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Editorials

European Immunization Week goes viral

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Immunisation is one of the most cost-effective public health interventions, saving between two and three million lives worldwide annually. In addition, an extra two million lives could be saved with the introduction of vaccines such as meningococcal, pneumoccocal and rotavirus vaccines. Each year, 2.5 million children worldwide still die of diseases that can be prevented with vaccination [1].

While many new vaccines will soon be on the market, several challenges still remain concerning the existing vaccines and immunisation policies, even in the World Health Organization (WHO) European Region where vaccination uptake at the national level is generally high, with rates over 90% [2]. However, these figures conceal the fact that many vaccinations are not administered in a timely way – i.e. according to the recommended national vaccination schedules – as well as the disparities in vaccination coverage at subnational levels. Both factors increase the risk of outbreaks of vaccine-preventable diseases, such as measles; and indeed outbreaks of measles have again been occurring in western Europe since 2006 [3]. Regardless of the European country there are pockets of susceptible populations, contributing to an estimated 600,000 children (based on the coverage rates) in the Region, that miss their routine vaccination annually.

These susceptible populations, which include certain ethnic and religious minorities as well as some migrant populations, are not vaccinated because they often lack the knowledge about the importance of immunisation or access to the services. In some extreme cases, the willingness to vaccinate is influenced by an unfounded scepticism among parents [4] about the effectiveness and safety of vaccines, fuelled by anti-vaccination movements with dubious motives.

These issues were recently pointed out in editorials published in Vaccine [5], the Weekly Epidemiological Record [6] and the European Journal of Public Health [7], which addressed the importance and the future of immunisation in Europe, and clearly stated the need to keep timely immunisation high on the agenda and boost routine immunisation programmes.

European Immunization Week

European Immunization Week (EIW) is an annual event, held in April. It provides a framework for politicians and health professionals in the WHO European Region to analyse and address the challenges of immunisation at national and subnational levels. Activities include the promotion of timely vaccination by carrying out a range of targeted advocacy activities as well as concrete outreach activities to reach vulnerable and hard-to-reach groups.

Since its inception in 2005, EIW has grown considerably. In 2008, 32 countries participated in the initiative, covering three quarters of the Region's population. They organised a wide range of immunisation-related activities involving parents, children, healthcare workers, policy-makers, politicians and the media. Fourteen countries reported targeting vulnerable and hard-to-reach groups, varying from minority populations, such as the Roma and migrants – including foreign workers and political refugees – to abandoned children, religious objectors, prisoners, the military, hepatitis B risk groups and geographically hard-to-reach groups.

Several countries organised outreach activities to assess people's vaccination status and inform them about the importance of timely vaccination and where these could be obtained. Supplementary immunisation activities resulted in almost two million persons being immunised during EIW.

As the initiative was born from a resolution adopted in 2005 by all the European Region's Member States to work towards the elimination of measles and rubella in the Region by 2010, many countries placed extra emphasis on measles vaccination, for example by organising consultations for policy-makers to address remaining challenges to measles elimination, trainings for healthcare workers to properly register administered vaccinations, as well as by addressing young adults directly and raising their awareness about the importance of knowing their immunisation status and following up on doses needed beyond childhood [8].

EIW 2009

For its fourth EIW, 20-26 April, the World Health Organization is leveraging innovative Internet-based viral techniques and social media to advocate for immunisation across Europe. The initiative, launched in 36 countries, is spearheaded by an animated YouTube video that aims to spread the EIW message by word-of-mouth (virally) online as well as drive users to an informative website (www.euro.who.int/eiw2009). Social networking sites Facebook, VKontakte and StudiVZ are being used to reinforce the message.

Starting on 22 April, millions of individuals were contacted electronically and encouraged to view a short video prepared by the WHO Regional Office for Europe. The potential perils facing young children are presented in a film available on 16 video-sharing websites and more than 120 social communication sites, blogs and discussion forums. The campaign website (www.euro.who.int/eiw2009) contains sections on reasons to vaccinate, myths about vaccination, questions and answers and links to recent reports on outbreaks of vaccine-preventable diseases in the European Region.

This week's edition of Eurosurveillance joins these efforts with a selection of articles on immunisation issues, which reminds us of the urgency of advocating for vaccination in Europe. For instance, D Schmid et al. [9] describe an ongoing outbreak of rubella in two provinces in Austria. One hundred and forty three cases have occurred since October 2008, 20 of them in soldiers in different military camps. The authors question whether the 2010 target for measles and rubella elimination in the entire European Region is realistic. In another article, D Whyte et al. [10] discuss the epidemiology of mumps in Ireland, noting a high proportion of cases in the age group 15-24 years in the Mid-West of Ireland. The authors therefore stress the importance to increase awareness of the disease in the school, college and university settings. Preventive measures implemented to limit mumps transmission in these settings over recent years in the Mid-West of Ireland include vaccination of close contacts, isolation for five days and hand hygiene.

Next, C Fazio et al. [11] report the results of molecular analyses of Neisseria meningitidis serogroup C strains obtained from two outbreaks of invasive meningococcal disease in northern Italy. The paper highlights the importance of molecular typing in identifying new variants and detecting hyper-virulent clones, which are crucial in monitoring and preventing the disease. The last paper in this issue describes the European Union-funded "Vaccine safety: attitudes, training and communication" (VACSATC) project [12], established in 2006 to study perceptions of immunisation and vaccine safety, to improve training of healthcare professionals on vaccine safety and to improve the availability of information on vaccine safety on the Internet that adheres to good information practices.

Beyond 2009

Given that at least 26 outbreaks of vaccine-preventable infections in the European Region have been described in the literature since early 2008 [13] (and there were likely many more not written up), there is good reason for all countries in the Region to be vigilant. It is also interesting to note that in 2005–2006, measles epidemics in six former Soviet Union countries accounted for over 75% of cases reported in the Region. This reversed in 2007–2008, when seven western European countries accounted for over 75% of the reported cases.

Hopefully, more parts of the world will join the efforts of Europe, as well as the Vaccine Week in the Americas, in marking European Immunization Week as an extra push to boost routine immunisation programmes. The vaccination of children and risk groups remains a year-round activity and should therefore be kept high on the national health policy agenda all year long.

Aknowledgements

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Outbreak of Clostridium difficile 027 in North Zealand, Denmark, 2008-2009

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We report an outbreak of *Clostridium difficile* PCR ribotype 027 in Denmark. The outbreak includes to date 73 cases from the area north of Copenhagen, but there may be related cases elsewhere in Zealand. Most infections are healthcare-associated and in patients who previously received antibiotic treatment. The strain is resistant to moxifloxacin, erythromycin, and clindamycin, and carries genes for toxin A, toxin B, and for the binary toxin. The antimicrobial pattern differs from that of the strain involved in a small cluster in Denmark in 2006-2007. Because of this outbreak, hygienic measures in the involved hospitals have been reinforced. Nationwide, microbiological laboratories were alerted to the outbreak and encouraged to send isolates for toxin profiling and PCR ribotyping.

Introduction

Clostridium difficile infection is the leading cause of nosocomial diarrhoea in industrialised countries. A specific subtype, *C. difficile* PCR ribotype 027 has been associated with more severe disease and caused outbreaks in North America and Europe [1-3]. The increased virulence is assumed to be associated with higher amounts of toxin production [2-4].

A cluster of 13 cases of *C. difficile* 027 occurring in southern Denmark between November 2006 and July 2007 was identified as part of a retrospective survey in 2007. The outbreak strain carried the binary toxin genes and was resistant to fluoroquinolones, and susceptible to erythromycin and clindamycin [5]. Since then, Danish departments of clinical microbiology were asked to report *C. difficile* findings and to forward selected isolates for toxin profiling and PCR ribotyping to the National Reference Laboratory at Statens Serum Institut, in particular whenever a severe disease or an outbreak was suspected.

A possible outbreak of infections caused by a strain of *C. difficile* resistant to moxifloxacin, erythromycin, and clindamycin, as determined by the Oxoid disk diffusion method, was recognised in January 2009 by the Department of Clinical Microbiology in Hillerød Hospital. This strain was confirmed by Statens Serum Institut as PCR ribotype 027. The Department of Clinical Microbiology undertakes diagnostics for the North Zealand area (i.e. north of Copenhagen), including four hospitals and one rehabilitation clinic. We conducted an investigation to assess whether there was an outbreak and to determine if the infections were healthcare-associated.

Methods

We used descriptive epidemiology to characterise the outbreak. Data on cultures and antibiotic resistance profile were collected at the Department of Clinical Microbiology, while toxin profiles and PCR ribotyping were obtained from the Statens Serum Institut. Additional information on symptoms, antibiotic treatment, and dates of hospital stay was collected from the electronic health records for the 60 days preceding the isolation of *C. difficile.*

For the purpose of the investigation, the following operational case definitions were adopted:

- A possible case was defined as a patient with a positive culture of *C. difficile* resistant to moxifloxacin, erythromycin, clindamycin;
- A probable case was defined as a patient with positive *C. difficile* culture and the presence of genes for toxin A, toxin B, and binary toxin;
- A confirmed case was defined by positive culture of *C. difficile* PCR ribotype 027;
- A relapse was defined as the occurrence of a second episode of *C. difficile* isolation (possible, probable, or confirmed as above) within 60 days from the first episode.

