptake rates in Northern Ireland have remained above those for the UK overall, and have now recovered to 92.4% when measured at the age of 24 months (Figure 1), and 97.1% for the first dose and 92.2% for two doses at the age of five years (Figure 2) [2,3].

From a peak of 12,647 cases in 1961, an average of 65 cases have been notified annually in Northern Ireland from 2000 to 2008. However only six of these cases were laboratory-confirmed in this period, with only one documented as a result of transmission within Northern Ireland. Between December 2009 and March 2010, 24 cases associated with the Irish Traveller community were reported. Sixteen of these were laboratory-confirmed. All occurred in unvaccinated children and young adults (median age seven years, range

three months – 23 years) and involved two different D4 genotypes. This occurred against the background of the ongoing outbreak of measles mainly affecting the Traveller community in the Republic of Ireland [4].

This is now the second outbreak to have been identified this year, following the report of the index case on 17 September 2010. As at 26 October, an additional four laboratory-confirmed cases and four epidemiologically linked cases have been reported. One confirmed case has had two MMR vaccine doses. The median age of cases is 19 years, the range is 12-24 years. Two of the cases have required hospitalisation. This outbreak is not linked with the Irish Traveller community.

A case is defined as laboratory-confirmed when, in the absence of a history of recent vaccination, a clinically suspected case has either a positive measles IgM result in blood or oral fluid, or a positive measles RNA detection. A case is defined as epidemiologically linked when a clinically suspected case has, within 7-18 days of onset of symptoms, been in contact with a laboratory-confirmed case during the infectious period.

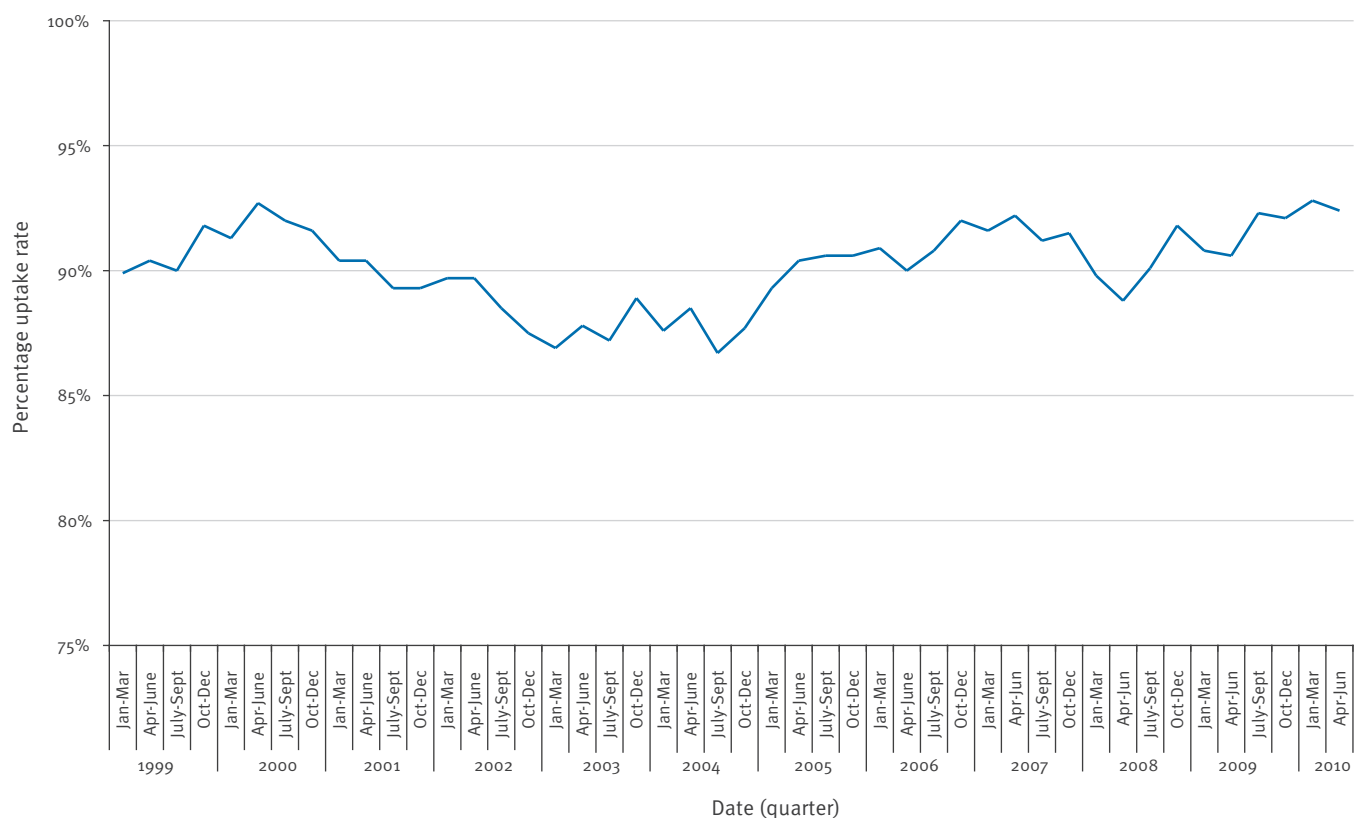
Outbreak description

The index case was an unvaccinated young adult who arrived in Northern Ireland on 3 September 2010 from another European country, where ongoing measles outbreaks had been previously reported, to work as a volunteer in a youth organisation. The onset of symptoms was 12 September and the case was notified on 17 September. The diagnosis was laboratory-confirmed by PCR detection, with D4 genotype subsequently identified.

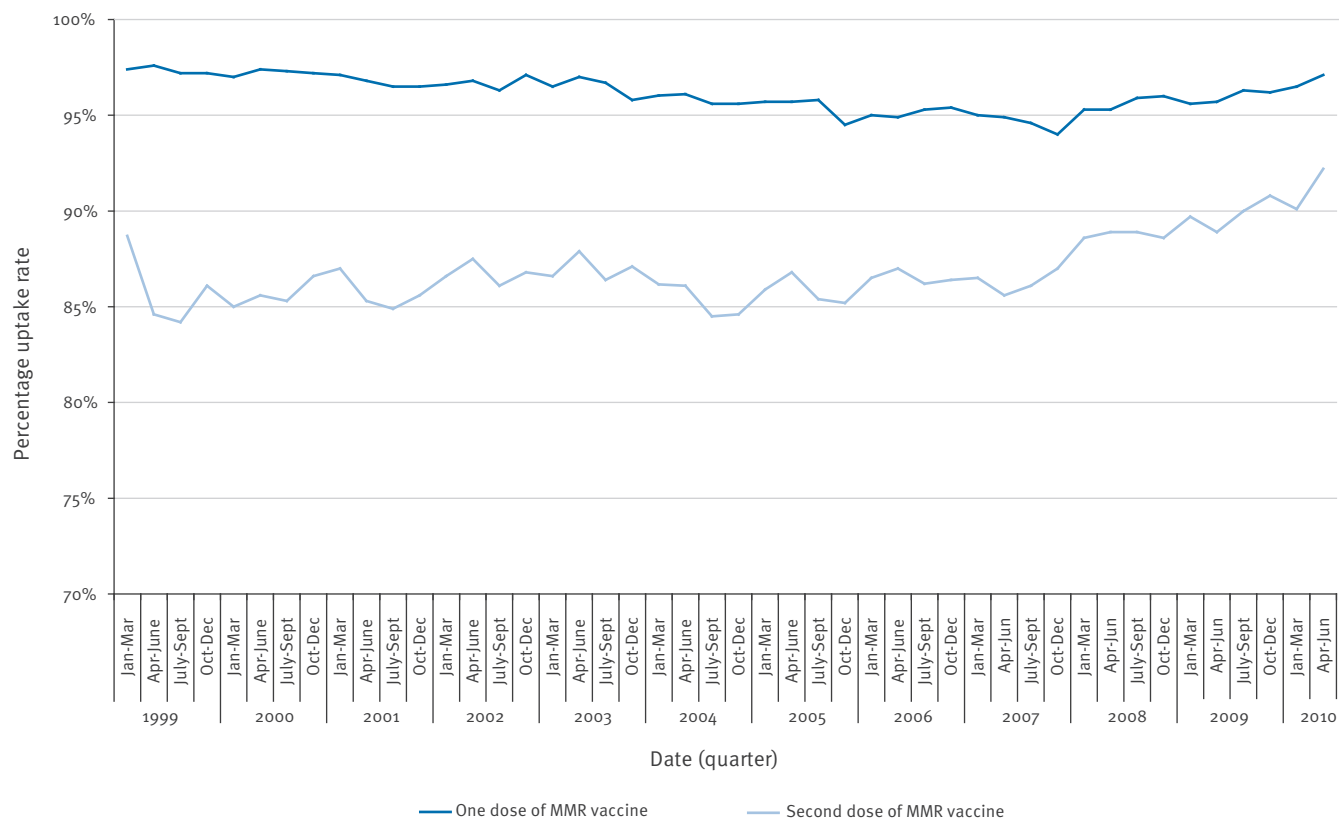
The second case, also laboratory-confirmed, was reported on 1 October in another unvaccinated volunteer with the same youth organisation, who had direct contact with the index case. Onset of symptoms was 28 September. This case had attended a weekend event organised by the youth organisation on 25-26

FIGURE 1

Measles-mumps-rubella vaccination uptake rate at the age of 24 months, Northern Ireland, 1999-2010

**FIGURE 2**

Measles-mumps-rubella vaccination uptake rate at the age of five years, Northern Ireland, 1999-2010



MMR: measles-mumps-rubella.

September, while infectious, at which 50-60 people were present.

