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EUROSURVEILLANCE ACHIEVEMENTS IN 2008 AND CHALLENGES FOR 2009

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2008 was yet another year of major innovations for Eurosurveillance. Since January 2008, Eurosurveillance has been published once a week online with short, rapid communications as well as longer papers on the surveillance, prevention and control of communicable diseases. In April we launched a new reader-friendly website with modern design and functionalities such as easy navigation between articles, display of related articles and improved search function.

A continuing rise in the number of subscribers to over 14,000 by the end of 2008 (see Figure 1) and an increasing number of submissions from European scientists as well as from experts from outside Europe proves that our efforts to raise the journal's scientific credibility have been successful. The new subscriptions in 2008 covered 121 different countries. The majority came from Europe, but many also from the United States (181), Canada (73) and Australia (52).

The geographical focus of the journal remains Europe even if we also publish articles from other countries if the topic is relevant for Europe. Figure 2 shows the wide distribution of countries from which we received contributions in 2008. We published 128 peer-reviewed rapid communications and 107 peer-reviewed long articles, additional 56 items were editorials, news, letters and meeting reports.

The possibility of peer-reviewed extremely rapid communications (published within as little as 24 to 48 hours) remained a unique feature of Eurosurveillance in 2008. As in previous years, they facilitated the rapid exchange of information for public health action, and in several cases contributed to the control of international outbreaks. Their impact was reinforced through the fact that the International Society for Infectious Diseases' Program for Monitoring Emerging Diseases (ProMED-mail) picked up at least one Eurosurveillance article per week for their world-wide mailings.

Among the long articles published in 2008, of particular value for the scientific community were the review articles covering areas from antimicrobial resistance in Europe to vaccination for seasonal influenza and tick-borne encephalitis in Europe. In 2008 we published eight special issues on meningococcal disease, tuberculosis, immunisation, molecular typing, hepatitis B and C, testing for recent human immunodeficiency virus (HIV) infections, seasonal influenza vaccination, antimicrobial resistance. Six Euroroundup articles covered the surveillance of viral meningitis and encephalitis, human salmonella infections acquired through contact with exotic pets, monitoring of congenital toxoplasmosis, hantavirus infections, managing patients with meningococcal disease and their contacts and *Clostridium difficile* O27.

FIGURE 1

Number of Eurosurveillance subscriptions in 2008 as of 18 December 2008 (n=14,204)

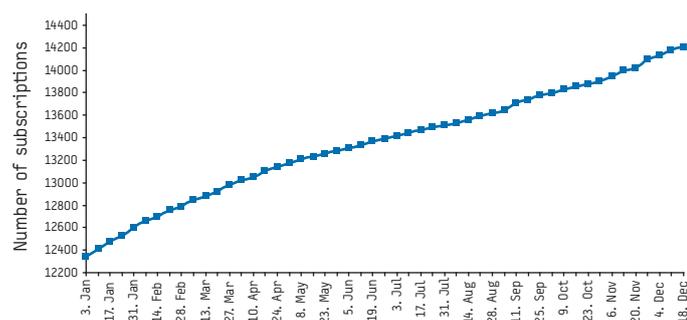
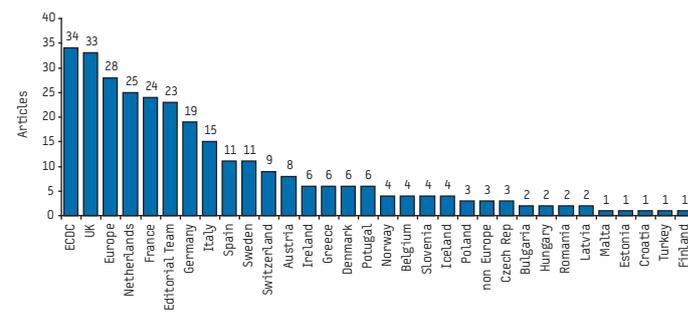


FIGURE 2

Articles published in Eurosurveillance, in 2008, by country of origin (n=291*)



* redundant counting when two or three countries involved; counted as "Europe" when more than three countries involved.

All this could not have been achieved without the continued support of our Associate Editors and Editorial Board members and, last but not least, our authors and readers to all of whom we are grateful. Furthermore, we thank all experts who dedicated their time to review articles for us, and we are obliged to those who provided us with helpful advice to guarantee the high quality of our publications. In this week's issue we want to acknowledge this help by publishing a list of otherwise invisible peer-reviewers in 2008.

What has been accomplished in 2008 will stimulate our work in 2009. We will continue to attract the most relevant high quality articles in the field and to provide our readers with timely information about important outbreaks and developments in infectious diseases. Attracting even more readers and contributors and strengthening our impact are additional challenges for 2009. We will persist in our vigilance to contribute to the prevention and control of infectious diseases in Europe and are looking forward to collaborating with you towards this goal.

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BOTULISM IN INJECTING DRUG USERS, DUBLIN, IRELAND, NOVEMBER-DECEMBER 2008

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In November and December 2008, six cases of suspect wound botulism were reported in heroin injecting drug users, all residents in Dublin, Ireland. Patients were aged between 23-42 years of age; four cases were male; one patient died shortly after admission. The patients presented to four different hospitals across the city. Botulism in injecting drug users in Ireland was last reported in 2002.

On Monday, 24 November 2008, public health authorities were notified that an injecting drug user (IDU) had been admitted to a hospital in Dublin, Ireland, with neurological signs suggestive of botulism including progressive bulbar palsy, diplopia, dysarthria, and an electromyography (EMG) test consistent with a diagnosis of botulism. The patient was treated with botulism anti-toxin and supportive measures. Serum samples taken prior to administration of anti-toxin were sent to the Foodborne Pathogen Reference Unit, London, United Kingdom (UK) for detection of *Clostridium botulinum* neurotoxin by mouse biotoxin assay. Laboratory results confirmed the diagnosis of botulism and identified the causative toxin as *C. botulinum* toxin type B.

By Friday, 28 November, three additional suspected cases of botulism had been notified, all of whom received anti-toxin. These four patients were admitted to three different hospitals in Dublin. Although two patients lived in the same area, they did not know each other. All were IDUs, but there was no evidence that they shared the same drug supply.