We considered the date of diagnosis as the date on the request form of the first positive stool sample in the Department of Clinical Microbiology. All stool samples from hospitalised patients were routinely tested for *C. difficile*. Toxin testing was performed on all cultures of *C. difficile* and on faeces in clinically obvious cases.

C. difficile isolates were characterised by toxin analysis (determining the genes for toxin A, toxin B and the binary toxin) and PCR ribotyping. On 48 isolates we also performed DNA sequencing searching for unique mutations in the regulating toxin gene tcdC (18 bp deletion and 1 bp deletion at position 117 of tcdC).

Current situation

From week 29, 2008 to week 15, 2009, a total of 73 cases (11 possible, eight probable and 54 confirmed cases) were recorded. As of week 15, 2009, all but one possible case have been confirmed

as 027. All 48 isolates DNA sequenced carried the mutations in the regulating toxin gene tcdC (the 18 bp deletion and the 1 bp deletion at position 117 of tcdC).

Three of the four North Zealand hospitals mentioned above and the rehabilitation clinic were involved.

We undertook a descriptive study of the first 59 consecutive cases since July 2008. A total of 32 of 59 cases were female and the median age was 81 years (interquartile range 73-87 years). A total of 53 of 59 cases were diagnosed among hospitalised patients; the mean time from admission to diagnosis was 9.5 days (range 0-72 days). Two other cases were sampled while in the emergency room; both had been previously hospitalised. The other four cases were diagnosed during an outpatient visit, or in a general practice. However, they had all had contact with a hospital in the 60 days prior to the diagnosis.

Forty-two of 59 cases were diagnosed more than two days after admission and therefore fulfil the criteria of healthcare-associated cases [4].

Up to week 10, 2009, we recorded 13 deaths occurring after the *C. difficile* diagnosis. Medical history was reviewed by two physicians and in eight cases, six of which had underlying conditions, *C. difficile* might have been a contributory cause of death.

Up to week 10, 2009, nine relapses were observed within 60 days after the first diagnosis. The median time between two infections was 31 days (range 23-50 days). Overall 68 episodes occurred (59 first infections and nine relapses). Diarrhoea with no systemic symptoms was reported in the medical records in 36 of them. Pseudomembranous colitis was reported in 20 episodes, toxic megacolon in two, and clinical sepsis in eight. In two of 68 episodes, symptoms were not described.

According to their hospital medical records, 55 of 59 cases had received antibiotics in the 60 days prior to the diagnosis, and 49 of the 59 cases had received two or more antibiotics. The most commonly used antibiotics were: cephalosporins in 41, penicillins in 27, fluoroquinolones, mainly ciprofloxacin, in 25, and metronidazole in 20 of 59 cases.

To date (mid April), *C. difficile* 027 has been identified in other hospitals in Zealand, especially in other parts of the Copenhagen region. More specifically, from week 42, 2008 to week 15, 2009, a total of 243 isolates, including those from our investigation, were PCR ribotyped as 027 (128 in 2008 and 115 in 2009) by the National Reference Laboratory at Statens Serum Institut. Besides a possible presence of the strain in the community, the common practice of transferring patients between hospitals of the region might have contributed to the spreading.

Control measures

During the outbreak, hospitals' control measures were reinforced by extensive communication of the outbreak to the hospitals and by implementing the evidence-based strategy for *C. difficile* outbreaks [6], emphasising the need for good hand hygiene, isolation of patients, revision of environmental cleaning procedures, and collecting and storing faecal samples from cases for typing and possibly other analyses.

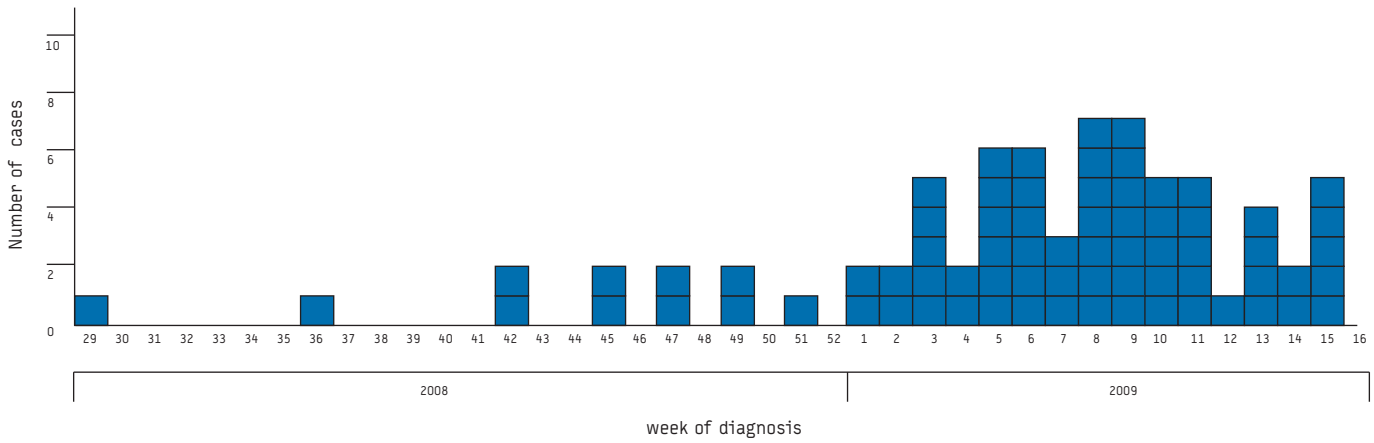
Because of the outbreak, the Danish National Board of Health decided to intensify the monitoring of *C. difficile* 027. All clinical microbiology departments, infection control organisations, and clinical departments in the country were advised to pay increased attention to possible cases of nosocomial diarrhoea, especially after antibiotic treatment. The National Board of Health also stressed that clinical microbiology departments are required to submit moxifloxacin-resistant isolates, isolates from cases with severe manifestations, and isolates collected during suspected outbreaks.

Discussion

We present preliminary data of the largest outbreak of *C. difficile* 027 recognised in Denmark. Most infections were healthcare associated, and almost all patients were treated with antibiotics

Figure

Distribution of confirmed (n=54), probable (n=8) and possible (n=11) *C. difficile* 027 cases, Denmark, week 29, 2008–week 16, 2009 (n=73)



Results are preliminary since PCR ribotyping of the isolates from the 19 probable/possible cases is pending.

in the two months prior to the *C. difficile* 027 isolation, foremost with penicillins, cephalosporins and fluroquinolones. The present outbreak may be a part of the cases that have been observed in the Copenhagen region in an overlapping time period, and may represent an emergence of CDAD 027 in the capital region of Denmark. Based on resistance profile, this strain is different from the one described in Jutland in 2006-2007. This indicates the possibility of existence of more than one clone of *C. difficile* 027, with epidemic potential in Denmark. MLVA typing will help in disentangling these relations [7].

The outbreak has prompted increased attention to hospital hygiene, a coordinated response from regional and national authorities concerning surveillance and control, and regular communications between different microbiological laboratories in Zealand.

The number of cases in the last five weeks has levelled out as compared to previous weeks, which may indicate that the measures have taken effect. However, further monitoring is needed, as is continued vigilance regarding hygienic measures.

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Ongoing rubella outbreak in Austria, 2008-2009

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Since October 2008, a total of 143 cases of rubella have affected the two Austrian provinces Styria and Burgenland. The index case occurred in mid-October 2008, but was not notified to the public health authorities until February 2009, when the Austrian Agency for Health and Food Safety was asked to investigate a cluster of 32 rubella cases (24 laboratory-confirmed and eight clinically suspected cases). No case of rubella had been reported in the two affected provinces between February 2007 - when statutory notification for rubella was implemented - and mid-October 2008. 113 of the 143 cases (79%) were confirmed: 101 (89.3% of the 113 cases) clinical-laboratory confirmed and 12 clinical-epidemiological confirmed. Thirty cases fulfilled the criteria of a probable outbreak case only (laboratory results or data on epidemiological link are pending). For 140 outbreak cases data on age was known; the median age was 19 years (range: 2-60 years). 20 cases occurred in soldiers in seven military camps in the area. 55 cases (38.5 %) were female. One case of a laboratory-confirmed rubella infection, affecting an unvaccinated pregnant 18-years old native Austrian in the early first trimenon of pregnancy, led to voluntary abortion.

Background

In Austria, rubella has been a notifiable disease since 2007. From February 2007 to the end of September 2008 a total of 13 cases of rubella were reported to the public health authority (seven in 2007 and six in 2008 including September). In the pre-vaccination aera, rubella was endemic in Austria, with large epidemics occurring every few years. Rubella vaccination was introduced in 1984 with a monocomponent vaccine targeting 11-13 year-old girls and seronegative mothers after delivery. Rubeaten® (Berna Biotech Ltd.) or Ervevax® (GlaxoSmithKline) were used until 1994. A two-dose measles, mumps and rubella (MMR) vaccination programme was launched nationwide in 1994; the two doses were given at the ages of 14-18 months and six years. The vaccine used throughout the programme was MMRII® (Merck). From 2001 until the end of 2008 the vaccine Priorix® (GlaxoSmithKline) was used; as of 2003, the vaccination scheme was changed and the second dose was given already four weeks after the first dose. Since 2009, the vaccine MMR VaxPro® (Sanofi Pasteure MSD) has been in use. The available nationwide data on the proportion of rubella susceptibles in the Austrian population by age-group and sex are limited.