At the beginning of the week starting on 11 October, a further seven cases, three of whom were laboratory-confirmed, were reported with onsets of illness at the end of the previous week. Three cases were volunteers with the youth organisation, and four cases were siblings of the second case. All four siblings were unvaccinated against measles as were two of the volunteers. The third case, who was a laboratory-confirmed measles case, had documentary evidence of two doses of MMR vaccine, administered in 1991 and 1997. The other two cases in volunteers were a separate set of siblings. One was laboratory-confirmed, the other was not tested. Of the four siblings of the second case one was laboratory confirmed, the others were not tested.

These further seven cases attended a secondary school, a primary school, a college and a university. To date, there have been no further cases reported in any of these institutions. However, active surveillance continues.

Public health actions

Following the first case notification, the immunisation status of those in the same living accommodation was checked and all had previously received measles-containing vaccines.

On notification of the second case, a letter was sent to all the young people and staff associated with the youth organisation, in particular those who had attended the weekend event on 25-26 September. This letter advised that they should ensure they had two doses of MMR vaccine and to stay at home if they developed any of the symptoms of measles. A press release was also issued giving similar messages to the public [5].

When the further cases occurred, a letter with the same message was issued to students and staff at the four institutions involved. A second press release was issued, now highlighting that this was an outbreak and

further explaining the importance of two doses of MMR vaccine [6].

A letter was also sent to general practitioners and to hospitals highlighting the importance of two doses of MMR and reinforcing the need to contact Public Health Agency should a suspected case be identified. This also signposted appropriate infection control and post-exposure prophylaxis guidance [7, 8].

Conclusion

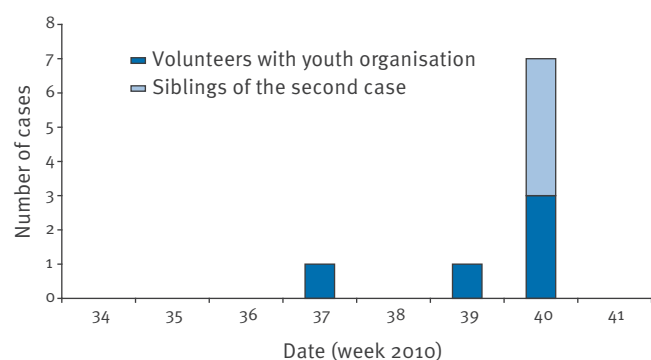
Recent outbreaks in countries such as Northern Ireland show that even in areas with high vaccination coverage there can be pockets of people that may be susceptible to measles infection. With current measles activity elsewhere in Europe, it is important to continue to strive to maintain and further improve MMR vaccine uptake in all European countries. It is not known whether the fully vaccinated case represents primary or secondary vaccine failure. The vaccination status of all cases will continue to be closely monitored.

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FIGURE 3

Date of rash onset in laboratory-confirmed and epidemiologically linked measles cases, Northern Ireland, September-October 2010



Spotlight on measles 2010: Measles outbreak among travellers returning from a mass gathering, Germany, September to October 2010

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In September and October 2010, 13 primary measles cases were identified among unvaccinated persons aged between 9 and 32 years (median: 16.5) in 11 districts in Germany. All cases had attended meetings in Taizé, France. This outbreak illustrates the risk of long distance spread of infectious diseases associated with international mass gatherings, and underlines the importance of closing immunisation gaps against measles by vaccinating non-immune adolescents and young adults.

Introduction

Reports on measles outbreaks in Europe point to the importance of travelling non-immune adolescents and young adults in spreading the disease. Measles outbreaks related to short commutes [1], intermediate, and long distance travel [2,3] have been reported in the past. We describe an outbreak that affected predominantly adolescents and young adults who had recently participated in meetings in Taizé, France. Taizé is home to an ecumenical Christian community of Protestant and Catholic traditions, and is one of the most important sites of Christian pilgrimage. Meetings draw thousands of young people from around the world for contemplation, Bible study and communal work.

Outbreak investigation

Between 13 and 21 September 2010, public health authorities in the German Laender of Baden-Wuerttemberg and North Rhine-Westphalia received notifications of six measles cases in adolescents who had recently returned from meetings in Taizé, France. This was communicated in a public health notice in the German epidemiological bulletin [4] in order to alert the public health community, and to identify any additional cases. A case was defined as clinically diagnosed or laboratory-confirmed measles infection notified in September or October 2010 in a person who had recently travelled to Taizé. French authorities were informed about the outbreak by the Robert Koch

Institute via the Early Warning and Response System (EWRS). The Taizé Community was contacted via electronic mail, and designated a contact person who responded to emails and telephone calls with helpful information about the setting. All patients were contacted by local health authorities via telephone or in writing and were interviewed about their history of measles, immunisation with measles virus-containing vaccine, and details of travel and accommodation, where available. Diagnostic confirmation of cases was sought by laboratory detection of measles virus-specific IgM in samples from the patient or any secondary or tertiary case. Whenever possible, samples of blood, oral fluid and urine were collected and forwarded to the National Reference Centre Measles, Mumps, Rubella to further confirm the diagnosis by measles virus genotyping and to investigate transmission chains.

Results

As of 31 October 2010, 13 primary cases who met the case definition had been identified from reports in Baden-Wuerttemberg (n=9), North Rhine-Westphalia (n=1), and Bavaria (n=3). Patients' ages ranged from 9 to 32 years (median: 16.5). Ten cases were female. None of the primary cases reported a history of clinical measles or having received measles virus-containing vaccine. Three cases were hospitalised for two – three days.

All 13 primary cases had travelled to Taizé from their various places of residence, either in youth groups (seven cases), with family (three cases) or a friend (one case). Cases 2 and 3 were persons who arrived in a bus chartered by their youth group. Cases 10 and 11 were siblings who had travelled in a private car with their parents. None of the other cases had shared the same means of transportation (e.g. charter bus, private car, hitchhiking), excluding a common source of exposure during outbound or return travel. Distances of the

cases' travel to Taizé by road varied between 390 km and 740 km (median: 520 km).

Periods of sojourn at Taizé ranged from six days to five weeks (the longest stay being for a volunteer helper, Case 4). Ten cases stayed for eight or nine days, mostly from Sunday to Sunday, which are the arrival and departure days recommended by the Community. Accommodation was in six – eight-bed dormitories (five cases) shared with youths from the same or other travel groups, in a family room (one case), or in their own tents that they brought with them (five cases); details of accommodation remain unknown for two cases.

Interviewed cases reported to have participated in a broad range of scheduled activities such as common prayers and meals, discussion groups, practical assignments, thematic workshops and informal gatherings at a common area, providing a picture of multiple possibilities for encounters with other persons in attendance. All primary cases were present on at least one weekend day between Friday 27 and Sunday 29 August 2010, and on a various number of days before or after this period (Figure 1).

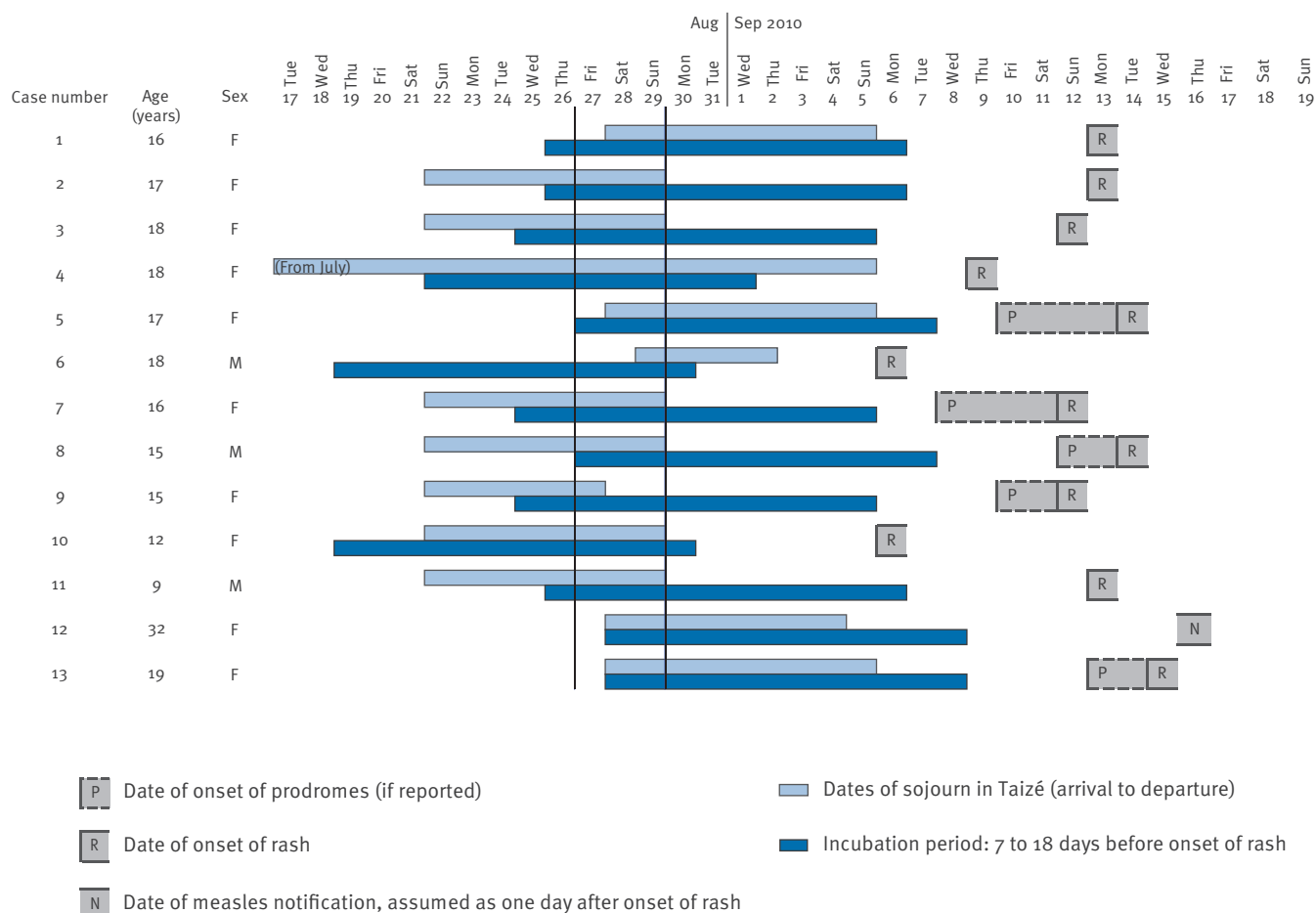
Eight of 13 primary measles cases did not cause secondary measles virus infections. Five primary cases resulted in 17 secondary cases (age range: 2–47 years, median: 15) and seven tertiary cases (age range: 5–18 years, median: 13). The persons affected were family members, friends and schoolmates, predominantly of a similar or younger age. In total, 37 measles cases could be attributed to this outbreak (Figure 2).