No additional cases were notified to the Departments of Public Health in Ireland during the week beginning on 1 December. However, during the 36-hour period from 8 to 10 December, two further patients were admitted to a fourth Dublin hospital with signs suggestive of botulism (difficulty breathing and speaking, ataxia, double vision). Both patients received botulism anti-toxin. Unfortunately, one of these patients died shortly after admission from overwhelming sepsis. At the time of writing this report, one case is laboratory confirmed, two cases are probable and three cases are possible (see next section and Table for further details).

For the purpose of this investigation, a *possible* case of drug injection-related wound botulism was defined as a person in the Republic of Ireland with a recent history (within four weeks of symptom onset) of injecting drug use and with acute onset since 1 November 2008 of either of the following symptoms in the absence of any other obvious cause:

- symmetrical cranial nerve palsy,
- difficulty in swallowing or speech,
- unexplained stridor,
- difficulty in breathing,
- or descending flaccid paralysis.

A *probable* case was defined as having the features of a possible case and laboratory results suggestive of *C. botulinum* infection but unconfirmed by neutralisation.

A *confirmed* case was defined as having the features of a probable case, with a confirmed diagnosis of botulism (by detection of botulinum toxin in serum or isolation of *C. botulinum* from a wound or abscess site).

An outbreak enhanced surveillance form was designed (available upon request) to collect relevant demographic, clinical and drug use data. This form was filled out in as much detail possible by hospital staff. Specific attempts were made to identify links between the six patients in terms of area of residence, social networks and drug supply.

A summary of selected demographic and clinical data as well as information about drug use of the cases is presented in the Table.

The outbreak has been managed by an outbreak control team led by the Department of Public Health, Health Service Executive-East (HSE-E) in Dublin. In addition to HSE-East staff, personnel from the Health Protection Surveillance Centre (HPSC), Dublin, the HSE Drug Services, Dublin, and a clinical microbiologist from one of the involved hospitals were included in the outbreak control team. As is the norm in outbreaks of suspected clostridial infections, the HPSC alerted clinical staff throughout the country (emergency medicine physicians, neurologists, infectious disease physicians, microbiology services, drug services and public health medicine physicians) through email alerts. Press releases were also issued to

the national media. Internationally, the European Centre for Disease Control (ECDC) and the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) were informed. HSE HPSC alerted other European countries using the Early Warning and Response System (EWRS), an internet based rapid alert system supported by the European Commission and run by ECDC. Advice in relation to 'skin popping' (subcutaneous injection of heroin) with potentially contaminated heroin was distributed to the drug using community through the drug services and the network of 13 local drugs task forces in Dublin.

Heroin used by one patient was obtained and has been sent to the Foodborne Pathogen Reference Unit for testing by the Irish police. However, *C. botulinum* could not be isolated from this sample. No other cases of wound botulism were reported in Ireland in 2008 apart from those reported here. There have been two cases of suspected wound botulism in drug users in different areas in the north of England since 25 December 2008. One of these is unconfirmed (serum sample collected several days after onset of symptoms), whilst testing for the second case is on going. Both cases had classic symptoms and have received anti-toxin. The authors are unaware of any other outbreak occurring in European countries in this time period.

Discussion

Since 2000, there have been three outbreaks of clostridial infections in IDUs in Dublin. In an outbreak of *Clostridium novyi* Type A in 2000, 22 patients were infected, of whom eight died [1-3]. A simultaneous outbreak occurred in the north of England and Glasgow, Scotland. In 2002, an outbreak of botulism involving three IDUs occurred in Ireland [4,5].

There is laboratory confirmation of a clinical diagnosis of botulism in approximately 40% of wound botulism cases, either by detection of botulinum neurotoxin in the patients' serum or by isolation of *C. botulinum* from wounds. Reasons for this low confirmation rate include delay in recognition of clinical signs and subsequent delays in specimen collection. Once toxin reaches the nerve endings, it binds irreversibly, thus reducing the amount of toxin in the serum to below detectable levels. In addition, inadequate volumes of serum sent for testing may reduce the sensitivity of the test, and the administration of systemic antibiotics prior to specimen collection

may reduce the viability of organisms in pus taken from associated wound abscesses.

The fact that only one case in this outbreak has been laboratory-confirmed, with the remaining cases classified as possible or probable, can be attributed to the difficulties mentioned in the paragraph above. Two of the cases were given anti-toxin before serum samples were obtained and thus toxin was not detectable.

Wound botulism became a notifiable disease in Ireland on 1 January 2004. Prior to this date, only food-borne botulism was notifiable under the disease category of *Acute Infectious Gastroenteritis*.

Wound botulism occurring among IDUs was first reported in the United States in 1982 [6]. Since then both sporadic botulism cases and outbreaks have been reported among this sub-population. A number of other European countries have also reported outbreaks among IDUs in recent years [7-11].

Heroin users who inject either subcutaneously or intramuscularly are at particular risk, as administration using this method is conducive to wound infection, abscess formation and generation of the anaerobic conditions for germination of *C. botulinum* spores and subsequent release of neurotoxin [7]. Spores of *C. botulinum* are often present in soil and may contaminate heroin or heroin taking equipment. Heating the heroin powder to solubilise it for subcutaneous injection does not kill the spores, and the acidulant used for solubilisation enhances tissue damage at the injection sites, facilitating the germination of botulinum spores and leading to release of neurotoxin.