Rubella is a viral disease that usually presents as a mild febrile rash illness with adenopathia in adults and children; 20%-50% of infected persons are asymptomatic. The infection is acquired through direct contact with nasopharyngeal secretions containing the virus or through droplet spread of nasopharyngeal secretions. Laboratory diagnosis of rubella is required, since clinical diagnosis is often inaccurate. According to the case definitions proposed by the European Commission [1],

laboratory confirmation should be based on the detection of a significant rise in rubella immunoglobulin G (IgG) antibody titres in the serum between acute and convalescent phase or on the isolation of rubella virus from nasal, blood, throat, urine, or cerebrospinal fluid specimens, on the detection of rubella virus nucleic acid by reverse transcription PCR (RT-PCR) in one of these clinical specimens, or – in an outbreak situation – on the detection of rubella-specific immunoglobulin M (IgM) antibody in serum or saliva [1]. An epidemiologically confirmed rubella case is defined as a patient with a febrile generalised rash illness of acute onset and an epidemiological link to a laboratory-confirmed case [1].

Rubella is of high public health importance owing to teratogenic effects that can result from congenital rubella infection (CRI) during the first trimester of pregnancy, leading to miscarriage, stillbirth, or infants with a pattern of birth defects, known as congenital rubella syndrome (CRS). CRS occurs in up to 90% of infants born to women who are infected with rubella during the first 10 weeks of pregnancy [2,3].

Outbreak description

On February 10, 2009 the Austrian Agency for Health and Food Safety (AGES) was informed about a cluster of 24 laboratory-confirmed cases of rubella infection and another eight clinical suspected cases by the provincial public health authority Styria. The 32 cases were notified between calendar week 3 and calendar week 7 from nine of the 17 public health districts in the Austrian province Styria (total population: approximately 1,208,000). Half of the 32 notified cases were soldiers who were currently doing their mandatory military service (six months duty). Seven military camps were affected in Styria and one in the province Burgenland (total population: approximately 283,000). All soldiers with rubella were hospitalised in a military hospital.

The index case - not related to the military camps – had already occurred in mid-October 2008; the case was not notified to the public health authorities until February 2009. Of the 32 cases, 29 cases resided in nine of the 17 public health districts in Styria and three cases in three of the nine public health districts in the Burgenland.

No case of rubella had been reported in the provinces Styria and Burgenland (combined population: 1.5 million) between February 2007 - when statutory notification for rubella was implemented - and mid-October 2008.

The following is a preliminary report of the ongoing outbreak of rubella in Austria. Aim of our ongoing outbreak investigation is to ascertain the vaccination coverage among the outbreak cases, the number of congenital rubella infections and to identify possible target groups for additional vaccination campaigns.

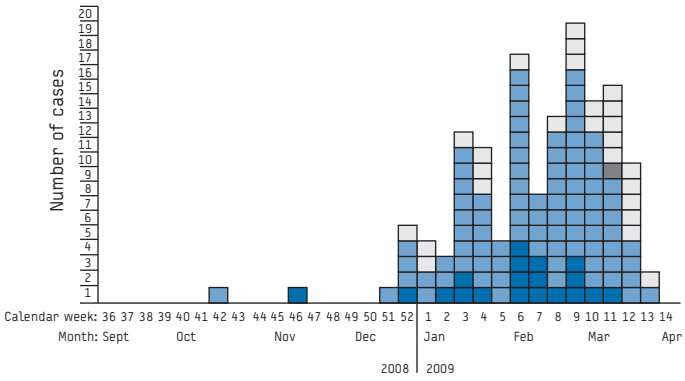
Methods

The outbreak was described by time, place and person. A confirmed outbreak case was defined (1) as a patient with a febrile generalised rash illness of acute onset, (2) who fulfilled one of the criteria of a laboratory-confirmed rubella infection or who was epidemiologically linked to a patient with laboratory-confirmed rubella infection, and (3) who fell sick after 15 October in the Austrian provinces Styria or Burgenland.

A probable outbreak case was defined (1) as a patient with a febrile generalised rash illness of acute onset and in whom a healthcare worker suspected rubella, and (2) who fell sick after 15 October in the provinces Styria or Burgenland.

Figure 1

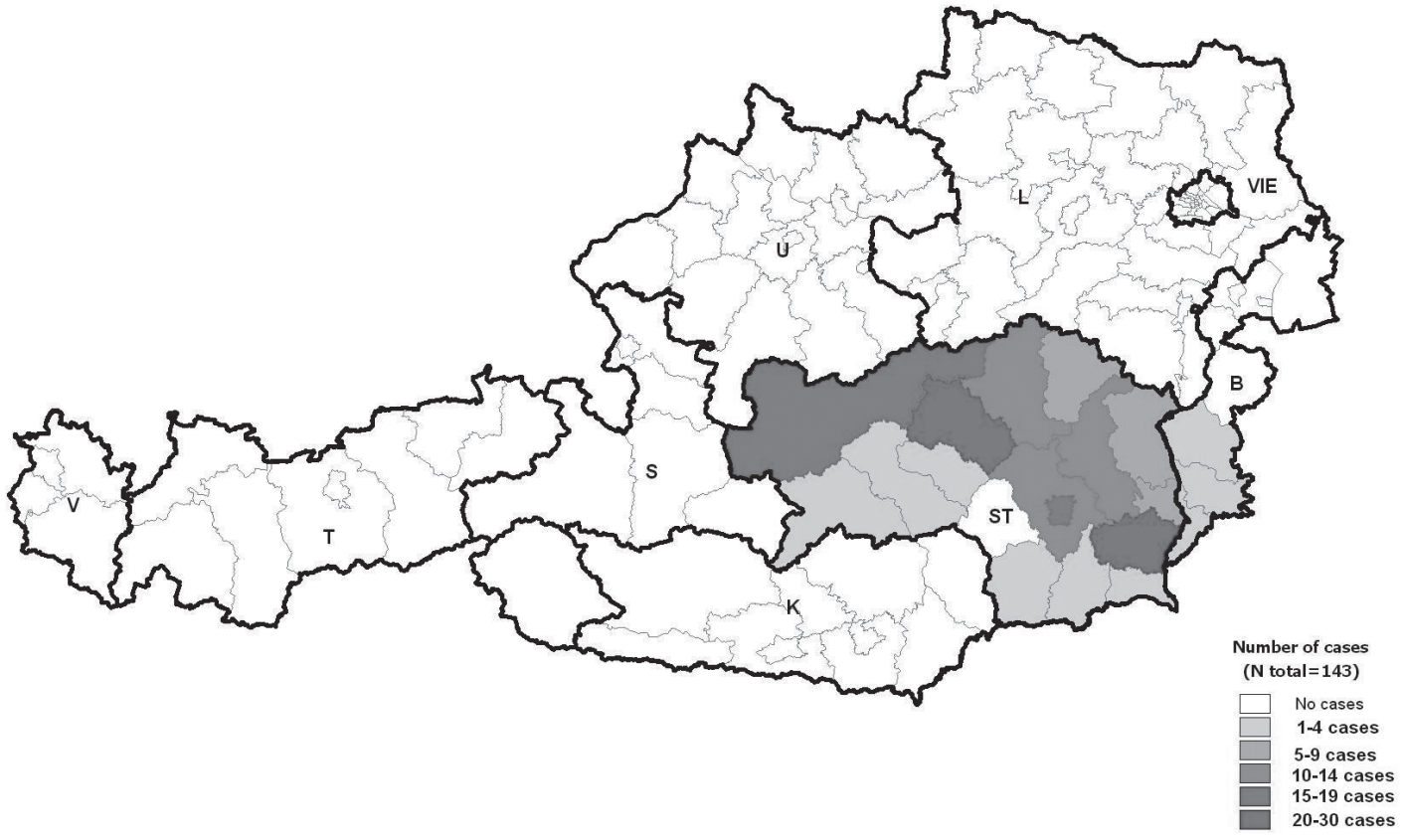
Rubella cases (including 20 army cases) by date of rash onset, Austria, October 2008-March 2009 (n=132, in which the date of rash onset was known)



Data as of 3 April 2009.
Grey squares: probable outbreak cases (n=27), including one soldier case (dark grey square); blue squares: confirmed outbreak cases (n=105), including 19 cases in soldiers (dark blue squares).

Figure 2

Rubella outbreak cases by public health district of residence in the affected provinces Styria and Burgenland, Austria, October 2008-March 2009 (n=143)



A suspected rubella case was defined as a patient who presented with fever and a maculopapular rash among the contact persons of outbreak cases, and was reported by the outbreak cases.

Case finding occurred as follows: Cases of rubella infection laboratory-confirmed by the Austrian reference laboratory and cases of rubella notified to the public health authority were reported to AGES. Rubella outbreak cases were asked to name further individuals with febrile generalised rash illness of acute onset among their contacts. Information on demographics, date of rash onset, and contact with laboratory-confirmed cases were obtained by telephone interviews conducted with 143 cases; for 57 of these cases the vaccination status could be ascertained based on their vaccination documents. For active case finding, local physicians were asked to collect blood samples from all incident patients with a generalised rash for serological examination.