One 15-year-old secondary case had received a single dose of measles virus-containing vaccine in 2000. All other primary, secondary and tertiary cases were reported as unvaccinated.

The diagnosis of measles was laboratory confirmed by enzyme-linked immunosorbent assay (ELISA) in 10 primary cases by IgM or by a rise in IgG antibody level. Laboratory confirmation was obtained for two secondary measles cases who had been in contact with two clinical primary cases during the infectious period upon return. One primary measles case was diagnosed clinically. Two primary cases were not laboratory-confirmed, but both were the infection source of at least one secondary case with laboratory-confirmed measles.

FIGURE 1

Dates of sojourn at Taizé, France, and of symptom onset of primary measles cases, Germany, August – September 2010 (n=13)



F: female; M: male.

The lines represent the weekend in which all primary cases were present in Taizé on at least one day.

The measles viruses isolated in Germany from mid-September until end of October 2010 were compared with prototypic measles viruses representing the predominant D4 sub-variants in western Europe.

FIGURE 2

Geographical spread of measles cases, Germany, September – October 2010 (n=37)

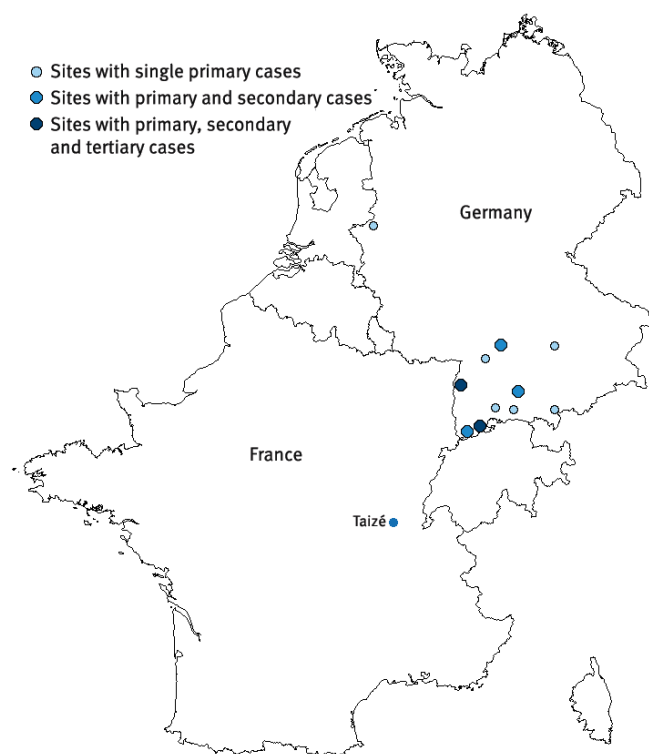
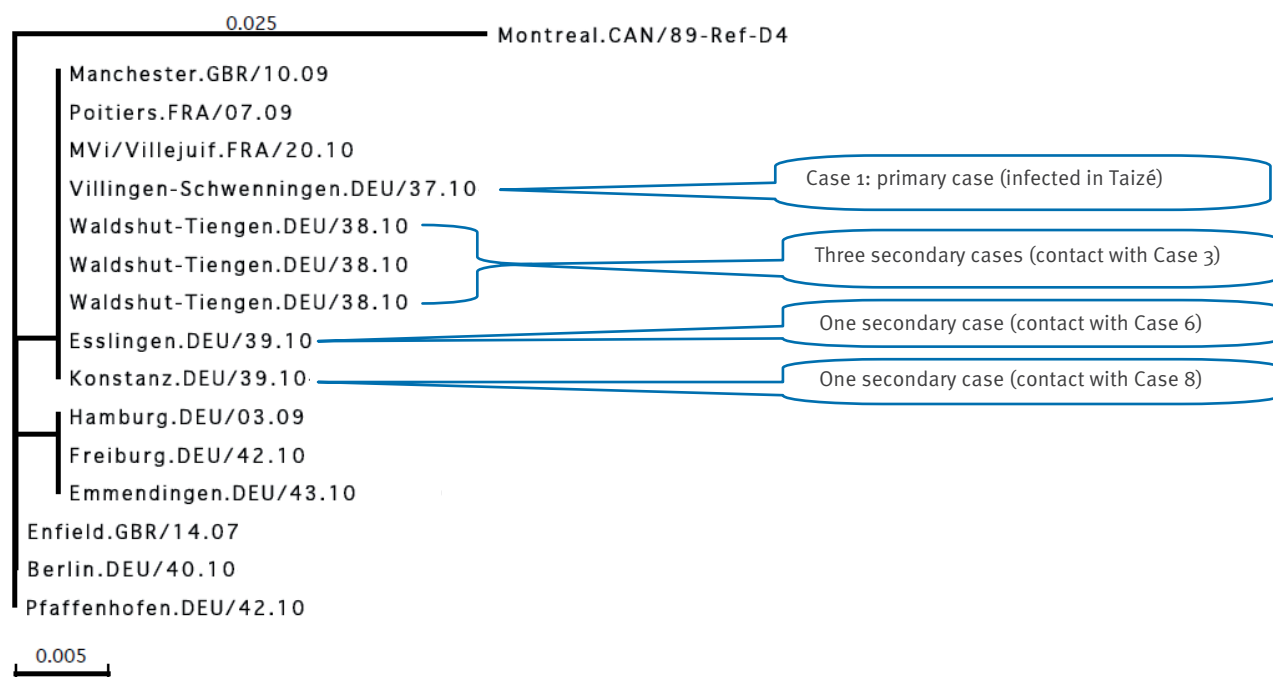


FIGURE 3

Phylogenetic relationships within measles virus genotype D4, measles outbreak, Germany, September – October 2010 (n=6)



The genotypes of the virus from the six cases are indicated in boxes. The other genotypes listed are shown for comparison (from GenBank).

Genotyping was performed for Case 1 (Villingen-Schwenningen.DEU/37.10) who had been infected in Taizé and for five secondary cases who had been in contact with either Case 3 (n=3), Case 6 (n=1) or Case 8 (n=1) (Figure 3). Phylogenetic analysis was based on a 456-nucleotide sequence encoding the C-terminus of the measles virus Nucleocapsid-protein. All five cases analysed showed the genotype D4 variant ‘D4-Manchester’ (MVs/Manchester.GBR/10.09[D4], GenBank accession number: GQ370461).

This suggests that the German cases with a suspected link to the meetings in Taizé belong to the same chain of measles virus transmission. Occurrence of measles virus variant D4-Manchester in western and central parts of Europe from 2008 onwards is reported in the GenBank and the MeaNS database. In 2010, this variant was identified several times in France [5].

Discussion

In Europe, measles outbreaks have been reported to occur in, among other settings, anthroposophical communities [6], minority populations [7] and unvaccinated preschool children [8]. In the United States where elimination has been achieved, the challenges to maintain elimination are considered to include outbreaks of measles resulting from travel to countries where measles is still endemic, frequent international travel and persons who remain unvaccinated because of personal belief [9].

This multilocal outbreak illustrates the risk of exposure to measles virus at mass gatherings while measles

elimination has not yet been achieved. In addition, it underlines the potential for long-distance spread of measles virus by mobile, non-immune adolescents and adults. We consider it likely that additional measles cases may have occurred among persons who visited Taizé at the end of August 2010 and returned to other destinations, where the possible source of exposure went unnoticed or remains unpublished.

In 2008, the nationwide measles vaccination coverage for German children at the time of their school entry examination (five to six years) was 95.9% for the first dose, and 89% for the second dose, with considerable geographical variation [10]. While measles vaccination coverage among younger children is on the rise, it should not be forgotten that immunisation coverage in older age cohorts may not yet have reached levels required for measles elimination.

In conclusion, measles may be reintroduced by returning travellers or visitors who have been infected with the virus. Public health policy should recognise the importance of proactive information of adolescents and young adults in order to address gaps in individual measles immunity, and by encouraging the vaccination of non-immune adolescents and young adults.

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Spotlight on measles 2010: Measles outbreak in the Provence-Alpes-Côte d'Azur region, France, January to November 2010 - substantial underreporting of cases

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In 2010, the Provence-Alpes-Côte d'Azur region in France has been experiencing a measles outbreak with at least 310 cases among the general population, which included 28 cases among healthcare workers (9% of all reported cases). There is, however, substantial underreporting in the notification systems of cases in both populations.

Background

In the Provence-Alpes-Côte d'Azur (PACA) region in France, the measles virus currently circulates in the general population [1]. Outbreaks have occurred in well-defined groups such as nomadic minorities and Roma communities that are not fully vaccinated, in childcare centres, schools, universities, healthcare facilities and a prison. Hospitals have been particularly affected, as many measles cases visited emergency units or were admitted to hospital with complications.