Botulism (both food-borne and wound) is extremely rare in Ireland, unlike many European countries which routinely see food-borne cases each year. Wound botulism is much rarer, but both sporadic cases and outbreaks have been reported in European countries in recent years [7-11]. Maintaining high levels of awareness of the risk of botulism among the population of injecting drug users is vital to insure that they are aware of the risk and urgently seek medical attention if they develop any of the signs or symptoms associated with the disease. Alerting clinicians to botulism increases the likelihood of rapid diagnosis, early hospitalisation and appropriate treatment with anti-toxin and other supportive treatment of these patients, thus decreasing mortality and complications. Delays in

TABLE

Demographic, clinical and drug use history, reported botulism cases, Dublin, 2008

| Case (No.) | Sex | Age (years) | Onset of symptoms | Clinical features/skin abscesses | Mechanical ventilation | Anti toxin given/date | Recent* heroin injection | Case classification | Outcome |
|------------|-----|-------------|-------------------|----------------------------------|------------------------|-----------------------|--------------------------|---------------------|---------|
| 1 | M | 33 | 20/11/2008 | Dysarthria, indurated area | No | Yes 21/11/2008 | Yes | Confirmed | Alive |
| 2 | M | 23 | 21/11/2008 | Respiratory problems | Yes | Yes 27/11/2008 | Yes | Probable | Alive |
| 3 | F | 34 | 17/11/2008 | Respiratory problems | Yes | Yes 27/11/2008 | Yes | Possible | Alive |
| 4 | M | 39 | 21/11/2008 | Respiratory problems/ abscess | Yes | Yes 27/11/2008 | Yes | Probable | Alive |
| 5 | M | 38 | 04/12/2008 | Dysarthria | No | Yes 8/12/2008 | Yes | Possible | Alive |
| 6 | F | 42 | 10/12/2008 | Dysarthria and ataxia/ abscess | No | Yes 10/12/2008 | Yes | Possible | Died |

*within four weeks of clinical disease onset

administration of anti-toxin treatment increase mortality, hospital stay and rehabilitation time. Raising the index of suspicion also increases the likelihood of additional cases being considered.

Our working hypothesis is that a contaminated supply of heroin is responsible for this outbreak, supported by the number of cases and focus in the Dublin area over a short period of time. However our investigation to date has failed to identify common links between cases. Such links were identified in the clostridial outbreak among IDUs in Dublin in 2000 [1-3], when common social networks and common drug dealers were identified for some of the cases. At that time, similar *C. novyi* outbreaks were occurring in northern England and Glasgow, Scotland, supporting the hypothesis of a common contaminated supply.

The fact that no further cases have been identified suggests that rapid dissemination of information and local action may have averted further cases. The authors would welcome hearing of any wound botulism cases seen in other countries around this time.

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IMPORTED ASEPTIC MENINGITIS DUE TO TOSCANA VIRUS ACQUIRED ON THE ISLAND OF ELBA, ITALY, AUGUST 2008

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We describe a case of aseptic meningitis due to Toscana Virus imported to Switzerland and discuss the epidemiological situation. To our knowledge this is the first description of this infection acquired on the Island of Elba.

Introduction

In Switzerland, aseptic meningitis is frequently encountered and most often caused by enteroviruses, flaviviruses (tick-borne encephalitis), herpes simplex virus type 1 and 2, varicella-zoster virus or mumps and measles viruses. Other arthropod-borne viruses that can cause clinical signs of meningoencephalitis, such as West Nile virus, have been detected in other parts of Europe and also in countries around Switzerland (e.g. Italy, France), but not as yet in Switzerland itself.

Toscana virus (TOSV) was first isolated from in a sandfly (*Phlebotomus peniciosus*) in central Italy in 1971 and identified as a common cause of aseptic meningitis in this country. Since then, it has been detected in other countries around the Mediterranean. Studies carried out in Italy have shown that the virus circulates not only in Tuscany but also in other regions such as Emilia Romagna, Marche, Umbria and Piedmont [1]. So far no data can be found about infections acquired on the islands off the coast of Tuscany, including Elba.

Case Report

On 10 August 2008, a man in his twenties was admitted to the emergency department of the Hospital of Lucerne, based in the central part of Switzerland. He suffered from a pronounced headache since the previous day and recurrent vomiting.

He had stayed on the island of Elba for two weeks and returned home on 8 August. From 27-31 July, he had stayed at a camp site east of Portoferraio, before moving to the southern part of the island (near Marina di Campo) for the remaining week. The entire holiday was spent exclusively on Elba, with no major stopovers on the way home from Piombino, the mainland port for the ferry to Elba.

At the camp site, the patient usually slept outside the tent on a canvas chair, the ground was sandy and hard

On admission, the patient had a neck rigidity without clinical signs of encephalitis or fever.

White blood cell count and C-reactive protein levels were normal. Cerebrospinal fluid (CSF), taken on the day of admission, was clear and showed a white blood cell count of 196/mm³ (85% mononuclear cells), protein levels of 0.75 g/L and glucose levels of 3.7 mmol/L (the glucose level in the blood was 6.9 mmol/L). Gram stain was negative and culture showed no microorganisms. PCRs for herpes simplex virus type 1 and 2, varicella-zoster virus and enteroviruses were negative. Serology for *Borrelia burgdorferi* and tick-borne encephalitis virus showed no signs of active infection.

Because the patient had stayed on the Island of Elba, TOSV meningitis was considered and confirmed by indirect immunofluorescence that showed high titres of anti-TOSV IgM and IgG, antibodies ("Sandfliegenfieber-Viren-Mosaik", Euroimmun, Lübeck, Germany). Antibody titres against other sandfly fever viruses (sandfly fever Naples virus (SFNV), sandfly fever Sicilian virus (SFSV), and sandfly fever Cyprus virus (SNCV)) were found to be low or negative.

Although a PCR of the CSF taken on the day of admission could not detect TOSV genome, the negative PCR result does not exclude an acute infection with TOSV as the virus rapidly becomes undetectable after the appearance of antibodies.

The patient recovered completely within three days. Apart from analgetic medication, no further treatment was necessary.

Discussion

TOSV belongs to the genus *Phlebovirus*, family *Bunyaviridae*. The *Phlebovirus* genus currently comprises 68 antigenically distinct serotypes, eight of which have been linked to diseases in humans. Three *Phlebovirus* serotypes are of importance in Europe: SFSV, SFNV and TOSV. While the first two cause a febrile illness, TOSV is characterised by its neurotropism and the clinical characteristics of meningitis, meningoencephalitis and influenza-like illness. As stated in several studies and case reports, TOSV is circulating not only in Italy but also in Algeria, Spain, Portugal, France and Cyprus [2-9]. In central Italy, a seroprevalence of approximately 20% could be detected [10] whereas in Granada, southern Spain, the overall prevalence of anti-TOSV IgG antibodies was almost 25% [11]. In both countries, the seroprevalence was significantly higher in older age groups and in the rural population, indicating exposition throughout life and a higher vector density in the rural areas.