Results

Between October 2008 and March 2009, a total of 143 cases fulfilled the outbreak case definition. Of these, 113 cases (79%) were confirmed outbreak cases of rubella: 101 (89.3% of the 113 cases) were confirmed clinically and by laboratory result, and 12 were confirmed clinically and epidemiologically. Thirty cases fulfilled only the criteria of a probable outbreak case; the procedure of laboratory or epidemiological confirmation is still ongoing for these cases. For 132 outbreak cases, the date of rash onset was known (illustrated in Figure 1).

Figure 2 shows the regional distribution by public health district of the cases' residence; 140 cases had their residence in Styria (affecting 16 of 17 public health districts) and three outbreak cases were resident in Burgenland (affecting three of the nine public health districts).

A further 21 suspected rubella cases (not included in Figure 1 and 2) were named by confirmed outbreak cases.

One case of laboratory-confirmed rubella infection occurred in an unvaccinated 18 year-old pregnant native Austrian. As the infection occurred in the early first trimenon of pregnancy, a voluntary abortion was performed. Already one year earlier, this woman had been identified as susceptible to rubella infection after delivery of her first child.

Of the 143 outbreak cases, 55 (38.5 %) were female. For 140 outbreak cases, data on age were known. The median age was 19 years (range: 2-60 years). A total of 136 cases (97% of 140 cases) were older than 15 years. The age group of 15-24 year-olds was most affected (88.6%; 124 of 140). Among the female cases, the age-group 15-19 years (67%; 35 of 52) was affected most, followed by the age-group 20-24 years (23%; 12 of 52). No female cases occurred in the age-group 25-39 years; two female cases occurred in the age-group 40-49 years (Figure 3).

To date, the vaccination status is known for 57 outbreak cases. Twelve cases (22%), including eight female cases, were vaccinated with one dose of rubella vaccine; none of them had received two doses. The remaining 45 outbreak cases were unvaccinated.

In the two most affected age groups, the 15-19 year-olds (n=32 in which vaccination status was known) and the 20-24 year-olds (n=24 in which vaccination status was known), the distribution of vaccination status by sex was as follows: in the age group 15-19 years, 11 of the 17 (65%) female cases were unvaccinated, while all 15 male cases were unvaccinated; in the age group 20-24 years, two of the four female cases and 14 of the 18 male cases were unvaccinated.

Outbreak control measures

MMR vaccination was immediately offered to any unvaccinated persons by public health officers and general practitioners in Styria. Although the rubella vaccine was offered at no cost, only 180 doses of MMR vaccine were administered as part of the outbreak control measures in February and March 2009.

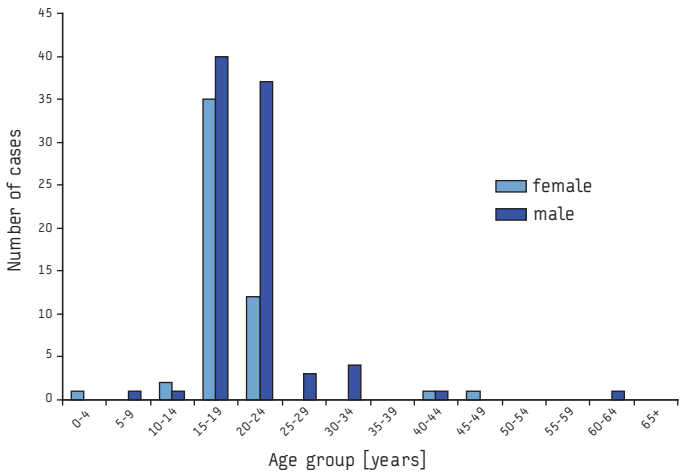
Discussion

Before the introduction of routine rubella vaccination, rubella outbreaks were common [4]. Recent outbreaks in Europe identified susceptible groups [5], e.g. in 2003 in immigrants from Latin America to Spain [6,7] and in 2005 in a religious community in the Netherlands [8]. Rubella, together with measles, is targeted for elimination in the WHO European region, with the objective for 2010 to eliminate endemic measles, endemic rubella, and to prevent congenital rubella infection (<1 case of CRS per 100,000 live births) [9]. Introduction of rubella vaccination programme has led to decreased circulation of the virus resulting in a reduced probability of wild virus exposure. If then vaccine coverage falls below a threshold of approximately 80%, there is an increase in CRS, due to accumulation of susceptibles among unvaccinated adult females [10]. According to the strategic plan for eliminating measles and rubella, and for preventing congenital rubella infection in the WHO European Region a total of 95% of the Member States should have administered, by January 2009, at least one dose of rubella vaccine to ≥95% of all children at the national level or to ≥90% of children in all first administrative levels [9]. In Austria there are no nationwide reliable data available on MMR vaccine coverage for individuals born before 1997. The official estimate of MMR vaccine coverage with at least one dose of the birth cohorts 1997 to 2007 was 84%.

Among the currently known outbreak cases, 90% of the female cases were 15-24 years-old. The index case, who occurred in mid-October 2008, was a teenage girl. No data on the contact pattern

Figure 3

Rubella outbreak cases by age-group and sex, Austria, October 2008-March 2009 (n=140, in which the date of birth was known)



during her infectious period are available to date. The second case occurred in mid-November 2008 and was the first case among soldiers. The other 19 outbreak cases in soldiers occurred between calendar week 52, 2008 and calendar week 11, 2009. To our knowledge the affected military camps implemented - except for isolation of the rubella patients in the military hospital - no other activities to control the outbreak.

Postnatal rubella is a mild infection and many cases are subclinical. Therefore, there may be substantial underreporting of cases among the general population. The clustering of cases among soldiers in this outbreak is more likely to be due to increased awareness and more reliable reporting to the public authorities in this population group.

In Austria, soldiers doing their mandatory military service are usually allowed to stay with their families during weekends, and in the second half of their six months duties may even sleep outside the barracks during the week. Three non-army outbreak cases had an epidemiological link to army cases.

In the setting of an outbreak, supplementary immunisation activities undertaken with the aim of interrupting transmission of rubella virus are the most effective preventive measure [11]. Obviously, the additional vaccination activities implemented by the local Austrian public health authorities have not been able to interrupt the rubella spread in the general population so far.

The documented voluntary abortion because of CRS risk affected a native Austrian who had been not vaccinated in childbed after her first delivery a year earlier although she had been identified as non-immune to rubella infection. This is a salutary reminder that vaccine programmes require a suitable public health infrastructure if unintended adverse consequences are to be avoided. However, national immunisation programmes are increasingly threatened by a combination of public and political complacency regarding the value of immunisation, and by the disturbing rise in the influence of anti-vaccination groups and their dangerously misleading advocacy campaigns.

An outbreak of mumps among adolescents and young adults in 2006 and an outbreak of measles affecting primarily the age-group ≥10 years in 2008, demonstrated already that additional MMR vaccination campaigns targeting the age group of ≥10 year-olds are highly required in order to prevent outbreaks of mumps, measles and rubella in Austria in the future [12,13]. Whether the statement *'The WHO European Region is well on its way to achieving targets for measles and rubella prevention and strengthening the control of vaccine preventable diseases in childhood'* as published in *Eurosurveillance* in June 2003 [14] still holds true in April 2009, might be a matter of controversy.

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Mumps epidemiology in the Mid-West of Ireland 2004-2008: increasing disease burden in the university/college setting

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Mumps is a contagious vaccine-preventable viral disease that is experiencing a revival in students attending second and third level colleges. Large mumps outbreaks have been reported in several countries despite the presence of childhood immunisation programmes over many years, including measles, mumps, and rubella (MMR) vaccination. In 2008, 1,377 cases of mumps were notified in Ireland and 1,734 in the first three months of 2009 (provisional data). This paper reviews the recent epidemiology of mumps in the Mid-West region of Ireland and highlights preventive measures. A substantial proportion of cases were not laboratory-confirmed and it is important that doctors continue to notify suspected cases. In the Irish Mid-West, data from enhanced surveillance show a high proportion of mumps in the age group 15-24 years. Complications were uncommon and rarely severe. Where data were available, over half of the cases did not recall having received two doses of MMR, but most recalled one dose. Parents should continue to ensure children receive both MMR vaccinations so that uptake is optimal for protection. Steps were taken to increase awareness of the disease in the school, college and university settings. Preventive measures implemented to limit mumps transmission in the school/college setting over recent years included vaccination of close contacts, isolation for five days and hand hygiene.

Introduction

Mumps (or infectious parotitis) is an acute infection caused by an RNA virus of the family *Paramyxoviridae*. It is spread directly from infected person to susceptible person by sneezing, droplets and close contact. Mumps can present with mild influenza-like symptoms which may include fever, headache and painful swollen salivary (usually parotid) glands [1]. Complications are usually infrequent but infection can progress to meningitis, deafness as well as orchitis, oophoritis or pancreatitis (inflammation of the testicles, ovaries or pancreas). Mumps infection during pregnancy is not associated with congenital malformations [2]. The incubation period is 16-18 days (range: 14-25 days), and recent data suggest an infected person is contagious during the period from two days before to five days after onset of symptoms [3].