In France, clinicians and microbiologists are requested to report suspected measles cases immediately to the regional public health authority (Agence régionale de santé, ARS), through the national mandatory notification system. The French Institute for Public Health Surveillance (Institut de veille sanitaire, InVS) collects and analyses this information. Where there is nosocomial infection, healthcare facilities are requested to notify the interregional infection control coordinating centres and the Agence régionale de santé, which in turn inform InVS, through the national early warning system [2]. As described fully elsewhere [1,2], the reporting includes the nature of the event, its main characteristics, as well as investigations and control measures carried out, and assistance can be requested.

Outbreak description

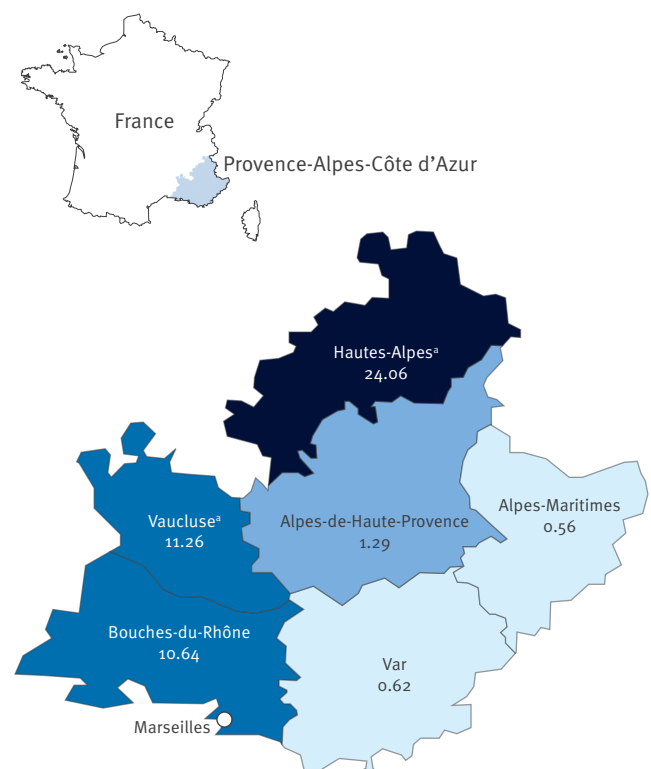
General population (preliminary data)

In the PACA region (4,780,986 inhabitants) increased measles transmission continued to be recorded in 2010. We included in our analysis the notified clinical

and laboratory-confirmed cases with a date of rash onset between January 2008 and November 2010 (preliminary data). A confirmed case can be: (i) laboratory-confirmed, by detecting either measles IgM antibodies or measles virus nucleic acid in serum or oral fluid

FIGURE 1

Incidence of reported measles cases, by district, Provence-Alpes-Côte d'Azur region, France, January – November 2010



The numbers shown are the incidence rates per 100,000 population.

^a Districts with active case finding.

Source : Regional Health Agency (Agence régionale de santé, ARS) of Provence-Alpes-Côte d'Azur, France.

using reverse transcription-polymerase chain reaction (RT-PCR), or (ii) epidemiologically confirmed, when a link with a laboratory-confirmed case is proven. Case definitions for measles are detailed on the InVS website [3]. As of 30 November, 384 measles cases had been reported (Figure 1). In 2008 and 2009, 51 and 44 cases were reported.

In our analysis, 74 of the 384 cases reported in 2010 were excluded because detailed data were unavailable. The majority of cases, 193 of the remaining 310, were reported by the Bouches-du-Rhône district (1,916,494 inhabitants) (Figure 2); 126 of the 193 cases were reported by Marseilles (852,395 inhabitants), the biggest town of the region. In the PACA region, the incidence increased from 1.07 per 100,000 population in 2008 to 6.37 per 100,000 population in 2010. The incidence in the Bouches-du-Rhône district reached 10.64 per 100,000 population and in Marseilles alone 14.78 per 100,000 population in 2010 (Figure 3). In France as a whole, 5,221 measles cases were reported between 1 January 2008 and 31 August 2010: the incidence rates in the general population increased from 0.95 per 100,000 population in 2008, 2.3 to 4.84 per 100,000 population in 2010 [1,3].

The male:female ratio of the 310 measles cases in the PACA region was 1:2. The disease affected all ages, but the people most affected were those under one year (10% of cases, n=31) and 20–29-year-olds (25% of cases, n=74). The highest incidence rate was observed in children under two years (51.07 per 100,000 population) (Figure 4).

Measles vaccination status was available in 81% of cases (n=250): 204 (82%) were unvaccinated, 37 (15%) had received a single dose of measles-mumps-rubella (MMR) vaccine, four (2%) two doses and five (2%) unspecified number of doses.

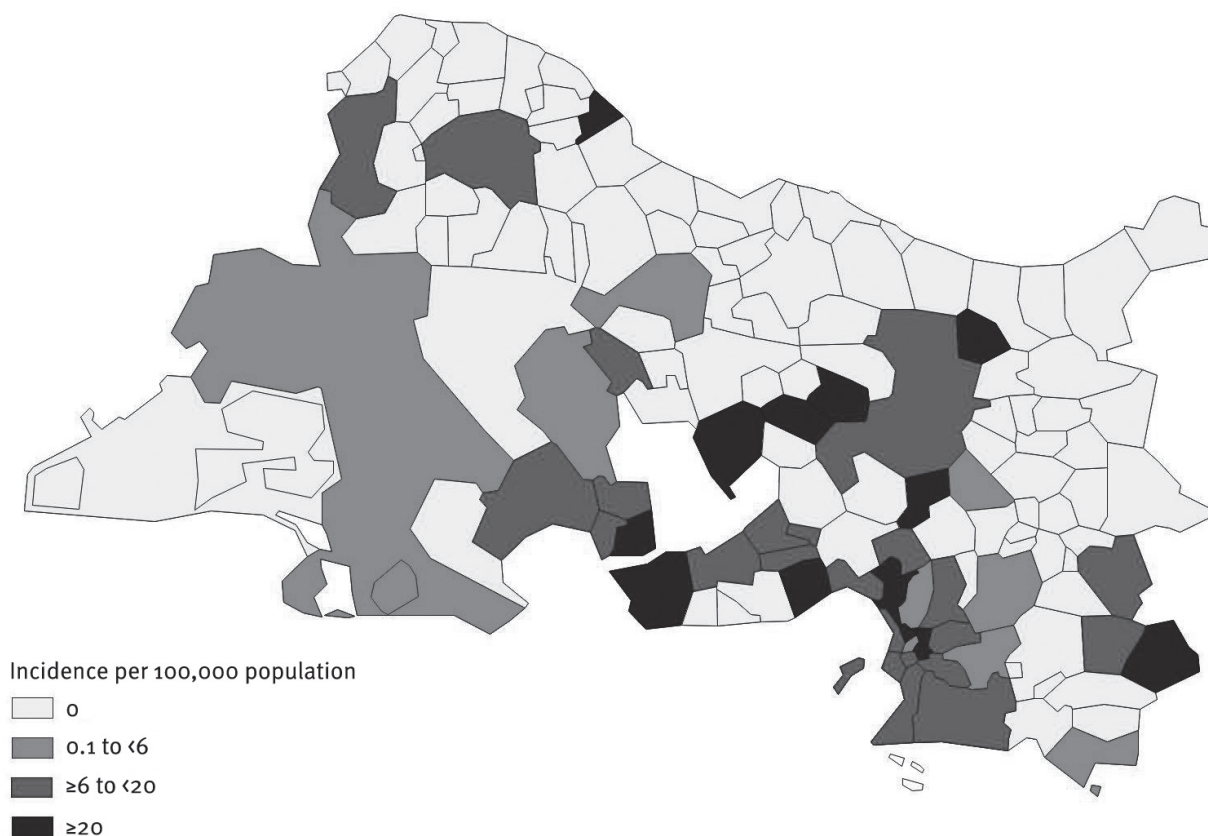
The proportion of laboratory-confirmed cases was 58% (n=180) and the D4 genotype was identified in 13 samples.

Information on hospital admission was available for all cases except one; 98 (32%) were admitted to hospital; of these, 29 were hospitalised in Marseilles.

A total of 34 cases had complications: 20 of these were in cases who had been hospitalised. There were no complications in infant cases, 11 cases with complications were aged 1–9 years, nine cases were 10–19

FIGURE 2

Incidence of reported measles cases in Bouches-du-Rhône district, Provence-Alpes-Côte d'Azur region, France, January – November 2010



Source : Regional Health Agency (Agence régionale de santé, ARS) of Provence-Alpes-Côte d'Azur, France.

years and 14 were older than 20 years. Acute encephalitis was reported in an unvaccinated six-year-old case and pneumonia in 23 cases. No measles-related deaths were reported.

Nosocomial infection of healthcare workers (preliminary data)

In the PACA region, healthcare workers were particularly affected by measles, with 28 cases reported in 2010 (as of 30 November) through the mandatory notification system, representing 9% of all cases in the general population. Four cases were nurses, four were medical doctors, 11 were students (two nursing students and nine medical students) and seven were other types of healthcare workers; for two cases, their type of healthcare work was unspecified. Of these 28 cases, 23 were reported from Bouches-du-Rhône district; 15 of the 23 were from Marseilles. Only two of the 28 cases were reported through the early warning system.

The male:female ratio of the 28 cases was 0:6. A total of 18 cases were aged 20–29 years and 10 were older than 30 years (the eldest was 55 years).