Transmission of the virus to humans results from the bite of small female phlebotomine sandflies (*P. perniciosus* und *P. perfiliewi*). The activity of sandflies is mainly crepuscular or nocturnal. During the summer months, concomitant with the period of maximum activity of the sandfly vectors in August, TOSV appears to be one of the major viral pathogens causing aseptic meningitis in tourists as well as in the local population of the Mediterranean countries [12].

TOSV infections have an incubation period of three to six days. The clinical picture is variable: In addition to meningitis and meningoencephalitis few cases of encephalitis without meningitis have been described [13]. The high seroprevalence suggests that asymptomatic infection is rather common and TOSV therefore probably under-recognised. In a study performed in the area around Florence, Siena and Arezzo, forestry workers with high occupational risk of TOSV infection showed a seropositivity rate of over 75% with negative history of neurological symptoms. This confirms that TOSV infection can be very mild or even completely free of symptoms [10].

To our knowledge, this is the first description of TOSV meningitis acquired on the Island of Elba. However, the geographic proximity to areas where the disease is endemic and which have a very similar climate, suggest that phlebotomes occur on Elba. Despite millions of visiting tourists and an increasing number of TOSV infections around the Mediterranean Basin, TOSV is still rarely considered as the cause of aseptic meningitis in returning travellers. Either it is not diagnosed, or the manifestation rate of severe infections is very low. Patients returning from the Mediterranean and also from the Island of Elba and complaining of CNS symptoms should be tested for TOSV infection.

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A MEASLES OUTBREAK IN CROATIA, 2008

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We report an outbreak of measles in Croatia, involving 49 cases with onset of symptoms between end of April and June 2008. Cases occurred in Zagreb and Slavonski Brod but investigations indicated a common epidemiological link between these two geographically separate regions.

Introduction

Following an almost four-year period with zero indigenous measles cases notified in Croatia the disease reappeared during the second quarter of 2008. With the exception of an import-related outbreak in winter 2003-4, less than 10 measles cases have been reported annually since 2000, although none of them had been laboratory confirmed. Measles is a statutorily notifiable disease in Croatia since 1949.

In Croatia, all vaccinations offered to children within the universal immunisation schedule are mandatory and free of charge. Measles vaccination was first introduced in the national childhood vaccination schedule in 1968 at 12 months of age and was replaced by the combined measles, mumps and rubella vaccine (MMR) in 1976. A second dose was given at seven years of age as monovalent measles vaccine since 1968, and was replaced by MMR in 1994. During the period 1997-99, the second dose was recommended at 12 years of age. Vaccine coverage rates for the first MMR dose at two years of age in Croatia are estimated to have been above 90% since the mid-1980s, and more than 95% since 2004. Vaccination coverage estimates are done by administrative method based on data submitted annually by immunisation providers and verified by competent epidemiologists.

Sequence of events

The first notified case was a 27-year-old man who fell ill on 26 April 2008. He was hospitalized initially as a case of staphylococcal sepsis based on clinical suspicion, and identified as measles case only after his brother was hospitalized ten days later as a case of measles. Both patients are from the greater Zagreb area. Until 15 May, further five cases were notified from the same municipality as the index case, and included three community acquired cases and two visitors to the hospital where the index case was admitted (Figure 1). In the following weeks, the outbreak spread further in other municipalities of Zagreb area (community and nosocomial transmission), reaching a total of 29 cases (37 suspected), the last one with onset of symptoms on 20 June 2008.

In May, a measles outbreak was also reported in the province of Slavonski Brod, affecting 20 persons (32 suspected cases) of a

migrant Roma community (Figure 1). Members of this community had recently returned from abroad, most of them from Italy. Mistakenly, the Slavonski Brod outbreak was initially believed to be due to erythema infectiosum. The last case in Slavonski Brod fell ill on 30 May.

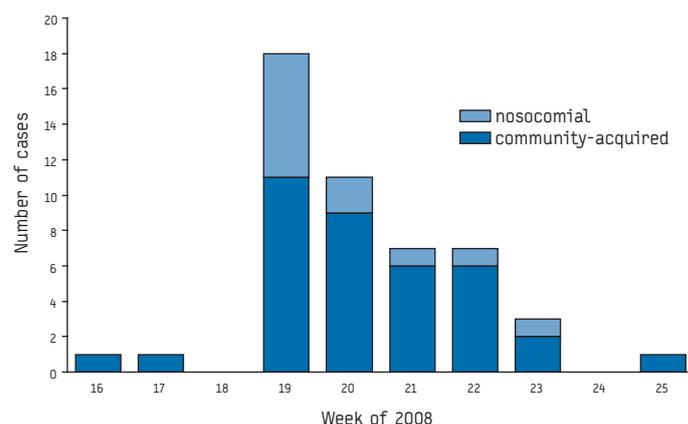
An additional case of measles was notified in a German tourist who stayed in Split and fell ill on 21 May, seven days after arrival to Croatia. However, there were no cases reported in connection with this case, so it was excluded from the analysis of the outbreak.

Laboratory and epidemiological investigations

Since the outbreak was first identified, 69 suspected cases of measles were notified. Of these, 40 (58%) were laboratory-confirmed using ELISA techniques on serum samples and/or polymerase-chain-reaction (PCR) analysis. Further four cases were epidemiologically linked and five were classified as clinical cases. The remaining 20 cases (35%) were discarded and excluded from further analysis.

Case classification was based on the European Commission case definition of measles [1]. In our classification a laboratory confirmed case corresponded to a confirmed case in the EC definition, an epidemiologically linked case corresponded to a probable case in the EC definition, and a clinical case corresponded to a possible case in the EC definition for which no laboratory information is

FIGURE 1
Cases reported in an outbreak of measles in Croatia, in 2008, by the week of onset of symptoms (n=49)



available. Discarded cases were clinical cases (possible cases in the EC definition) with negative serology and/or negative detection of measles virus/antigen from a clinical specimen.