Mumps is a vaccine-preventable disease. The measles, mumps and rubella (MMR) vaccine offers safe and effective protection against these diseases and is provided free of charge to children at the age of 12-15 months (MMR1) as part of the Irish Primary Childhood Immunisation Programme (PCIP) [4]. Prior to 1996, there was no structured PCIP, only recommendations on immunisation. Electronic records of childhood vaccinations in Ireland for national and regional uptake monitoring are only available from 1996. Documentation of MMR status in people born prior to 1996 relies on manual records. Immunisation programmes rely on achieving over 95% uptake of MMR vaccine to protect the population from disease – especially the most susceptible, children under two years of age. Vaccine uptake in some areas of Ireland has only lately recovered to levels of over 90% after public confidence in combination vaccines was eroded by published research about possible side effects that has since been rejected [5]. Uptake levels in Ireland for MMR1 at the age of 24 months averaged below 80% until 2004 but reached 89% in 2008 (90% in the Mid-West) [6].

In 1989, about 700 mumps cases were notified in Ireland, but this number declined to between 30 and 40 cases annually after MMR1 was introduced in 1988. MMR2 (second dose of vaccination) was introduced in 1992 for 11-12 year-olds. Case numbers rose again in 1996-1997 (300-400) but subsequently fell back to 30-40 annual cases until the year 2002. In line with a recommendation from 1999, the age for MMR2 was brought forward to the age of 4-5 years in 2001. In 2008, 1,377 cases were reported in Ireland, half of whom were laboratory-confirmed. In the context of even higher infection levels observed in Ireland since the beginning of 2009, (a greater than ten-fold increase on 2008), it is timely to review the epidemiology of mumps infection in the Irish Mid-West over the preceding five year period to help explain the factors which may have been of influence.

In recent years a large number of cases of mumps have been reported in young adults, arising from transmission of the virus in so-called 'third level colleges' (colleges/universities attended by students aged 18 years and over), but also in some secondary schools (with 12-18 year-old students). Mumps outbreaks in third level colleges have been reported in Ireland since 2004 [7] and in several other countries [8-11]. This paper reviews the epidemiology of mumps infection in the Mid-West of Ireland from 2004 to 2008 and describes the source, demography of cases, risk factors and the spectrum of illness and examines the role of preventive measures.

Geographically, the Mid-West of Ireland includes the administrative counties of Clare, Limerick and North Tipperary with a population of 361,028 people. There are three large university/college institutes in Limerick city and smaller third level colleges in Tipperary including the national Garda (Police) Training College.

Methods

Suspected or confirmed mumps cases have been subject to mandatory notification in Ireland since 1988 (and outbreaks since 2004) and must be reported to the Medical Officer of Health (MOH) in the Mid-West by medical doctors and laboratories [12]. Notifiers should have regard to Irish case definitions for mumps [13], which is based on the case definition of the European Union, but it adds the classification 'possible case' for clinical cases that are not laboratory-confirmed or are epidemiologically linked to a confirmed case. Where possible, enhanced surveillance data (on complications, symptoms, travel, etc.) were collected by medical officers in the regional public health department. Data on MMR vaccination history were based largely on family or doctor recall rather than on records. A copy of the national enhanced surveillance form for mumps is available online (http://www.ndsc.ie/hpsc/A-Z/VaccinePreventable/Mumps/SurveillanceForms/) from the Health Protection Surveillance Centre in Dublin. This core dataset is larger and more disease-specific than the minimal dataset required under legislation for the generic list of notifiable diseases.

Data on clinical notifications from general practitioners and hospital doctors were collated by the Department of Public Health where notifications to the MOH are recorded. Laboratory data notified from the Department of Serology, Mid-Western Regional Hospital, Limerick and the National Virus Reference Laboratory (UCD) were collated. Laboratory notified cases were confirmed by the detection of mumps specific IgM immunoglobulin in serum or oral fluid specimens. The test is an IgM class capture enzyme immunoassay (MACEIA, Microimmune Ltd., United Kingdom). The reported sensitivity and specificity of the assay for serum samples is 94.7% and 95.9%, respectively, when compared to IgM antibody capture radioimmunoassay (MACRIA). For oral fluid samples, the sensitivity and specificity compared to MACRIA is 92.6% and 100%, respectively. Data were collected, entered into secure databases and analysed in MS Excel and SPSS. Analysis by age, sex, symptoms, complications and vaccination history was confined to the enhanced surveillance dataset.

Results

From 1 January 2004 to 31 December 2008, 319 mumps notifications were received by the Mid-West MOH. Three records were removed as duplicates and 14 were re-classified as denotified as laboratory data became available, leaving 302 records. Over the five year period, 109 laboratory-confirmed notifications (36%) and 193 clinical notifications (64%) were recorded. Enhanced surveillance was completed for 186 mumps cases (71% of 262 notified cases); 116 of them were clinical notifications only, 50 were laboratory confirmed only, and 20 were notified clinically and laboratory-confirmed (see Table 1).

Figure 1 shows all notified mumps cases, inclusive of those cases for whom enhanced surveillance information was available. With the exception of the academic year 2006-7, the number of mumps cases was relatively low in summer, and peaked in autumn in the months after third level colleges resume (Figure 1). An intervention with MMR vaccination was carried out by public

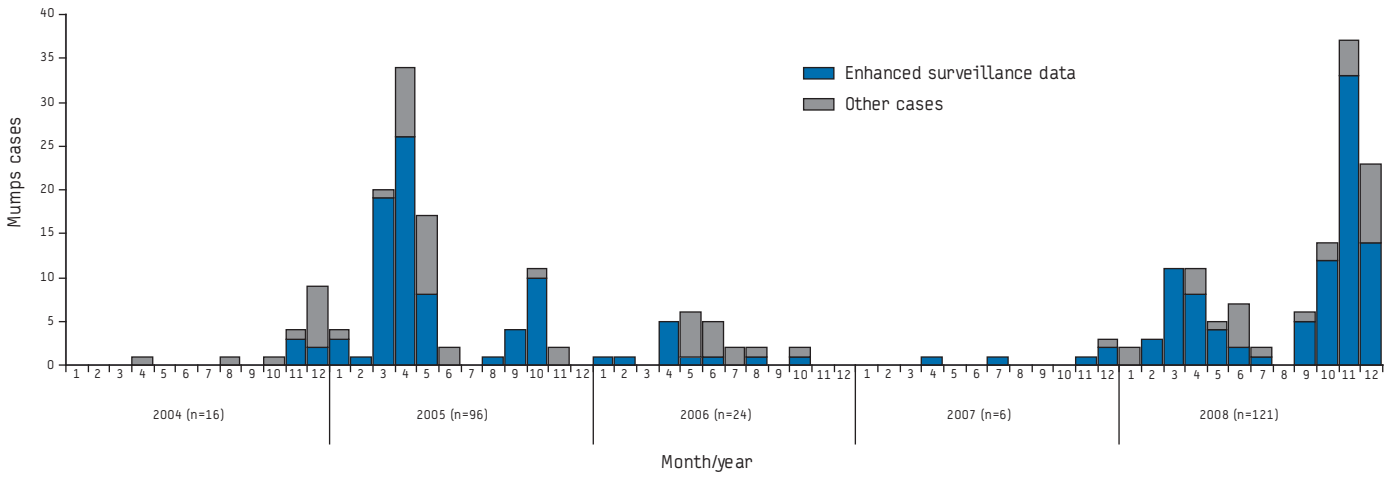
Table 1

Mumps cases for whom enhanced surveillance data were available, by notification type, Mid-West of Ireland, 2004-2008 (n=186)

	Notification Type (enhanced surveillance)			
Year Notified	Clinical	Laboratory and clinical	Laboratory	Total
2004	4	0	1	5
2005	57	3	12	72
2006	8	0	3	11
2007	4	0	1	5
2008	43	17	33	93
2004-2008	116 (62%)	20 (11%)	50 (27%)	186 (100%)

Figure 1

Mumps cases with enhanced surveillance data and other mumps notifications, by year and month, Mid-West of Ireland, 2004-2008 (n=263)

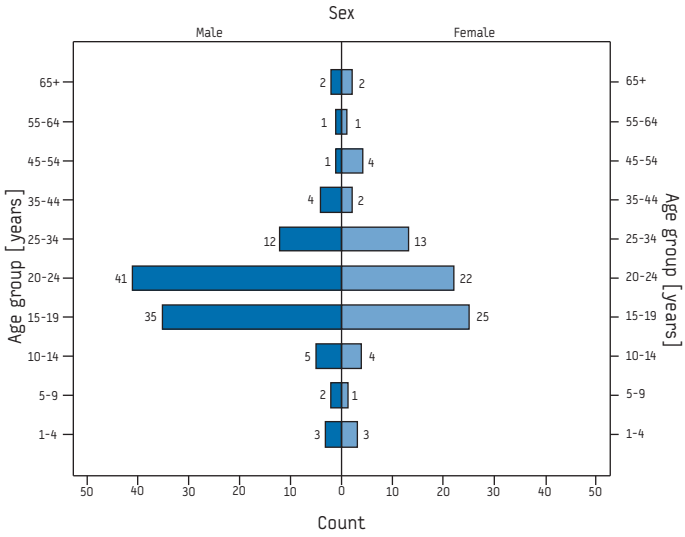


health/university student health services in one large university following a peak in mumps infections in April 2005. This could be an explanation for the change in pattern in 2006-7.