FIGURE 3

Incidence of reported measles cases in Provence-Alpes-Côte d'Azur region, France, by year, January 2008 – November 2010

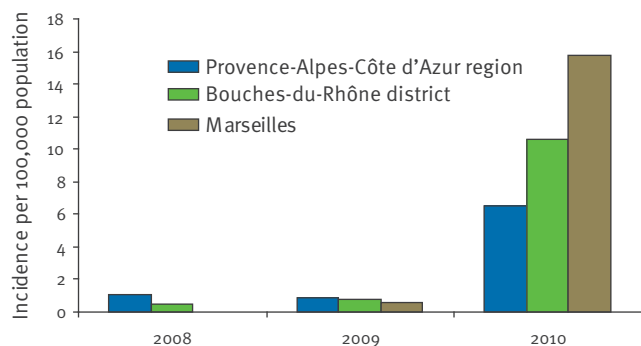
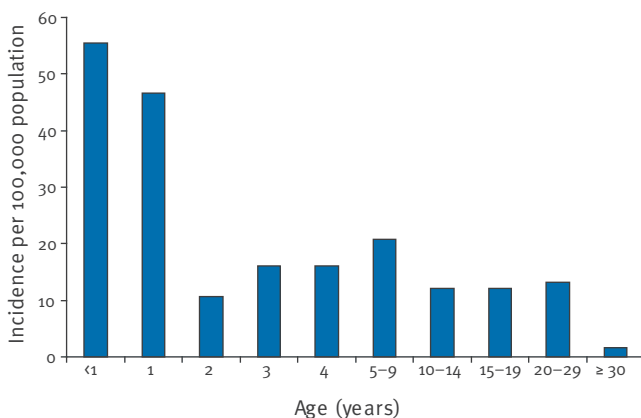


FIGURE 4

Incidence of reported measles cases in Provence-Alpes-Côte d'Azur region, France, January 2008 – November 2010



Measles vaccination status was known for 22 of the cases: 14 were unvaccinated, six had received a single dose of vaccine and two had had two doses.

Nine cases were admitted to hospital, of whom six were hospitalised in Marseilles.

Control measures

Several control measures were implemented by the Agence régionale de santé according to the national guidelines [4]. They included providing information to the general public and providing targeted information to healthcare professionals, by individual letter to general practitioners and heads of nursing schools in the Bouches-du-Rhône district. The communication was focused on vaccinating the general population and healthcare workers according to the national immunisation schedule and proposed post-exposure vaccination or immunoglobulin for people at high risk for severe disease as a result of measles virus infection.

During measles transmission among healthcare workers and/or hospitalised patients, most healthcare workers implemented barrier measures, and unvaccinated or non-immune healthcare workers and patients' contacts were vaccinated locally. Contacts outside the hospital, relatives and external patients that could have been infected by a case were identified, informed and invited to contact their general practitioner in order to ascertain their vaccination status and to complete their vaccinations if necessary.

Discussion

A high number of measles cases has been reported in 2010 in the PACA region, in particular in Marseilles. However, the number of measles cases reported is less than the true number of cases, for various reasons: cases were excluded from the analysis because of missing data, and clinicians and microbiologists did not report all cases to health authorities. InVS demonstrated that during investigations of measles outbreaks in 2008, cases reported through the national mandatory notification system represented only 10% of all detected cases [5]. Often, only the first case in a household is reported: any secondary cases are not. The high proportion of hospitalised cases from the general population seems to reflect a better compliance in notification by their health professionals than by general practitioners.

In healthcare facilities, underreporting through mandatory notification and early warning systems is the main reason for underestimating the number of cases. For example, more cases have been identified by the public hospitals of Marseilles than have been declared to the Agence régionale de santé [6,7].

The low measles immunisation coverage among the general population and healthcare workers, who can infect vulnerable persons who they treat, facilitates the expansion of the outbreak in the region [8]. In 2007,

among children aged 24 months, the vaccination coverage (one dose) reached 92% in the Alpes-Maritimes district, 89% in the Bouches-du-Rhône district and 87% in Var district (no data are available from the other districts of the PACA region); at national level, it was 90% [9]. Clinical diagnosis of measles cases must be better understood by general practitioners, and case notification and the implementation of preventive measures, including catch-up and post-exposure vaccinations, must be improved.

Insufficient implementation by healthcare workers and general practitioners of the current recommendations issued by the French health authorities [4] and unsuitable control measures in some healthcare facilities are the cause of measles transmission in healthcare workers and hospitalised patients [8]. Awareness among the healthcare workers, particularly occupational medical staff, must be raised to implement specially adapted preventive and control measures in hospitals units, especially in emergency rooms and wards where all patients admitted to hospital with rash and fever must be isolated and strict infection control procedures applied before diagnostic confirmation. Preventive measures need also to focus on improving the hospital's knowledge of the serological status of their patients and on vaccinating them if they are not immunised, because immunisation is the only reliable protection against nosocomial spread of measles [10].

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Spotlight on measles 2010: Increased measles transmission in Ferrara, Italy, despite high vaccination coverage, March to May 2010

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We report an increase in the incidence of measles in a population with consistently high and improving immunisation coverage in Ferrara province, northern Italy. During the first six months of 2010, 19 cases were confirmed, 10 of which were hospitalised. General practitioners, paediatricians and local health-care authorities were alerted about the outbreak and asked to notify all suspected cases. We need to further increase immunisation coverage and to maintain and implement the monitoring system.

Background

In Italy measles vaccination is recommended with a two-dose schedule, with the first dose of measles-containing vaccine administered to children between 12 and 15 months of age and the second dose at the age of five to six years. The combined measles-mumps-rubella (MMR) vaccine was included in the national vaccination schedule in 1999, and has been provided free-of charge to all children since 2002.

Thanks to the implementation of surveillance plans and interventions to improve vaccination coverage, the incidence of measles in Italy has decreased considerably

in the past decades from 150 per 100,000 0-14 year-old inhabitants in the 1960s to 15 in 2000 and 1 in 2006 [1-2]. At the same time, the national vaccination coverage at the age of 24 months increased significantly from 84% in 2003 to 90% in 2006, although with differences between regions [3]. Since 1998, the surveillance on vaccination coverage rates at national level has collected data on immunisations in newborns by a cluster sampling method. The same methodology is used to evaluate vaccination coverage rates in 16 year-old adolescents. Thus, national data on vaccination coverage for the first dose in children over two years of age and for the second dose are not available [4]. Despite recent improvements, the vaccine coverage in Italy, similar to other European countries, remains below the threshold suggested by the World Health Organization to reach elimination of the disease, i.e. country-wide at least 95% of children at the age of two years [5]. Epidemic outbreaks in several Italian regions (Piedmont, Lombardy and Emilia-Romagna) have been described in the past three years [6], an indication that measles virus is circulating. Therefore, specific preventive interventions should be strengthened. Here we describe a measles outbreak that occurred in the first

FIGURE 1

Coverage with first dose of measles-containing vaccine by the age of 24 months in Ferrara province and Emilia-Romagna region, Italy, 1999-2008

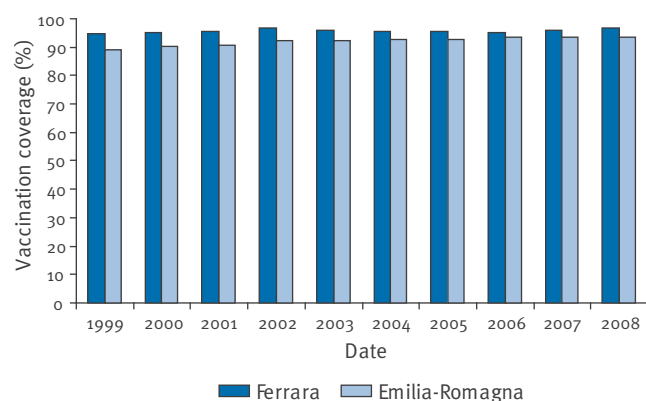
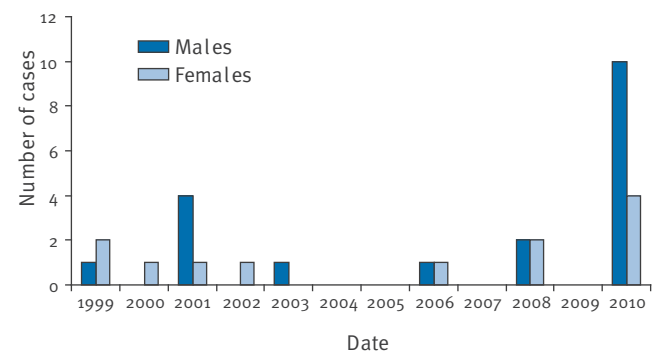


FIGURE 2

Laboratory-confirmed measles cases by sex, Ferrara province, Italy, 1 January 1999–30 June 2010 (n=31)



six months of 2010 in the province of Ferrara, in the Emilia-Romagna region, north-east Italy, an area with historically high immunisation coverage rates [7].

Epidemiological update and outbreak description

Ferrara had a population of approximately 360,000 inhabitants, and 2,813 newborns in 2009 [8]. According to national legislation [1] and the European case definition for measles [9], the identification of a case requires the detection of measles-specific IgM antibodies in the serum of a person notified with clinical symptoms of measles who had no record of recent vaccination. Since 1999, only notified and laboratory-confirmed (IgM-positive) cases have been reported by the healthcare workers in the local health unit to the regional information system of infectious diseases in Emilia-Romagna. Epidemiologically linked cases are notified but not reported to the information system. For each case, this database collects personal data (age, sex, place of residence), clinical information (if complications or hospitalisation occurred) and vaccination status.

In 1999 the vaccine coverage at 24 months of age was 94.9% in Ferrara province, and it has increased over the years, reaching in 2008 96.7% with one dose at 24 months of age and 91.1% with two doses at six years of age. The vaccine coverage has been higher in Ferrara than in the region of Emilia-Romagna as a whole since 1999 (Figure 1) [7]. Over the past ten years the measles incidence has been stable in the province and transmission has ceased spontaneously, indicating that vac-

ination coverage has been high enough to break the chain of infection.