Genotype D4 was identified in six PCR-positive cases all from cases reported in Zagreb area. There was no sequence diversity (unpublished data). Comparison of the isolated genotype with strains circulating in Europe is underway.

This outbreak was limited to greater Zagreb area (n=29, 59%) and the Slavonski Brod province (n=20, 41%). The mean age of all cases was 21 years (range 7 months - 50 years). The mean age of the cases from Zagreb was 27 years and that of the cases from the Slavonski Brod province was 12 years (Figure 2).

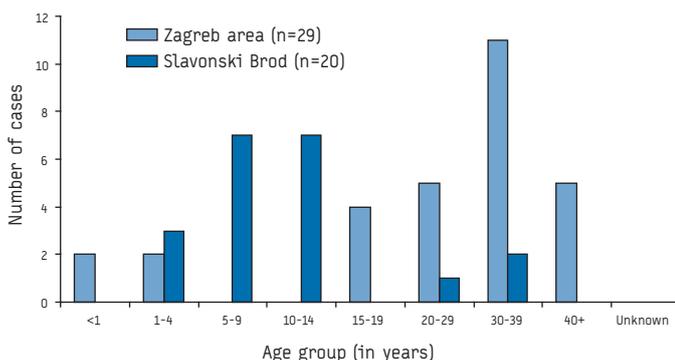
The vaccination status of cases was determined by interview and review of personal medical records. Overall, 32 cases had not been vaccinated against measles, three had received only one measles-containing vaccine (MCV), two cases had been vaccinated with two MCV doses and two had been vaccinated but the number of MCV doses was unspecified. In 10 cases the vaccination status was unknown. Of those with a known vaccination status there was a significant difference in the number of unvaccinated cases in the two affected areas: 16 out of 23 (70%) in Zagreb and all 16 (100%) in Slavonski Brod ($p<0.05$)

Of the 49 cases included in the outbreak, 11 (22%) were hospitalised and five (10%) had an unknown hospitalisation status. In two cases complications with pneumonia occurred. Nosocomial transmission was reported in 12 (24%) cases, all from Zagreb area.

Further investigations

Upon further enquiry to identify a possible source of infection and reveal further contacts, it transpired that a Roma girl developed a rash whilst visiting the family of the 27-year-old man in Zagreb whom we had identified as the outbreak index case. The paediatrician who suspected rubella referred the child for laboratory testing to the University Hospital for the Infectious Disease in Zagreb. However, the child never attended the clinic, because she and her mother left Croatia. They were both Italian citizens who were visiting Serbia and Croatia on their way to Germany.

FIGURE 2
Number of reported measles cases by area of notification and age group, Croatia, 2008 (n=49)



It was later revealed that this child and her mother had travelled from Italy to visit family members in the Slavonski Brod province before they visited the family in Zagreb. This led to the hypothesis that this child with an undiagnosed rash was the source of infection in both geographically separate areas of Croatia.

Control measures

After notification of this first generation of cases, a circular letter was sent to all health-care institutions notifying them of the outbreak and providing guidelines on reporting and investigating suspected measles cases.

To control the outbreak, the Department of Infectious Disease Epidemiology performed contact tracing, vaccinated susceptible contacts and recommended voluntary quarantine of susceptible contacts to those who could not be vaccinated due to contraindications to vaccination or because it was too late to vaccinate them because their exposure had occurred more than 72 hours before. Paediatricians were instructed to invite parents to vaccinate all previously unvaccinated children above 12 months of age. Recommendations for vaccination were also issued to healthcare workers without evidence of immunity. It is not known, however, how many people were vaccinated as a result of these outbreak control measures.

Discussion

With the outbreak described in this paper, Croatia joins some other European countries that have recently experienced a resurgence of measles [2]. The presence of pools of individuals in the general population and amongst members of the Roma community susceptible to measles infection still exists in Croatia and is brought to light when the measles virus is imported from abroad. A serological survey carried out on samples collected in 1999-2000 showed a high susceptibility to acquire measles in those aged 16-40 years [3]. This conclusion is compatible with our findings, as the proportion of cases in this age group (particularly in Zagreb) was high. It is believed that the vaccination coverage amongst members of the Roma community living in Croatia, i.e. non-migrating Roma, does not differ largely from the coverage of the rest of the population, since they are well integrated into the primary health care system, which provides immunisation. However, migratory members of the Roma community, who spend a substantial time abroad do not benefit from the immunisation system, although the services are free of charge and available to everyone regardless of insurance status and citizenship. There is, therefore, a need to improve vaccination coverage using innovative ways in such groups that are hard to reach by normal vaccination programmes. In doing so, the herd immunity would be maintained at level conducive of measles elimination from Croatia.

The outbreak clearly demonstrates the role of nosocomial transmission in the spread of infection. Nosocomial transmission of measles virus has also recently been described elsewhere [4,5]. In the import-related outbreak in winter 2003-4, nosocomial transmission had also played a significant role (unpublished data). This shows the importance for health-care workers to be fully vaccinated against measles if they have no history of the disease. This investigation also demonstrates the potential of measles to be misdiagnosed as other infectious diseases presenting with a rash and fever. It is also evident that at least in some healthcare settings, health personnel's awareness of measles should be increased, in order to suspect measles in a timely manner. This also stresses the

importance of laboratory testing of suspected measles cases and to identify the circulating measles virus genotype.

As part of the measles and rubella elimination plan by 2010 from the WHO European Region [6], the Croatian Ministry of Health has on several occasions sent circular letters to all healthcare workers urging all suspected cases of measles and rubella to be notified immediately, emphasizing the need for enhanced surveillance, and providing instructions on sampling and transportation of specimens to the national measles and rubella reference laboratories affiliated to the National Institute of Public Health.