The age range of mumps cases was 1.4 years to 79 years (average 22.9 years, median 20.4 years). There was a slight preponderance of cases in males over females in all years except 2007 (data not shown): from 2004 to 2008, the male:female ratio was 1.4:1. For the period from 2004 to 2008, Figure 2 illustrates the age distribution of mumps cases by sex in the Mid-West. Of 186 cases, 123 were in the age group of 15-24 year-olds (66%). This distribution reflects the ongoing transmission since 2004 of mumps virus in susceptible people attending third level colleges in Ireland.

Figure 2

Age distribution of mumps cases for whom enhanced surveillance data were available, by sex, Mid-West of Ireland, 2004-2008 (n=183*)



*Age for three of the 186 cases unknown.

For 186 cases over the five year period, symptoms and complications are shown by sex in Table 2. Nausea, earache, headache and vomiting were mentioned by seven cases as symptoms or complications. Complications of mumps disease were uncommon in female patients (1/78) while 13% of the male cases (14/108) reported complications. Seven cases (four male and three female) were hospitalised, 5% of the 144 cases for whom such information was available. The outcome 'recovered' was stated for 28% of cases (52/186). No deaths were reported.

Investigation of the cases to determine the likely place of acquisition of mumps infection implicated several settings but university/college and secondary schools were reported in 54 cases (71% of 75 cases for whom this information was acquired), four in secondary schools and three in primary schools. The University of Limerick, a campus-style third level college, was associated with the vast majority of the infections acquired in university/college and with some related cases. Two mumps outbreaks were reported from the Mid-West – one in the community and one mixed community/college event.

Twelve cases (8% of cases where data were given) occurred in foreign-born nationals. Travel (25 days before onset) was reported in 16 cases, but only four had travelled "overseas" (two to the United Kingdom, one to North America and one to Africa). One case was reported as acquired overseas. Travel within Ireland appeared consistent with students commuting to their home counties.

Data on childhood MMR vaccination were ascertained for a large proportion of these mumps cases (78%; 146/186) and are shown in Table 3. MMR vaccination was not evident in the older cases (over 25 years of age), which is not unexpected. Where data were provided in young adults (15-24 years), 7% of cases (7/103) reported not receiving any MMR, 49% (51/103) had at least one MMR (MMR1) and 44% (45/103) reported receiving two doses (MMR2).

Discussion

Historically, in the Irish setting, mumps occurred in children between the ages of five and 15 years, although the disease

Table 2

Mumps cases with enhanced surveillance data showing symptoms and complications, by sex, Mid-West of Ireland, 2004-2008 (n=186)

	Males (n=108)			Females (n=78)		
Symptoms	Yes	No	Not given/unknown	Yes	No	Not given/unknown
Parotitis swelling	98 (91%)	3	7	69 (88%)	5	4
Bilateral parotitis	46 (43%)	49	13	26 (33%)	43	9
Fever	53 (49%)	41	14	20 (26%)	44	14
Complications						
Meningitis	1 (1%)	95	12	0	69	9
Encephalitis	1 (1%)	94	13	0	69	9
Orchitis/Oophoritis	12 (11%)	82	14	0	69	9
Deafness	0	95	13	0	69	9
Mastitis	0	94	14	0	68	10
Pancreatitis	1 (1%)	94	13	1 (1%)	69	8

Due to the small numbers, we did not undertake a statistical analysis.

was also seen in adults. The current epidemiological picture of mumps in the Mid-West of Ireland is an ongoing upsurge of cases in third level colleges and the wider community. Transmission of mumps virus in college students occurs in classroom, residential settings and social or sports activities, and contacts may require public health follow-up over a large geographic area. ProMED mail reported, in April 2009, that two third level college students in the United States (US), both having had two doses of mumps vaccine, have suspected mumps after returning from Ireland. US public health authorities think further cases are likely [14].

In many students mumps was probably prevented by MMR vaccination, and the immunity conferred probably limited outbreaks in the community. Nevertheless, mumps outbreaks are continuing in third level colleges. Slightly more males than females are affected but this may reflect attendance patterns to third level colleges. While complications were more commonly reported in males, a similar proportion of males and females were hospitalised. Students ill with mumps and absent from lectures/studies may experience negative effects on academic progress.

Since 2004, public health authorities maintained ongoing contact with all Mid-West third level college authorities and student health services to promote mumps and MMR awareness in students and staff. College services sent email alerts to the students where possible. Clear information in the college setting is essential for foreign-born students from countries that may not have MMR vaccination. Letters were issued to general practitioners and hospital doctors advising them of the upsurge in cases and reminding them of the requirement to notify mumps cases. Cases were advised to stay off work/college for five days after the onset of symptoms. Vaccination of close contacts, isolation and hand hygiene were promoted as key measures to prevent further disease transmission. The national outbreak control team, convened in 2004 in Ireland, recommended that new third level students under the age of 25 years and attending college during the academic years 2005-6 to 2007-8, who had not already had two doses of MMR should have one dose of MMR vaccine [7]. Advisory measures, unless supported by specific, ring-fenced resources, may be considered too passive as interventions to control continued mumps transmission. A strategic, national, targeted immunisation campaign in third level colleges was not undertaken in Ireland, but some regional public health departments did implement some active outbreak management measures in institutions. In March and April 2005, an outbreak was declared by the MOH in the largest third level college in the Mid-West, which resulted in an active targeted vaccination campaign involving several thousand students and staff. This may have had an impact by increasing herd immunity for that cohort of students and reduced mumps transmission in this institution in the subsequent years, 2006 and 2007.

People who received only one MMR dose may not be protected against mumps. The level of protection against mumps given in different reports varies from 65% to 90% after one dose [11]. Cases of mumps in people who reported receiving two MMR doses may indicate a combination of primary and secondary vaccine failure [15]: Immunity may wane after a number of years [16], owing to the comparatively low immunogenicity of the mumps component of MMR [8,17], There may be a genotype mismatch between circulating wildtype virus and the vaccine virus [18]; Lastly, true vaccine failure may be responsible. Several reasons could explain uncommon primary vaccine failure (e.g. incorrect storage, transport), and some have implications for the protective effect of the other two components of the vaccine. Nevertheless, parents should continue to have their child vaccinated with MMR according to national immunisation recommendations.

DiRenzi et al. reported in 2004 using ESEN2 data that approximately 80-85% of individuals in Ireland aged between 15 and 24 years were immune to mumps and that this relatively low level of immunity may be a reflection of the impact of MMR vaccination and subsequent decrease in exposure to wild mumps virus circulation [19]. It is likely that a proportion of susceptible individuals from this cohort will be attending secondary schools and higher education colleges between now and 2013. More individuals who are susceptible to mumps may arise from a global shortage of MMR that occurred in 1994 during which MR (measles, rubella vaccine) was used instead, as preventing a measles epidemic was a priority [20].

Our analysis underlines some particular issues in mumps surveillance in Ireland. Missing data was a limiting factor in the analysis of the mumps enhanced surveillance dataset and illustrates the competing objectives in public health infectious disease surveillance. In crisis situations such as an outbreak priorities are shifted to outbreak management and clinical follow-up at the expense of timely and complete surveillance. Analysis was confined to mumps notifications where enhanced surveillance was undertaken, hence the representativeness of this sample may be prone to some bias. Accuracy and objectivity of MMR vaccination status is open to question where the classification depended on recall rather than records.

Traditional epidemiological measures, like mumps incidence, are difficult to interpret as geography and census data do not provide a clear denominator for these cases in this setting due to the mobile cohort of students commuting to colleges in the Mid-West from neighbouring counties. Validating mumps notifications nationally to

Table 3

Mumps cases with enhanced surveillance by age group and measles, mumps, rubella (MMR) vaccination, Mid-West of Ireland, 2004-2008 (n=186)

	MMR vaccination				
Age group (years)	MMR1	MMR2	None	Data not given	All
1-4	5	0	1	0	6
5-9	2	0	1	0	3
10-14	5	3	1	0	9
15-19	21	23	4	12	60
20-24	30	22	3	8	63
25-34	6	2	4	13	25
35-44	0	0	4	2	6
45-54	0	0	2	3	5
55-64	0	0	2	0	2
>65	0	0	2	2	4
Not given	0	2	1	0	3
Total	69 (37%)	52 (28%)	25 (13%)	40 (22%)	186

MMR1: reported receiving one dose of MMR vaccine; MMR2: reported receiving two doses of MMR vaccine.

avoid duplication and overestimation remains a challenge, although the full implementation of a national computerised infectious disease reporting system (CIDR) may improve surveillance in future. Public health relies greatly on general practitioners and hospital clinicians notifying cases. More cases of mumps are reported clinically than are confirmed and notified by the laboratories. While mumps may have some classical symptoms and signs on presentation, clinicians may confirm cases by either serum IgM serology or by non-invasive salivary IgM testing. However, testing at the appropriate time in the clinical course of disease is important consideration in order to avoid apparently conflicting results [21,22].

A national outbreak control team was re-convened in 2009 and has recommended re-enforcing the present measures and adopting further active interventions, regionally and nationally, to control future transmission of mumps at secondary schools and third level colleges in Ireland.