Only 17 laboratory-confirmed cases of measles were observed between 1999 and 2009, with between 0 and 5 cases per year (Figure 2). During the first six months of 2010, however, 23 cases were reported, 14 of whom were laboratory-confirmed and are shown in Figure 2. Five cases were epidemiologically linked to one of the confirmed cases but not laboratory-confirmed and hence not included in the regional information system of infectious diseases. The remaining four cases were neither laboratory-confirmed nor linked and are not further analysed here.

General practitioners, paediatricians and local healthcare authorities were alerted about the outbreak and asked to notify all cases with symptoms suggestive of measles. The following case classification was used:

- *Suspected*: a person with any febrile illness accompanied by rash;
- *Probable*: a case that met the clinical case definition [9], had non-contributory or no serological or virological test results, and was not epidemiologically linked to a confirmed case;
- *Confirmed*: a case that was laboratory-confirmed or that met the clinical case definition and is epidemiologically linked to a confirmed case. A laboratory-confirmed case did not need to meet the clinical case definition.

TABLE

Characteristics of measles cases, Ferrara province, Italy, 1 January–30 June 2010 (n=19)

Case	Age	Sex	MMR vaccination status	Hospitalisation	Complication	Epidemiological link
1	16 years	F	Unvaccinated	No	No	No (index case)
2	48 years	F	Unvaccinated	Yes	Pneumonia	No
3	44 years	M	Unvaccinated	Yes	No	No
4	12 months	M	Unvaccinated	No	No	No
5	19 years	M	Unvaccinated	Yes	No	No
6	11 months	M	Unvaccinated	No	No	No
7	11 years	M	Unvaccinated	Yes	No	No (index case of the linked cluster)
8	42 years	F	Unvaccinated	Yes	No	No
9	11 years	F	Unvaccinated	No	No	Yes (primary school)
10	20 years	M	Unvaccinated	Yes	No	No
11	54 years	F	Unvaccinated	Yes	No	No
12	49 years	M	Unvaccinated	Yes	No	No
13	10 years	M	Unvaccinated	No	No	Yes (primary school)
14	14 months	M	Unvaccinated	Yes	No	No
15	36 years	M	Unvaccinated	No	No	No
16	10 years	F	Unvaccinated	No	No	Yes (primary school)
17	5 years	F	Vaccinated ^a	No	No	Yes (primary school)
18	13 months	F	Vaccinated ^a	No	No	Yes (sister of number 17)
19	34 years	M	Unvaccinated	Yes	No	No

M: male; F: female;

^aVaccination with one single dose of MMR vaccine, coincidentally administered three to five days before the onset of exanthema.

Laboratory criteria for diagnosis were a positive serologic test for measles immunoglobulin M antibody, or significant rise in measles antibody level by any standard serologic assay, or isolation of measles virus from a clinical specimen [9]. A linked case was defined as a person who showed clinical signs of disease following close contact with a confirmed case during infectious period [10].

The index case, notified on 5 March, was a 16-year-old unvaccinated girl. She had no close contact with any other case nor a history of travel in areas where recent outbreaks were described. Therefore, a clear source of infection could not be identified for this case. The five epidemiologically linked cases formed a cluster notified in the period from 9 to 29 April. An 11-year-old boy was identified the index case; all cases attended the same primary school, except for a 13-month-old girl, the sister of a pupil.

The mean age among the 19 confirmed cases was 21.7 years (range 11 months to 54 years) (Table). The mean delay between the onset of the exanthema and the notification to the authorities was 3.3 days. Ten patients required hospitalisation. One patient had a complication (pneumonia). Two of the 19 cases had been vaccinated against measles with one single dose of MMR vaccine, three to five days before the onset of exanthema. Considering the incubation period for measles of 8-12 days, these two patients probably acquired the infection before immunisation and were in the incubation period at the time of vaccination [11].

Control measures

In accordance with current legislation [1], vaccination of the cases' families and other contacts has been proposed. Moreover, as a measure to control the spread of the disease, students and teachers who had no history of measles vaccination or illness were encouraged to not to attend school until there were no more cases. Recreational and work activities of each case were also recorded. General practitioners, doctors, paediatricians and local healthcare authorities were requested to rapidly notify all patients with clinical symptoms suggestive of measles and to confirm the diagnosis by appropriate laboratory tests. All hospitalised patients suspected to have measles were isolated and no nosocomial transmission has been seen. No further cases were reported after 12 May. It is therefore likely that the measles outbreak has been contained through implementation of adequate control measures by the department of public health of the local healthcare unit of Ferrara.

Discussion

In 2005 the World Health Organization (WHO) had planned the elimination of measles in Europe no later than 2010 [12], but this deadline has recently been extended to 2015 [13]. In order to achieve this target, a minimum of 95% vaccination coverage with at least one dose in children at the age of two years should

be reached. However, several outbreaks that occurred in recent years in Italy and other European countries are an indication that this goal has been only partially achieved. Historically, immunisation coverage in the province of Ferrara has been high, and in 1999 a vaccine coverage of 94.9% at the age of 24 months was recorded. This coverage was maintained over the following years, but the present outbreak shows how difficult it is to reduce the incidence of measles to less than one in 100,000 live births, even in an area with high vaccine coverage. It is noteworthy that the cases reported here did not give rise to large outbreaks, indicating that, together with control measures, population immunity was high enough for the outbreak to die out.

However, as long as the measles virus is imported from neighbouring areas or from other countries, a population will not be entirely without measles cases because the number of susceptible people will accumulate over time and will sustain smaller or larger outbreaks depending on how large and how concentrated the accumulated susceptible population is. Most measles outbreaks in Europe in recent years have started as a result of importation of measles from another European country, and Europe has on several occasions exported measles to measles-free areas of the world such as the Americas.

It is therefore necessary to make an extra effort to further increase immunisation coverage and to maintain and implement the monitoring system, especially in terms of quickness, completeness and accuracy of reporting.

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Spotlight on measles 2010: An ongoing outbreak of measles in an unvaccinated population in Granada, Spain, October to November 2010

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On 13 October 2010, the Andalusian Epidemiological Surveillance Network was notified of one case of measles. By 15 November 2010, 25 confirmed cases of measles had been reported from Granada, southern Spain, of whom 22 were unvaccinated children under the age of 15 years. This ongoing outbreak involved a subpopulation with low vaccination coverage and parents with ideological objections to vaccination. As of 7 December the number of cases has reached 59.

Background

In Andalusia, Spain, a Plan of Action for Measles Elimination was approved in 2001 [1], following the recommendations of the World Health Organization (WHO) [2]. This Plan was created with the objective of eliminating indigenous measles by the year 2005, but elimination has not yet been achieved. The two strategic goals of the Andalusian Plan were to enhance the epidemiological surveillance system to facilitate early detection of cases and transmission control, and to increase the vaccination coverage in children in order to improve population immunity.

The measles-mumps-rubella (MMR) vaccine was introduced in 1984 in the Andalusian vaccination calendar for children at 15 months of age. In year 1990, a second dose was included in the calendar for children at 11 years of age. The age of administration of the second dose was changed to six years in 1999, and to three years in 2004 [3]. These changes were made in order to adapt the levels of immunity against measles in different age cohorts to the WHO proposals regarding the elimination of indigenous measles in the European Region.

Since 2001, two important measles outbreaks have occurred in Andalusia: one in 2003 in Almería (180 cases; unpublished data) and the other in 2008 in Algeciras (155 cases) [4]. Both outbreaks mainly affected unvaccinated young adults, although

unvaccinated children under 16 months of age were subsequently also affected.

Here we present preliminary data until 15 November on an ongoing outbreak of measles in Granada, southern Spain, a city with a population of approximately 234,000 inhabitants.

Outbreak description

On 13 October 2010, a suspected case of measles [5] in a 13-year-old girl was notified, and confirmed by serology (IgM-positive) two days later. The second case, in a 13-month-old child from the same neighbourhood was reported on 19 October 2010 by the same health centre. Both cases had attended a wedding reception where they had been in contact with a girl from another region in Spain who was diagnosed with measles when she returned home. Until 15 November 2010, a total of 25 cases of measles were confirmed (Figure 1).

The age of the cases ranged from seven months to 38 years. Nine of the 25 cases were under one year of age and 14 cases were under three years of age. Only three cases were older than 15 years.

Of the 25 cases, 21 were living in the same neighbourhood in Granada. Of these 21, 19 cases were younger than 15 years, and the other two were 24 and 29 years-old. Eight of these children were too young to attend any educational centres, while the remaining 11 were attending the following centres:

- A secondary school located outside the affected neighbourhood: one case (living in the affected neighbourhood), no secondary cases;
- Primary school A, located in the affected neighbourhood: six cases;
- Primary school B, located in the affected neighbourhood: one case, no secondary cases;

- Day care centre A, located in the affected neighbourhood: two cases;
- Day care centre B, located in the affected neighbourhood: one case, no secondary cases.

Four cases were living in other neighbourhoods in Granada or in nearby towns and were infected through transmission in hospital. These cases were 38 years, 7 months, 13 months and 16 months of age.

All cases were treated at the same hospital, 14 as outpatients, and 11 as inpatients. Two cases were diagnosed with bronchiolitis and pneumonia, respectively. Only one case, a six-year-old, had been vaccinated previously with one dose of MMR. The remaining cases were unvaccinated. Nineteen cases were laboratory-confirmed and six cases were confirmed by epidemiological link with a confirmed case. To date measles virus

genotype B3 was identified in two cases. Genotyping of the other cases is ongoing.