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AN OUTBREAK OF NON-TYPEABLE MRSA WITHIN A RESIDENTIAL CARE FACILITY

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In a household setting within a residential care facility for visually and intellectually disabled people, a resident (index case) was diagnosed with dermal abscesses caused by a methicillin-resistant *Staphylococcus aureus* (MRSA) which was non-typeable by standard pulsed-field gel electrophoresis. In the process of 'search and destroy', all residents and staff in contact with the index case (a total of 200 people) were screened for MRSA. Five people (three personnel and two residents) carried non-typeable MRSA and were treated with antibiotics to eradicate the infection. The 'search and destroy' efforts did not result in the identification of a source. Goats and rabbits which were kept on the premises tested negative for MRSA. The condition of the index case is improving. Further restrictive measures were implemented within the facility to prevent wider spread of the MRSA. This discovery and spread within a residential care facility of a non-typeable MRSA which is often associated with livestock, is remarkable.

Introduction

A new methicillin-resistant *Staphylococcus aureus* (MRSA) isolate belonging to multi-locus sequence type ST398 was first described in a French study in 1998 [1]. No further reports concerning ST398 MRSA strains were mentioned until 2004, when a MRSA isolate belonging to ST398 was detected in the Netherlands [2]. This isolate could not be typed with *Sma*I pulsed-field gel electrophoresis (PFGE) and was termed non-typeable MRSA (NT-MRSA). All NT-MRSA isolated so far belong to ST398.

Voss and colleagues were the first to report the isolation of NT-MRSA strains from people taking care of pigs [2]. Since then, NT-MRSA has become increasingly common among Dutch MRSA isolates. In 2007, 29% of the MRSA isolates forwarded to the Dutch National Institute of Public Health and the Environment (Rijksinstituut voor Volksgezondheid en Milieu, RIVM) belonged to this group of MRSA. Publications about a connection between NT-MRSA in various animal species and NT-MRSA in humans soon followed. A French study reported increased NT-MRSA carriage rate in pig farmers caused by transmission of the strain ST398 [1]. A later retrospective case-control study showed a strong association between human NT-MRSA carriage and contact with pigs or calves [3]. New data revealed that family members living on pig farms can also be NT-MRSA carriers, even when they have not been in direct

contact with animals [4]. In reaction, screening of various animal species was performed. A survey of pigs in Dutch slaughterhouses showed that nearly 40% of the pigs were colonised with NT-MRSA ST398 [5]. NT-MRSA has also been isolated from horses and poultry [6,7].

On the basis of these results, it can be concluded that an NT-MRSA reservoir is established within a variety of animal species and could spread to humans. The emergence of NT-MRSA outside hospitals threatens the MRSA 'search and destroy' policy in Dutch healthcare facilities. It was considered only a matter of time before NT-MRSA would be transmitted from animals via farmers into healthcare settings. Indeed, both NT-MRSA colonisation of personnel and patients, and outbreaks within Dutch hospitals have recently been described [8-10]. It has been suggested that MRSA ST398 isolates are less virulent than other MRSA strains and have limited capacity to spread between humans, but recent reports have shown clinical manifestations of NT-MRSA such as wound infections [4] and endocarditis [11].

Here we describe an outbreak of NT-MRSA in a residential care facility for visually and intellectually disabled people.

One of the residents (index case) was diagnosed with abscessing acne and chronic hydradenitis in his armpits, loins, scrotum and between the buttocks. The index case was fully blind, had a severe intellectual disability and had been suffering from this skin condition since 2004. *S. aureus* isolated from wound swabs in the period between 2004 and 2007 were methicillin-sensitive. The patient was treated with several antibiotics (tetracycline, erythromycin, flucloxacillin, trimethoprim/sulfamethoxazole, clindamycin, minocycline, rifampicin), but this did not result in a significant clinical improvement. In October 2007, the abscesses were surgically treated, in combination with vitamin A therapy, but without success. All swabs taken at that time were suddenly positive for MRSA. Additional screening showed that nose, throat and perineum were colonised with MRSA.

The risk of MRSA transmission within the residential care facility to other residents and personnel was considered high because the index patient had already suffered from staphylococcal disease for

a long period. In the Netherlands, active 'search and destroy' efforts are taken to stop further transmission of MRSA within healthcare settings. The residential care facility therefore contacted the department of infectious diseases of the local municipal health service for advice. A multidisciplinary outbreak team was set up to assess all possible routes of MRSA transmission within the facility, and to identify all at-risk contacts of the index case.

Methodology and results

Assessment of the risk of MRSA transmission

The index patient lived in a household-like setting together with seven other residents and 15 staff members. Other contacts included staff members who also worked at various other units within the residential care facility, such as doctors and nurses, household, day care and facility personnel. The unit consisted of two groups living separately but sharing sanitation. The whole residential care facility has 35 units, situated in various buildings on the premises.

The outbreak team decided to screen all residents living and personnel working in the same unit as the index case, as well as doctors, nurses and family who had been in direct contact with the index case. A total of 43 people were identified as being at risk. Nose and throat cultures were collected from all those screened.

In addition, perineum and/or wound cultures were set up from samples from residents.

Preventive measures

In order to reduce the risk of further MRSA transmission, hygienic measures were implemented around the index case. His private room as well as the sanitation area he was using were disinfected daily, and nurses wore gloves, aprons and surgical masks during direct contact with the index case. He started using a private shower and toilet within the sanitary room. No other residents were allowed in the sanitary room while the index case was there, and the room was cleaned with hypochlorite after he used it. The index case's social contacts with other residents who lived in other units were restricted to a minimum, organised group day care was changed into private day care, and the whole unit is considered contaminated until the cultures of all included individuals are MRSA negative.

Screening results

Two other residents and three staff members from the same unit as the index case tested positive for MRSA. Three of them had positive nose cultures only, one had positive nose, perineum and skin cultures, and one person was MRSA-positive in nose and

TABLE 1

Antibiogram of isolates from residents and staff, NT-MRSA outbreak, the Netherlands, 2007

| | Resident A (index) | Resident A (index) | Resident B | Resident C | Staff A | Staff B | Staff C |
|------------------------------|--------------------|--------------------|------------|------------|----------|----------|----------|
| Date of sample | Nov 2005 | Oct 2007 | Oct 2007 | Oct 2007 | Oct 2007 | Oct 2007 | Oct 2007 |
| Penicillin | | R | R | R | R | R | R |
| Flucloxacillin | S | R | R | R | R | R | R |
| Gentamicin | S | R | R | R | R | I | R |
| Trimethoprim/Sulfamethoxazol | S | S | R | R | R | S | R |
| Doxycylin | | R | R | R | R | R | R |
| Erythromycin | R | R | R | R | R | R | R |
| Clindamycin | R | R | R | R | R | R | R |
| Rifampicin | | S | S | S | S | S | S |
| Fusidine acid | | S | | | | | |

S: sensitive; R: resistant; I: intermediate sensitive.