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Characterisation of Neisseria meningitidis C strains causing two clusters in the north of Italy in 2007 and 2008

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Two clusters of invasive meningococcal disease in the north of Italy both due to serogroup C/ST-11 clonal complex are here described. The objective of the investigation was to analyse the phenotype and the genotype of meningococci involved in the two clusters which were of national relevance due to the fatal outcome of the majority of cases (six of the total of 10 cases). All the strains were C:2a:P1.5 ST-11/ET-37 clonal complex. Two pulsed field gel electrophoresis (PFGE) and variable number tandem repeats (VNTR) profiles were identified, one for each cluster. VNTRs were different from those detected in Italy for C/ST-11 strains isolated from sporadic cases in the same period.

This laboratory surveillance report highlights the importance and the crucial role of molecular characterisation to confirm the relatedness among meningococci responsible for clusters of cases.

Introduction

Meningococcal disease remains a major childhood infection in Europe, with a considerable number of cases appearing also in other age groups, notably young adults. The incidence of serogroup C disease substantially declined with the introduction of conjugate meningococcal C vaccine in the national vaccination programmes of several countries [1]. However, the C/ST-8 and the C/ST-11 strains are currently the two hyper-virulent meningococcal lineages involved in a significant proportion of serogroup C invasive disease worldwide [2].

In Italy, the notification of invasive meningococcal disease to the local health authorities and to the Ministry of Health has been mandatory since 1983. Through national surveillance of bacterial meningitis, established in 1994, the National Reference Laboratory (NRL) at the Istituto Superiore di Sanità in Rome each year receives an average of 80% of strains isolated by local hospital laboratories throughout the country. The disease, characterised by low national incidence (0.3/100,000 inhabitants) and by sporadic cases, has in the last three years mainly been caused by serogroup B meningococci (64%).

Since the end of 2007, two clusters of serogroup C meningococcal disease have been detected in two different administrative regions in Italy. Due to the severity and fatal outcome of cases, these clusters were of national relevance, and the strains have been fully characterised at the NRL. The molecular characteristics of the ten strains involved in the two clusters are reported here.

Methods

Isolates of meningococci received at the NRL were subcultured for serogroup confirmation by slide agglutination with commercial antiserum (Remel Europe, United Kingdom). Serotypes and serosubtypes were determined by standard whole-cell ELISA with monoclonal antibodies (purchased from NIBSC, UK) [3]. Susceptibilities to penicillin G, rifampicin, ciprofloxacin and ceftriaxone were determined by E-test method (AB Biodisk, Solna, Sweden), according to the manufacturer's instructions.

The breakpoints were those recommended by the European Monitoring Group for Meningococci EMGM [4].

Molecular analyses by multilocus sequence typing (MLST), variable number of tandem repeats (VNTR) typing and pulsed field gel electrophoresis (PFGE) were performed following the procedures described elsewhere [5-7].

Results

The two clusters of serogroup C meningococci occurred in a group of seven adolescents/young adults and in three adults in two different but bordering Italian regions, Veneto and Lombardy, in December 2007 and in July 2008, respectively.

The outbreak in Veneto has already been described from an epidemiological aspect and in terms of management [8]. The outcome was fatal in three of the seven cases.

From 13 to 15 July 2008, three cases of fatal septicaemia in patients aged 34, 48 and 51 years occurred in a limited geographical area of the Lombardy region. Family members and people who had been in contact with the patients were given chemoprophylaxis. Thorough investigation by the local health authorities did not show any social or institutional link between the three cases, and none could be identified as specifically at risk on the basis of the information obtained. All cases from both events, were laboratory-confirmed at the regional level by culture and the serogroup of *Neisseria meningitidis* was identified. At the NRL, the phenotypic and genotypic characteristics of the ten isolates were further determined. The strains showed the antigenic formula C:2a:P1.5 and were fully susceptible to penicillin, rifampicin, ceftriaxone and ciprofloxacin. All of them belonged to ST-11/ET37 clonal complex (cpx) as identified by MLST.

PFGE confirmed the relatedness of strains within each cluster (Figure, Panel A, lanes 3-9 and 11-13). In particular, the presence of a single pattern from each cluster was observed.

VNTR analysis was also performed to further discriminate among ST-11 strains. The isolates showed a high degree of similarity in the patterns identified for each cluster and were different compared to VNTR profiles found among C/ST-11 strains isolated sporadically in the country in the same period (Figure, Panel B, lanes 3-9 and 11-13).

Discussion

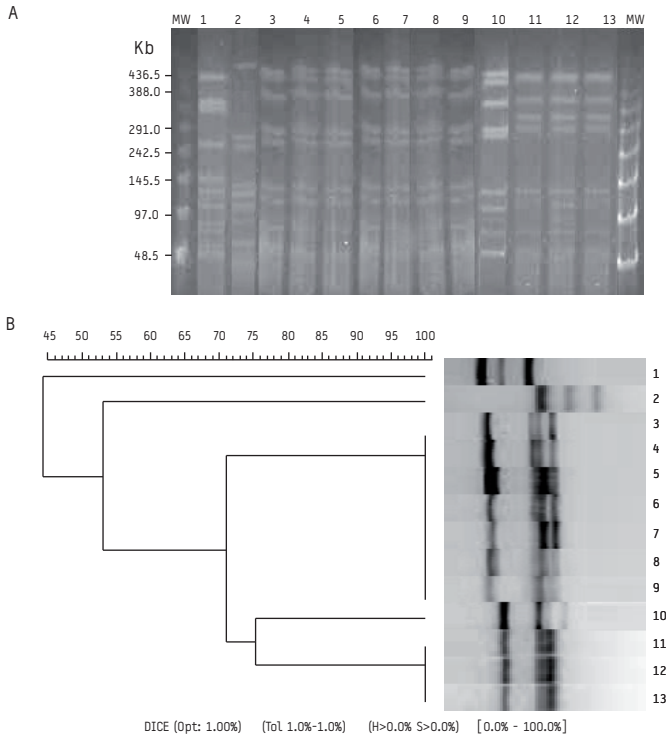
Vaccination campaigns in Europe [1,9] against *N. meningitidis* serogroup C have been very effective and have contributed significantly to its decline mainly among children and adolescents. However, the spread of ST-11 hyper-virulent meningococci among non-vaccinees is noteworthy due to the high transmissibility and low carriage rate, as documented by the literature [1,10]. A thorough assessment based on clinical and laboratory diagnosis combined with genotyping of all strains isolated during a cluster is highly recommended to confirm the clonality and to detect the circulation of new variants in this hypervirulent complex [1].

In this report, two clusters caused by C:2a:P1.5/ST-11 meningococci in December 2007 and July 2008 in northern Italy, have been reported. The two events are of national relevance due to the high fatality rate of the disease. The molecular studies (PFGE and VNTR) performed at the NRL demonstrated the involvement of two different clones, each responsible for a cluster. Interestingly, VNTR analysis identified profiles not yet detected among other C:2a:P1.5/ST-11 strains circulating in the country over the last few years.

The present analysis confirms that, from a public health perspective, genotyping in the investigation of a cluster is crucial to detect the circulation of a hyper-virulent clone, to identify new variants and to monitor the spread in the area.

FIGURE

Genetic relationship among meningococci C:2a:P1.5/ST-11 by PFGE (panel A) and VNTR analysis (panel B). Molecular analyses of isolates from clusters of *Neisseria meningitidis* infection in Veneto and Lombardy, Italy, between December 2007 and July 2008



Lanes 1-2 and 10, C:2a:P1.5/ST11 meningococci isolated sporadically in Italy; lanes 3-9 and 11-13, C:2a:P1.5/ST-11 from clusters in Veneto and Lombardy, respectively. MW: molecular weights (New England, Biolabs). The left side of the VNTR gel photo is the top of the gel. VNTR: Variable number tandem repeat

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VACSATC (Vaccine safety: attitudes, training and communication): Why such a project?

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The Vaccine safety: attitudes, training and communication (VACSATC) project was established in 2006 to study perceptions of immunisation and vaccine safety, to improve training of healthcare professionals on vaccine safety and to improve the availability of information on vaccine safety on the internet that adheres to good information practices. The three year project is funded by the European Commission's Directorate General for Health and Consumers and by the partners. The project complements the activities of the Vaccine Safety Net project and the Vaccine European New Integrated Collaboration Effort (VENICE) project.

Background

Vaccinations against life-threatening diseases are one of the greatest public health achievements in history. Literally millions of premature deaths have been prevented, and countless more children have been saved from disfiguring illness [1]. Though some risks are unavoidable when dealing with vaccines, the medical, social and economic benefits they confer have led countries in Europe to establish childhood vaccination programmes to stop the spread of preventable diseases. In some countries, the programmes are based on recommendations while in others childhood immunisations have been made mandatory [2,3].

Today, however, vaccines are becoming a victim of their own successes. Many individuals have never witnessed the debilitating diseases against which vaccines protect, and this has led to complacency about necessary immunisations [1]. The risk of side effects of medicinal products - and therefore also of vaccines - are often not effectively communicated to the public, media and healthcare professionals. Especially the relation between risks and benefits of vaccination and the risk of not being vaccinated are not communicated well, as is information on how the number and seriousness of side effects relate to the number of vaccines administered. Anti-vaccination sentiment is growing in many European countries, in large part due to the controversial and hotly disputed link between immunisation and autism, between Hepatitis B vaccination and multiple sclerosis in France, and between sudden death and convulsions and human papillomavirus immunisation in Austria, Germany, Spain and other countries, despite a lack of evidence for such a causal relationship.