Control measures

Control measures have been implemented in the four affected schools and the day care centre, in accordance with the Plan of Action for Measles Elimination and to Protocol of Alert of the Regional Ministry of Health [5]. The vaccination status of all children in the affected schools was reviewed and an MMR vaccine dose was offered to all children who were not fully vaccinated. Cases were excluded from school for at least four days after appearance of the exanthema. All affected school and day care staff younger than 40 years and without a history of the disease or documented evidence of vaccination were tested for susceptibility to measles and offered a dose of MMR vaccine.

FIGURE 1

Confirmed measles cases by day of onset of rash, Granada, Spain, October-November 2010 (n=25 as of 15 November)

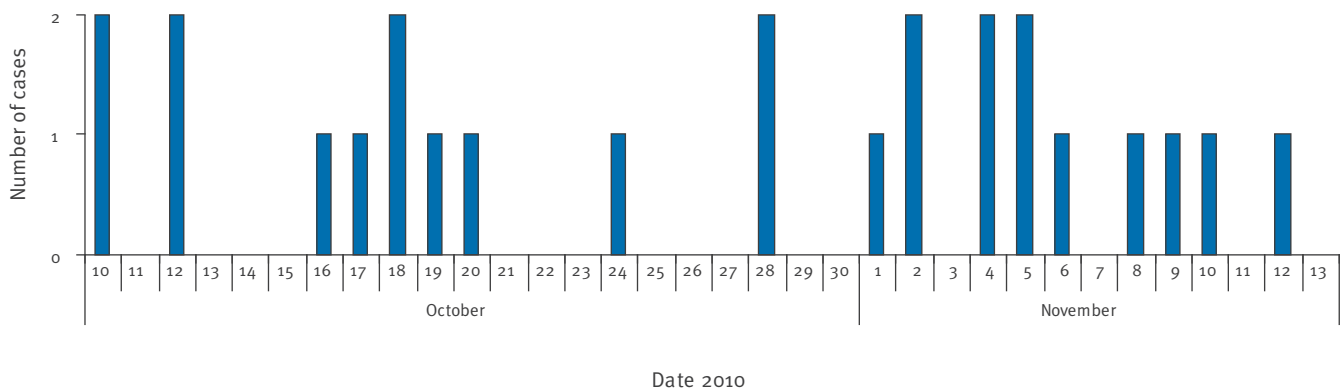
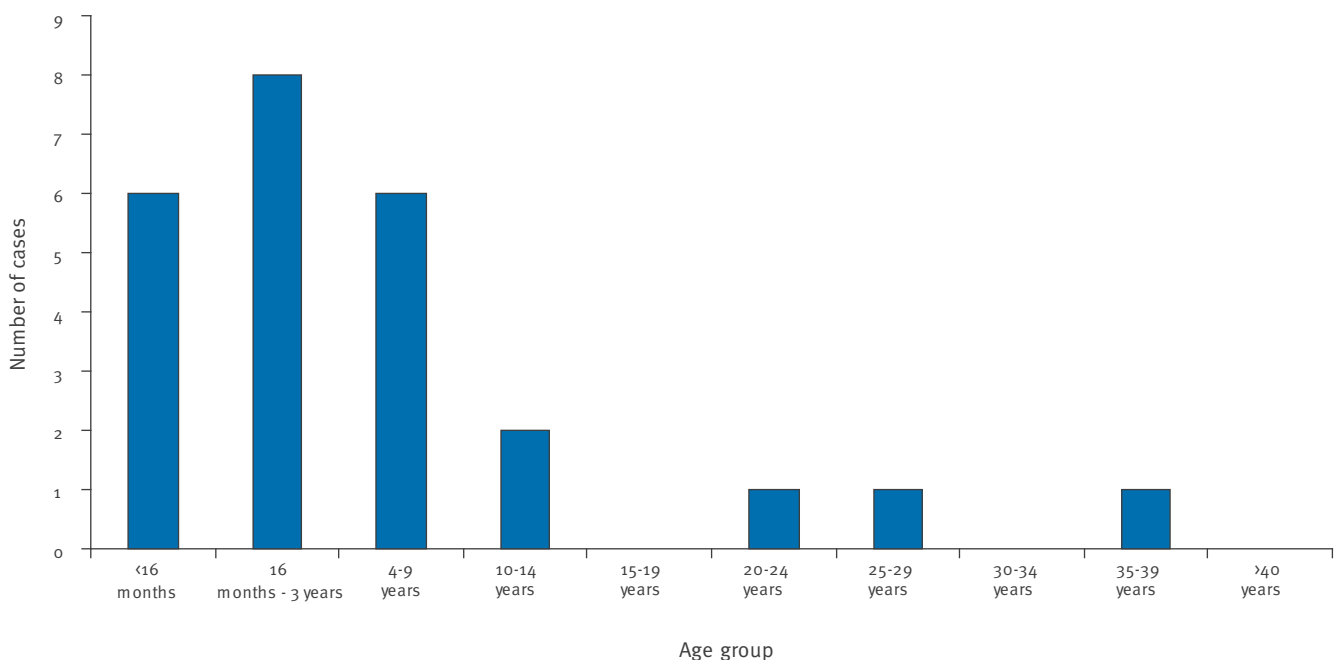


FIGURE 2

Confirmed measles cases by age, Granada, Spain, October-November 2010 (n=25, as of 15 November)



In the affected day care centre, unvaccinated children aged between 12 and 15 months received one dose of MMR vaccine, and children aged between 6 and 11 months received one dose in the context of the current outbreak and are scheduled for a second dose at the age of 15 months according to the vaccination calendar. The unvaccinated contacts of cases or contacts with no history of measles were immunised with MMR vaccine in the first 72 hours after exposure, except for infants younger than six months, pregnant women and immunocompromised people, who were treated with anti-measles immunoglobulin.

It was recommended, until there are no more cases, to exclude from the affected centres individuals who were not vaccinated because of contraindications or another reason that excluded vaccination and who had no history of measles illness.

As a pre-exposure measure at the population level, a first dose of MMR vaccine is being administered to all children older than 11 months in the city of Granada and nearby towns that have reported one or more cases. A second dose of MMR vaccine will be administered to these children at three years of age according to the vaccination calendar. All health workers younger than 40 years working at healthcare centres in the outbreak area who had no history of measles or documented evidence of vaccination were vaccinated.

Discussion

There is an ongoing measles outbreak in Granada that began in a small community in the Albaycin neighbourhood who were not vaccinated due to ideological objections. The outbreak then spread to other unvaccinated people in the neighbourhood, mainly unvaccinated children under the age of 16 months. Outside this neighbourhood, secondary cases have to date only been detected in family contacts of the first cases (four cases) or people who had contact with the first cases in hospital (four cases). In 2010, similar outbreaks have been described in other European countries [6].

In the school with the highest number of cases (primary school A) and a low MMR vaccination coverage (about 60%), the response to vaccination proposals was low at the beginning of the outbreak. We are currently working with parents of unvaccinated children in order to increase the response to vaccination, since many of these parents have no firm position against vaccination and there is a possible change of attitude. With these interventions vaccination coverage with one dose in this school has been increased to 95%.

It is important to emphasise the hospital transmission in four cases admitted to the same hospital at the beginning of the outbreak, although there has not been any case among healthcare workers so far. To avoid transmission in waiting rooms, emergency services and inpatients in health centres of Granada, training sessions for the staff were organised reinforcing the preventive aspects.

As of 7 December 2010, a total of 59 confirmed cases of measles have been reported from Granada. Most of the cases were very small children or schoolchildren under the age of 15 years (n=46). Few cases in young adults have been detected, in contrast to measles outbreaks in Algeciras (2008) [4] and Almeria (2003) (unpublished data). However, although coverage with MMR vaccine in Andalusia overall is appropriate to interrupt transmission of the disease in the population (above 95%), a seroprevalence survey done in Spain and Andalusia in 1996 in the population between two and 40 years of age shows that there are more than 5% of susceptibles in the age cohorts born between 1997 and 1986 (currently between 24 and 33 years of age) [7]. Catch-up vaccination of these age groups has not been considered until now, so it is possible that the number of cases in this age group will further increase.

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Letter to the editor. Spotlight on measles 2010: Measles in healthcare workers – vaccination should be revisited

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To the editor: In the light of the current outbreak of measles in France reported by Parent du Chatelet *et al.* [1], we would like to report a case of hospital-acquired measles in a nurse who had not received the measles-mumps-rubella (MMR) vaccine. Working in our department of infectious diseases, she was infected in spite of barrier measures.

On 8 August 2010 a woman in her 20s was admitted to our department with a maculopapular rash associated with high-grade fever and cough. The cause was rapidly laboratory-confirmed as measles. From the moment of her admission in our ward to her discharge on 13 August she was confined to a single room and respiratory isolation measures were in place. As of 9 August, a nurse in her 20s took care of the patient using protective personal equipment including an FFP2 facial mask and alcohol-based hand rub.

Thirteen days after the first contact with the patient, the nurse presented with fever and four days later developed a maculopapular rash. She was laboratory-confirmed with measles which was complicated by keratitis. Following a 15-day sick leave the nurse recovered. She had had no contact with a case of measles in the community. A survey of other members of staff and patients in contact with the nurse was carried out. No other secondary cases of measles were described. One medical student without immunity to measles was vaccinated. It was not possible to establish a molecular link between the viruses in our two cases as all the measles virus genotypes circulating during the current local outbreak were identical.