TABLE 2

Isolate typing, NT-MRSA outbreak, the Netherlands, 2007

| | Resident A (index) | Resident A (index) | Resident B | Resident C | Staff A | Staff B | Staff C |
|----------------|--------------------|--------------------|------------|------------|----------|----------|----------|
| Date of sample | Nov 2005 | Oct 2007 | Oct 2007 | Oct 2007 | Oct 2007 | Oct 2007 | Oct 2007 |
| Spa-type | Not done | t2383 | t011 | t2383 | t011 | t2383 | t2383 |
| SSCmec | Not done | IV | IV | IV | IV | IV | IV* |
| PVL | Not done | Negative | Negative | Negative | Negative | Negative | Negative |
| MLST | Not done | ST398 | ST398 | ST398 | ST398 | ST398 | ST398 |
| PFGE SmaI | Not done | NT | NT | NT | NT | NT | NT |
| PFGE Crf9I | Not done | ** | ** | ** | ** | ** | ** |

* SSCmec typing by multiplex PCR-typing according to the method of Kondo *et al.* [12] showed a PCR product for multiplex 1 and 3, but not for multiplex 2.

** PFGE Crf9I is shown in Figure 1.

PVL: Panton-Valentine leucocidin; MLST: multi-locus sequence typing; PFGE: pulsed-field gel electrophoresis.

throat. These results indicated considerable MRSA transmission within the unit and prompted the expansion of the ring for MRSA screening to the relevant direct contacts of all six MRSA-positive individuals. This resulted in the screening of a further 160 people. In this group, no new MRSA infections were detected; the outbreak seemed to be restricted to the unit of the index case. Personnel who work at various units, such as cleaning personnel and medical doctors, did not test positive for MRSA.

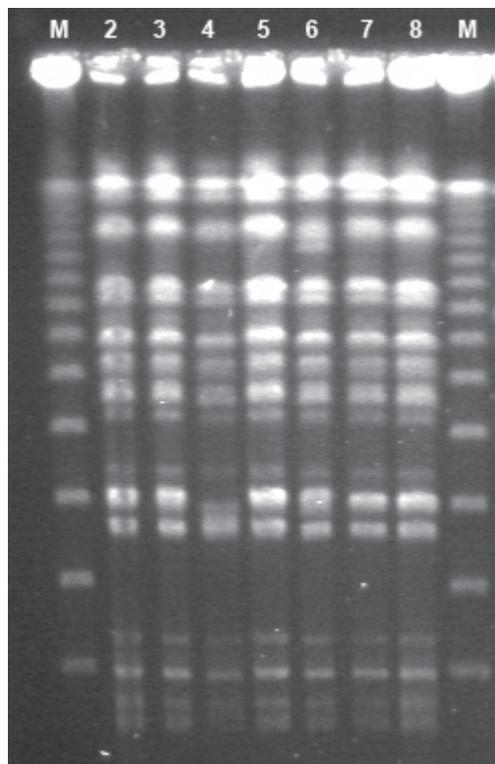
MRSA typing

In order to evaluate the transmission of MRSA strains, the bacterial isolates were typed. All six MRSA isolates had an almost identical antibiogram (see Table 1) and carried staphylococcal cassette chromosome *mec* (SSC*mec*) type IV* according to the method of Kondo *et al.* [12] (see Table 2).

All isolates were Panton-Valentine leucocidin (PVL)-negative and their genome did not contain the restriction site *Sma*I (Table 2). Therefore, they could not be typed by PFGE using *Sma*I and were considered NT-MRSA. In PFGE analyses using the restriction enzyme *Crf9I* (a neoschizomer of *Sma*I that is less sensitive to methylation), all isolates showed very similar banding patterns (Figure 1).

FIGURE 1

PFGE of *Crf9I* macro-restriction fragments of non-typeable (ST398) isolates, NT-MRSA outbreak, the Netherlands, 2007



Lane 2: resident A (index), lane 3: resident B, lane 4: resident B, lane 5: staff B, lane 6: staff A, lane 7: resident C, lane 8: staff C.
M: molecular length marker.
PFGE: pulsed field gel electrophoresis.

Spa-typing revealed two *spa*-types t011 and t2383, both belonging to the ST398 family, which in the Netherlands are primarily found among livestock (cattle and pigs) and people working with livestock (see www.spaserver.ridom.de). Two patients carried *spa*-type t011. The remaining four isolates, including the strain obtained from the index patient, had an uncommon *spa*-type t2383. Multi-locus sequence typing (MLST) confirmed that all strains belonged to the ST398 family (www.mlst.net).

Outbreak source and transmission

The index patient's lesions continued producing pus. The index could thus have functioned as a reservoir and may have maintained the outbreak. It is unclear if the index was the source of the outbreak.

This outbreak in a residential care setting indicates that NT-MRSA is also a public health issue. NT-MRSA is most often associated with direct contact with pigs or calves [4,13], but none of the MRSA-positive individuals had any contact with livestock. However, rabbits, chickens and goats were living on a farm on the premises of the residential care facility. The outbreak team decided to screen the goats and rabbits because various animals have been described as a source of MRSA and there had been sporadic contact between the residents and these animals. All cultures of the animals' anterior nares (three goats and four rabbits) were MRSA-negative.

A definite source for the NT-MRSA could not be traced. The outbreak of NT-MRSA was most probably caused by direct human to human transmission facilitated by the intensive contact between the residents and staff living and working in the unit. The contact between staff and clients is randomly organised, frequent and intense. An exact route of NT-MRSA transmission within the unit is therefore indistinct. Furthermore, there was no significant difference between MRSA-positive and negative staff regarding the intensity of physical contact with MRSA-positive residents.