The results of many surveys on attitudes to immunisation demonstrate that mothers believe that the measles, mumps, rubella (MMR) vaccine protects against diseases that are not serious. The surveys have also shown that MMR is the vaccine least likely to be considered safe [4-10]. On the other hand a study by Smith et al. published in 2007 found that the proportion of parents in the United Kingdom (UK) who believe the MMR vaccine to be a greater risk than the diseases against which it protects had fallen from 24% to 14% since 2002. The proportion of people in that study in the UK who rejected vaccination completely remained stable in 2006 at just 6% [11]. The most significant finding from this latest survey is that there was a gradual and sustained increase in the proportion of parents who considered that the MMR vaccine was completely safe or posed just a slight risk, from 60% in 2002 to 74% in 2006. Clearly parents in the UK are not sure about the safety of the vaccine and the danger posed by the diseases that it protects against [11]. Not much is known about the situation in other countries and how it is changing.

The consequences of low vaccination coverage are serious not only for unvaccinated children, but also for society as a whole. 'Herd immunity' (a critical proportion of the population being immune to a particular infection that is spread from person to person, so that natural transmission of the infection is effectively inhibited) is threatened, and outbreaks of diseases reoccur that were thought to be under control [12]. The decision-making process regarding childhood immunisation is complex. Parents require information that is up to date, tailored to their individual needs and provided by health professionals who are well informed [13]. The role of well-trained healthcare staff in giving advice and an opportunity to discuss vaccination with concerned parents cannot be overemphasised [11,14].

Given the impact of concerns about vaccine safety on vaccine coverage, the issue needs to be addressed by healthcare professionals offering vaccines [9]. Primary care physicians, paediatricians, family doctors, nurses and midwives as the most common contact points between parents and the immunisation delivery system, are most likely to be exposed to parental concerns about vaccine safety and have an important role to play in providing parents with balanced advice on this topic [10,15,16]. Physicians,

nurses, midwifes and other healthcare professionals should increase their efforts to build honest and respectful relationships with patients, especially when parents express concerns about vaccine safety or have misconceptions about the benefits and risks of vaccination [17,18]. Medical and paramedical students should therefore receive adequate pre-service training in vaccinology already at the level of nursing schools and universities, although other strategies could be used in the post-graduate period (training, reminder/recall interventions, incentives, etc.).

Not only healthcare professionals but also school personnel trained in vaccine safety may serve as a valuable source of vaccine information for parents. Public information campaigns [19] and the use of mobile teams [20] also play a role in disseminating reliable information on vaccines. Among the factors influencing individuals' perception of vaccines are religious and philosophical beliefs, freedom of choice and individualism, as well as misinformation and over-perception of risk [1,10,21,22].

The context in which patients search for health information has changed dramatically with the growth of the internet, progress in telemedicine, and changes in the coverage of health issues in the media. Increasingly, individuals search for information online before talking with their physician [23]. Although the precise effect of increasing use of the internet for health information is unclear, it seems that the internet worsens fears regarding vaccination safety. Anti-vaccination sites express a range of concerns related to vaccine safety, relying heavily on emotional appeal to convey their messages [24]. The most common characteristic of vaccine-critical websites is the inclusion of statements linking vaccinations with specific adverse events, especially idiopathic chronic diseases such as multiple sclerosis, autism, and diabetes [25]. Sites with factual refutation strategies alone are unlikely to counter the highly rhetorical appeals of such sites [26].

Responding to the needs of improved information on immunisations

Recognising the need of web-based information that is objective and based on science, the World Health Organization (WHO) Global Advisory Committee on Vaccine Safety established the Vaccine Safety Net Project in 2003. The project has developed criteria for good quality websites. Websites are evaluated and those that meet the criteria in content and credibility are listed on the WHO website at http://www.who.int/immunization_safety/safety_quality/vaccine_safety_websites/en/index.html.

The need for good training of healthcare personnel has also been recognised by WHO and educational material has been made available at http://www.who.int/immunization_safety/.

Another initiative to improve training is the tutorial "Addressing Parents Concerns About Childhood Immunizations: A Tutorial for Primary Care Providers", developed by B. Levi (Penn State College of Medicine in the United States). This tutorial has the potential to enhance communication between parents and primary healthcare providers and, more generally, to improve clinicians' response to the growing resistance toward routine childhood immunisations [27].

In Europe, training materials have been produced as well, such as: the brochure *"Argumentarium: Kinder impfen? Ja! Wieso?" ("Argumentarium: Vaccinating children? Yes! Why?")* in Switzerland (http://www.bag.admin.ch/shop/00047/00140/index.html?lang=de), an Immunization Update Net by Junta de Andalucía in Spain (http://www.juntadeandalucia.es/salud/andaluciaessalud/bolet/portada.asp?id=14), and a complete document about immunisation learning standards *"National Minimum Standards for Immunisation Training"* in the UK, which offers a wide range of information (http://www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1196942164323).

The Vaccine safety: attitudes, training and communication (VACSATC) project

The Vaccine safety, attitudes, training and communication (VACSATC) project (www.vacsatc.eu) was established in 2006 to study perceptions of immunisation and vaccine safety, to improve training of healthcare professionals regarding vaccine safety and to improve the availability of information on vaccine safety on the internet which adheres to good information practices. The project, funded by the European Commission's Directorate General for Health and Consumers and by the partners in the project, will run for three years. The project complements the activities of WHO and the Vaccine European New Integrated Collaboration Effort (VENICE) project (http://venice.cineca.org/the_project.html) coordinated by the Istituto Superiore di Sanitá in Rome.

The reasons for establishing the VACSATC project were:

- The infectious agents as well as rumours and concerns about vaccine safety cross country borders. The problems cannot be resolved by action in a single country.
- Further improvements could be made through sharing of experiences in different countries, for instance on risk communication, perception of the population's attitudes regarding vaccines, etc.
- The participation of centres of excellence will lead to improved quality and rapid dissemination of best practices, for example in training on immunisation, information about vaccines for the public, etc.
- Vaccine safety initiatives in individual countries are often inadequately funded [28].

The activities of the project are divided into work packages (WP). The objectives of three of them are given below:

WP5: To collect and summarise published material on perceptions of vaccination and carry out pilot and full scale studies on attitudes and perception,

WP6: To improve immunisation training for medical and paramedical personnel.

WP7: To increase the number of websites with information on vaccine safety and the number of websites that meet the WHO Vaccine Safety Net criteria for good information practices.

These three work packages use the same approach, namely to review the current status of the three aspects, attitudes, training and communication about immunisation, to share the expertise in partner organisations in order to develop a tool kit of best practices and to implement improvements at national level.

WP 5 is concerned with attitudes to vaccine-preventable diseases, immunisations and adverse events following immunisation (AEFI). At the beginning of the project, participants were invited to share studies on the subject, and at the same time the UK Department of Health performed a literature search. The number of good quality

studies in the published literature was limited. Partners were also asked to identify studies in their own countries that examined attitudes to vaccine-preventable diseases, immunisations and AEFI. The main purpose was to describe the work already done and to gain a better understanding of parental attitudes across Europe. A secondary aim was to explore the possibility of developing a common approach for the participating countries. Thirty papers were assessed and emerging issues noted. Twenty-eight papers focused on childhood immunisations and the remaining two focused on high-risk groups above the age of 65 years who refused influenza immunisation. The main practical conclusions arising from this review were that the level of investigation into parental attitudes varies widely from country to country and that such approaches are not well developed: There was no common methodology to investigate the parental attitudes. Financial resources and number of staff available for this kind of research vary widely across the participating countries. The participants agreed on ten themes for future questionnaires that can be used to prepare questionnaires locally.

WP6 focuses on training on immunisation including vaccine safety and communication on vaccination. At the kick-off meeting in Lund, Sweden, in October 2006 it was agreed that due to the diversity of the healthcare systems, a definition of target groups in the participating countries was needed: Who immunises and who provides information on immunisation? In February 2007, a 'Setting the scene' questionnaire was drafted and distributed to the participating countries. One conclusion of the 'Setting the scene' phase was the necessity to improve the training on immunisation, and a strategy and tool were developed to evaluate the current training in immunisation and vaccine safety, addressed to curriculum managers and students at medical universities and nursing schools. As vaccinology is poorly addressed during the training of future healthcare workers although immunisation is a responsibility of all healthcare workers, an international vaccination course will be offered to medical, nursing and midwifery students in summer 2009 at the University of Antwerp (Belgium) that probably will be repeated every year. (see: http://www.ua.ac.be/main.aspx?c=.CEVSUMMERSCHOOL&n=71545). A set of common criteria for good training in immunisation and vaccine safety will be identified by the end of the project.

The aim of WP7 is to improve dissemination of information on vaccine safety on the websites of the partner organisation and to increase the number of websites that meet the quality criteria of Vaccine Safety Net. An assessment of the partners' websites has been carried out. Documents on best practices and a web-based "library" have been developed in http://www.vacsatc.eu/LibraryWindow.aspx. There are now 16 websites in Europe that are certified by the WHO Vaccine Safety Net Project.

The VACSATC project started with 16 partners in 14 countries. Subsequently, a further five partners from four different institutions started collaborating with the project. Plans to expand the work and the number of partners are on the way.

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