The case reported here is noteworthy because an unvaccinated nurse trained in infectious diseases contracted measles in spite of efficient use of respiratory protective measures and alcohol-based hand rub. A recrudescence of measles is currently occurring in France, especially among children and young adults, due to insufficient vaccine coverage in these population groups [1]. Consequently young healthcare workers (HCW) are at risk of occupational measles if they are not immunised. In the literature, nosocomial transmission of measles from HCW to patients and from patients to unimmunised HCW has been reported

[2,3]. Indeed measles is a highly contagious disease with a basic reproduction number ranging from 7.7 to 15 [4], as the transmission airborne droplets leads to a high risk of infection for unvaccinated or not naturally immunised individuals even if isolation measures are correctly applied. Vaccination is the only reliable protection against nosocomial spread of measles. Reports of susceptibility to measles showed a high level of immunity, including natural immunity, among HCW in Europe [5]. Therefore, even if the prevalence of non-immune HCW seems to be low, the low uptake of MMR immunisation and the increase in measles outbreaks [1] may increase the risk of nosocomial transmission.

It should be mandatory to identify non-immune HCW and offer them vaccination. Only HCW who are vaccinated or willing to be vaccinated should be recruited to work on medical wards, especially high risk wards such as infectious disease, emergency room, paediatric, maternity and oncology wards. This recommendation should also extend to medical students who are often poorly protected against vaccine-preventable diseases as seen in our case.

If mandatory vaccination is not possible in France as we saw during the 2009 influenza pandemic, a strategy of voluntary vaccination for HCW should be rapidly implemented in hospitals, especially in high risk areas and even on infectious disease wards where isolation barriers are usually used carefully.

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Authors' reply. Spotlight on measles 2010: Measles in healthcare workers – vaccination should be revisited

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To the editor: We thank Botelho-Nevers *et al.* for their interest in our paper [1] and for illustrating the risk for non-immune healthcare workers (HCWs) of contracting the disease in a context of high measles virus circulation in the community [2].

Since the beginning of the outbreak in 2008 and through the national early warning system [3], the French Institute for Public Health Surveillance (InVS) received a total of 42 notifications of nosocomial transmission events (three in 2008, 10 in 2009 and 29 since January 2010). Among the notified events, 30 involved at least one HCW, and 44 of 61 cases (72%) were HCWs. Two of the three nosocomial transmission events in 2008 occurred in spite of a low prevalence of measles susceptibility in HCWs [4-7].

We agree with Botelho-Nevers *et al.* that due to the high contagiousness of measles, its control in healthcare settings can not rely only on barrier measures and that all efforts should be made to ensure that HCW are properly immunised. According to national recommendations, HCWs born in 1980 or later are targeted by the general catch-up immunisation strategy which consists in a single dose of measles-containing vaccine for all adults, HCW or not [8].

A control of measles serology among HCWs (in position as well as students or applicants) born before 1980 without a reliable history of measles or vaccination is recommended and vaccination should be proposed in case of a negative result. Mandatory measles serology for hospital staff would certainly increase the knowledge of HCWs of their immune status for measles. However recruiting only immunised HCWs for at-risk medical wards would be very difficult to implement in the current context of staff shortage, and quite impossible for medical students.

Our data confirm the insufficient implementation of current recommendations issued by the French health authorities and therefore the difficulty in preventing measles in healthcare settings. However, this difficulty is partly offset by the recommendation, to administrate

immediately after a contact with a confirmed measles case one dose of measles-mumps-rubella (MMR) vaccine to HCWs who were not previously vaccinated with two doses of MMR vaccine or who can not provide a serological proof of immunity.

It would be helpful to identify the reason behind the low compliance of healthcare professionals regarding the knowledge of their serological status and/or the updating of their vaccination status. Ongoing efforts to sensitize HCWs regarding the risk of transmission from pre-symptomatic contagious HCWs measles cases to severe measles at-risk patients (e.g. immunocompromized patients) should be maintained.

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Letter to the editor. Spotlight on measles 2010: Timely administration of the first dose of measles vaccine in the context of an ongoing measles outbreak in France

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To the editor: Parent du Châtelet *et al.* recently described the ongoing measles outbreak in France [1]. We would like to highlight a specific aspect of this outbreak: the significant change in the age distribution of measles cases. In fact, the proportion of cases aged under one year has increased significantly from 2008 to 2010 and this population represents to date the highest incidence rate [1]. Several factors could explain this phenomenon, leading to the question of the necessity of specific control measures in response to the increase of measles cases in the under one year-olds.

During the first year of life, protection against measles is conferred by transferred maternal antibodies. Since the introduction of the measles vaccine, changes in epidemiology have had major effects on the transmission of protective antibodies. The majority of women of childbearing age are now vaccinated and transfer fewer antibodies than naturally immune mothers, conferring protection over a shorter period of time than before to their offspring [2]. A recent French study confirms this fact, showing first that measles antibodies titres were significantly lower in women born after the implementation of the vaccine [2] and secondly that at six months of age, 90% of infants were not protected whatever the mothers' immunisation status (vaccinated or naturally immune) [3]. Several studies confirm this fact, notably Leuridan *et al.* demonstrating a median presence of maternal measles antibodies of 3.78 months for infants of naturally immune mothers and 0.97 for infants of vaccinated mothers [4]. Furthermore, the decrease in antibody levels in women of childbearing age may be amplified by three phenomena: first, childbearing age is increasing, with an increased interval between childhood vaccination in the mother and childbirth, resulting in a diminution in antibody levels; and second, boosting by wild type viruses occurs less often as vaccination coverage increases, and this may contribute further to lowering antibody levels in both vaccinated and naturally immune women. In addition, an increasing number of unprotected mothers is being observed, due to failure in catch-up strategies [3].

The result of this early loss of maternal antibodies is the apparition of a critical window of risk for measles infection during the first year of life, which should give rise to several modifications of the measles vaccination programme. One of the barriers to earlier vaccination is the presumed immaturity of the neonatal immunological system. However several studies demonstrate both humoral and cellular responses at an early age [4]. For example, Gans *et al.* demonstrated priming of infant T-cells with measles antigen as early as six months of age, despite the presence of maternal antibodies [5].

In France, recommendations have been made for vaccination at 12 months of age, and a second dose during the second year of life. Specific recommendations have been made for vaccination at nine months of age for infants in day care centres, with a second dose between 12 to 15 months. In case of contact between infants aged six to eight months and people with measles, vaccination with monovalent vaccine is recommended within 72 hours after contact [3]. Considering that the highest age-specific incidence rate is found in children under one year [1], demonstrating early loss of maternal antibodies, policy makers could consider advancing the measles vaccination programme to, for example, nine months for all infants. In fact, these infants need direct protection until the catch-up vaccination programme can reduce the susceptible population as well as disease transmission.

Early loss of maternal measles antibodies is well documented to date [2-4]. The high number of measles cases in the population under one year of age illustrates this fact. This underscores the importance of timely administration of the first dose of measles vaccine in the context of the ongoing measles outbreak in France and Europe.

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Authors' reply. Spotlight on measles 2010: Timely administration of the first dose of measles vaccine in the context of measles outbreak in France

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To the editor: We thank Gagneur and Pinquier for their interest to the paper [1] and share their concern with respect to the high incidence of measles in children under one year of age, as observed in the ongoing measles epidemics in France.

General immunisation at the age of nine months has been discussed in 2005 when the immunisation schedule has been modified in the context of the implementation of the French National Plan for elimination of measles and congenital rubella [2]. At that time, this was considered not relevant because the majority of childbearing women had acquired immunity through natural infection and would thus transfer to their newborn a high level of antibodies able to inhibit living vaccine measles virus for a long time. We agree with Gagneur and Pinquier that the situation has changed and that at present, the majority of childbearing women, born in 1983 or later, have acquired immunity through vaccination, which results in more rapidly waning antibody levels in the newborns. In theory, administration of measles-mumps-rubella (MMR) vaccine at nine months of age seems now possible.

However, in the opinion of doctors who provide vaccination, repeated modifications of immunisation schedules appear worrisome. Measles vaccine was recommended for children in France in 1983 and changed to one dose of MMR vaccine in 1986. A second dose at the age of 11-13 years was recommended in 1993, then at the age of 3-6 years in 1997. In 2005, the immunisation schedule was again changed with the first dose at one year of age and the second dose during the second year of life. Other modifications in the general immunisation schedule of young children might be considered in the near future. It would probably be more convenient to reconsider the age of first administration of MMR vaccine at that time. Furthermore, our immunisation schedule is somewhat crowded in the first year of life and could become more so if new vaccines (such as meningococcal B vaccines) are introduced.

As stressed by Gagneur and Pinquier, some studies [3] have demonstrated the existence of both a humoral and cellular immune response to measles vaccine when administered early in life, even in the presence of maternal antibodies. "However, since a modification of the summary of product characteristics (SPC) of the M-M-R-VAXPRO vaccine was needed to allow its administration at nine months of age, the immune response according to the age of administration has been studied [4]: after the second dose (administered three months after the first), children who had received the first dose at nine months of age had a seroprotection rate against measles of 94.6%, (95% confidence interval (CI): 92.3–96.4) compared to 98.9% (95% CI: 97.5–99.6) for those vaccinated at 12 months of age. Similarly, geometric mean antibodies titres for measles was significantly lower in children immunised at age nine months. So, the SPC mentions that administration of this vaccine at nine months of age should be reserved to certain circumstances (for example for children admitted to day-care centres, for epidemics and for travel in countries with high incidence of measles) and that an additional dose (i.e. a third dose) of vaccine should be provided to children who received the first dose at nine months of age [4].

In our study 135 (56%) of the notified cases in children aged under one year were under nine months-old. Thus, starting the immunisation at nine months of age would have left the majority of them unprotected.

Finally, we know that the current prolonged outbreak of measles in our country is due to the existence of a large cohort of susceptible children, adolescents and young adults who had neither the vaccination nor the disease. In our opinion, reducing the size of this cohort by catch-up vaccination campaigns in the unvaccinated population (according to the official recommendations) is the best way to interrupt the circulation of measles virus and to protect the infants through herd immunity.

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