MRSA eradication

To eradicate the MRSA, all MRSA-positive residents and staff (except the index case) were given oral and topical therapy (mupirocin nose gel and washing with chlorhexidine for five days), followed by three successive control cultures taken from the nose and throat. MRSA-positive residents were temporarily banned from group activities and MRSA-positive staff had to stay at home during the period of eradication. The residents' sanitary room and sleeping rooms were cleaned daily. Also hand-touch sites, such as door handles were thoroughly cleaned on a daily basis. All control cultures taken after completion of the eradication therapy tested MRSA-negative.

The preventive measurements were restricted to the unit of the index case. To date, the index patient is being treated with a combination therapy with rifampicin and trimethoprim/sulfamethoxazole and surgical incision of the abscesses. The skin lesions are slowly diminishing, and recent cultures taken from wounds, nose and throat in late December were MRSA-negative. Once his skin lesions have healed, eradication therapy will be started.

Discussion and conclusions

This MRSA outbreak in a residential care setting highlighted particular challenges. Firstly, the healthcare setting described in this article is not a hospital, but a permanent care facility for people with visual and intellectual disabilities. The outbreak

caused commotion among the staff members, and they had a lot of practical questions as they were unfamiliar with MRSA and an MRSA-outbreak in particular. Furthermore, it turned out that the use of gloves, surgical masks and aprons during washing and clothing was perceived as threatening by the clients.

The restriction of the index case's social contacts was difficult to implement. His wounds were resolving slowly, and hygiene measures were lifted to some extent after six months. In addition, follow-up samples of the wounds proved to be MRSA-negative under antibiotic treatment. It was therefore decided that after careful bandaging of the wounds, social contacts could be allowed within the unit.

To our surprise, two different *spa*-types were discovered by molecular typing. The rare *spa*-type t2383 only contains the first two repeats (08-16) of the seven repeats present in the t011 gene (08-16-02-25-34-24-25). Considering that the strains share the same antibiogram and have very similar PFGE patterns, it is tempting to speculate that the initial introduced strain had *spa*-type t011. It could very well be that one of the individuals carrying the t011 strain was the primary source for the other case. After a deletion of five repeats, this strain could then have colonised the cases infected with the t2383 strain. Alternatively, we can not exclude that both *spa*-types were introduced independently.

NT-MRSA is not only a Dutch problem, but has been discovered in a number of European countries, as well as in Canada, China and Singapore [14-16]. *Spa*-type t2383 (Figure 2) is a rare relative of t011 (Figure 3) (see <https://mrsa.rivm.nl/flash/flash.aspx>).

NT-MRSA transmission from human to human is relevant for the impact of NT-MRSA in public health care. Inter-human transmission of NT-MRSA has been described earlier within families of animal

farmers [2] and on a larger scale in patients and personnel of a Dutch hospital [9]. This outbreak within a non-hospital healthcare setting adds proof for the potential of NT-MRSA for inter-human transmission. Therefore, NT-MRSA might be able to gain a foothold in the human population.

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An earlier report of this outbreak was published in Dutch [17].

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FIGURE 2

NT-MRSA *spa*-type t2383 isolated in the Netherlands in 2007-2008

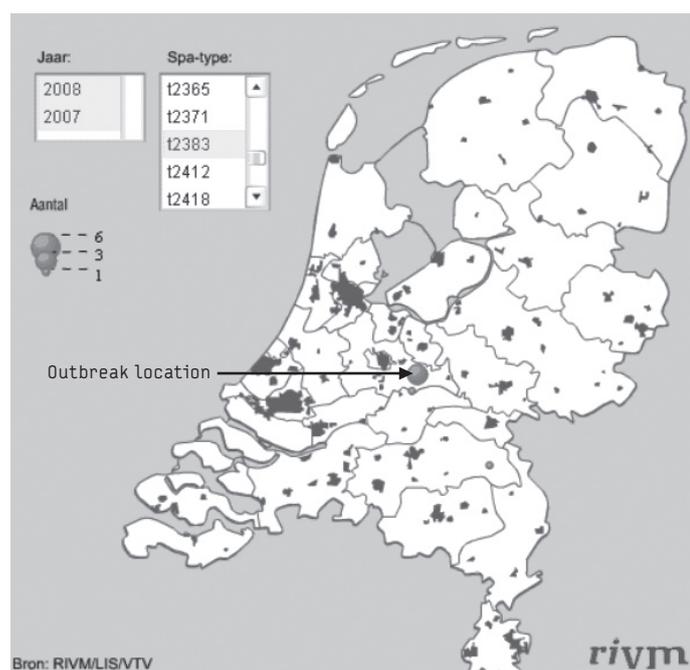
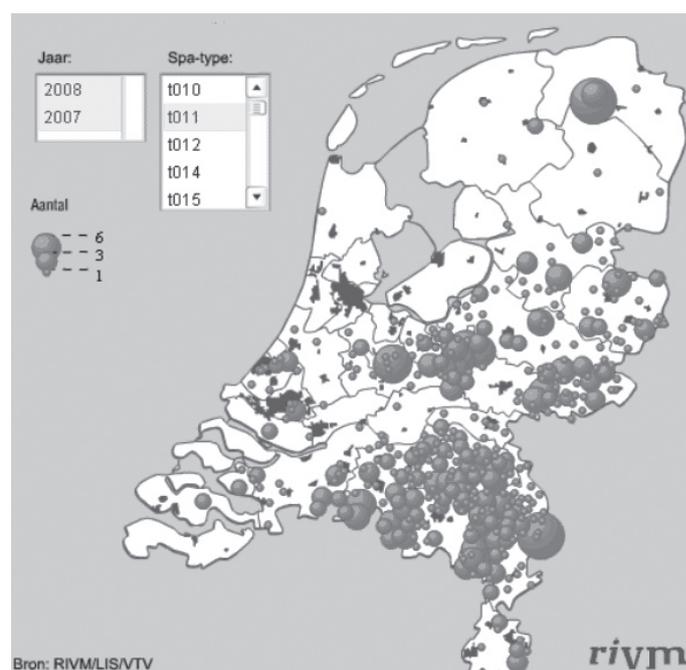


FIGURE 3

NT-MRSA *spa*-type t011 isolated in the Netherlands in 2007-2008



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