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

Vol. 16 | Weekly issue 16 | 21 April 2011

ecdc EUROPEAN CENTRE FOR DISEASE PREVENTION AND CONTROL

www.eurosurveillance.org

Measles resurgence in Belgium from January to mid-April 2011: a preliminary report

M Sabbe (martine.sabbe@wiv-isp.be)[1], D Hue[1], V Hutse[1], P Goubau[2,3]
1. Scientific Institute of Public Health, Brussels, Belgium
2. Department of Virology, Université Catholique de Louvain, Brussels, Belgium
3. National committee for the elimination of measles and rubella in Belgium

Citation style for this article:
Sabbe M, Hue D, Hutse V, Goubau P. Measles resurgence in Belgium from January to mid-April 2011: a preliminary report. Euro Surveill. 2011;16(16):pii=19848. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19848

Article published on 21 April 2011

From 1 January to 14 April 2011, a total of 155 measles cases were notified in Belgium, whereas throughout 2010, there were only 40. Of the 103 cases with known vaccination status, 87% had not been vaccinated with measles-mumps-rubella vaccine. The resurgence of measles is the consequence of insufficient vaccine coverage in previous years. Efforts to communicate the benefits of measles vaccination to the public and to advise health professionals on control measures and outbreak management are ongoing.

Resurgence of measles in Belgium in 2011

Since the beginning of 2011, Belgium has seen an increase in the number of measles cases. As of 14 April 2011, a total of 155 cases were reported through mandatory notification. In 2009 and 2010, only 33 and 40 cases, respectively, were reported. This in contrast to the period between April 2007 and May 2008, when a large measles outbreak, with more than 130 cases, occurred in Orthodox Jewish families in Belgium [1].

Background

Since 2003, paediatricians in a sentinel network surveillance system (PediSurv) and general practitioners in Belgium have recorded the number of measles cases [2]. Mandatory notification of the disease was adopted in the French-speaking community (in Wallonia) in 2006 and in the Flemish-speaking community (in Flanders) and in Brussels in 2009, as recommended in the national plan for elimination of measles and congenital rubella [3]. Physicians and microbiologists have to report suspected measles cases without delay to the regional health authorities or to PediSurv [2]. Laboratory confirmation is strongly recommended for sporadic cases, preferably by testing of oral fluid. Samples are sent to the Belgian National Reference Laboratory, where detection of measles virus-specific IgM and measles virus detection by PCR is carried out, as well as genotyping of the circulating viruses [4]. Notification forms are collected and analysed centrally at the Belgian Scientific Institute of Public Health.

Vaccination of measles-mumps-rubella (MMR) vaccine was introduced in Belgium in 1985 (one dose) and 1995 (two doses). The current measles vaccination strategy consists of two doses of MMR vaccine, the first at 12 months of age and the second between the age of 10 years and 13 years. Vaccination is free of charge and systematically offered through the childhood immunisation and school health programmes. Immunisation status is verified by childcare and public school services. If necessary, a catch-up dose is offered at the age of 5–7 years and 14–16 years. Despite these programmes, vaccination coverage of more than 95% with one dose of MMR vaccine – needed to meet the measles elimination goal for 2010 [5] – was reached in 2008 in only one of the three regions in Belgium (Flanders) (Table). Coverage of two MMR doses is lagging further behind. The coverage for children aged 18–24 months and second-year secondary school students (aged 14–16 years) is estimated in Flanders by a stratified multistage random sampling method; in Wallonia, a cluster sample survey method is used [6-8], The coverage shown in the Table is as reported by the communities, who are in charge of the vaccine programmes.

Outbreak description

Measles resurgence in Belgium this year began with an outbreak in anthroposophical schools in Ghent (Flanders) in February. A total of 56 children were affected – most of their parents were opposed to MMR vaccination. At the same time, outbreaks and sporadic cases were reported elsewhere in the country, especially in Brussels and Wallonia (Figure 1).These outbreaks often occurred after people had travelled to France, with spread of the measles virus to unvaccinated family members or pupils at school. Besides the outbreak in Ghent, we identified at least six small interfamilial outbreaks, two in schools and one in a Roma community. In 16 cases, an epidemiological link or recent ski trip to France was reported, and one case fell ill after travelling to Italy. In France, more than 3,700 measles cases were reported in January and February 2011 [9].

Virus transmission is still ongoing, with 151 cases reported in Belgium during January to March 2011, compared with five for the same period in 2010 (Figure 2). A further four cases were reported during 1 to 14 April 2011.

Table

Vaccination coverage of measles-mumps-rubella vaccine in Belgium by region, 1995–2009[a]

Region and MMR dose	Percentage MMR vaccination coverage							
	1995	1999	2000	2003	2005	2006	2008	2009
Brussels								
First dose	68.1	–	74.5	–	–	91.1	–	–
Second dose	–	–	–	–	–	70.5	–	–
Flanders								
First dose	–	83.4	–	–	94.0	–	96.6	–
Second dose	–	–	–	–	83.6	–	90.6	–
Wallonia								
First dose	–	82.4	–	82.5	–	89.0	–	92.4
Second dose	–	–	–	–	–	70.5	–	75.5

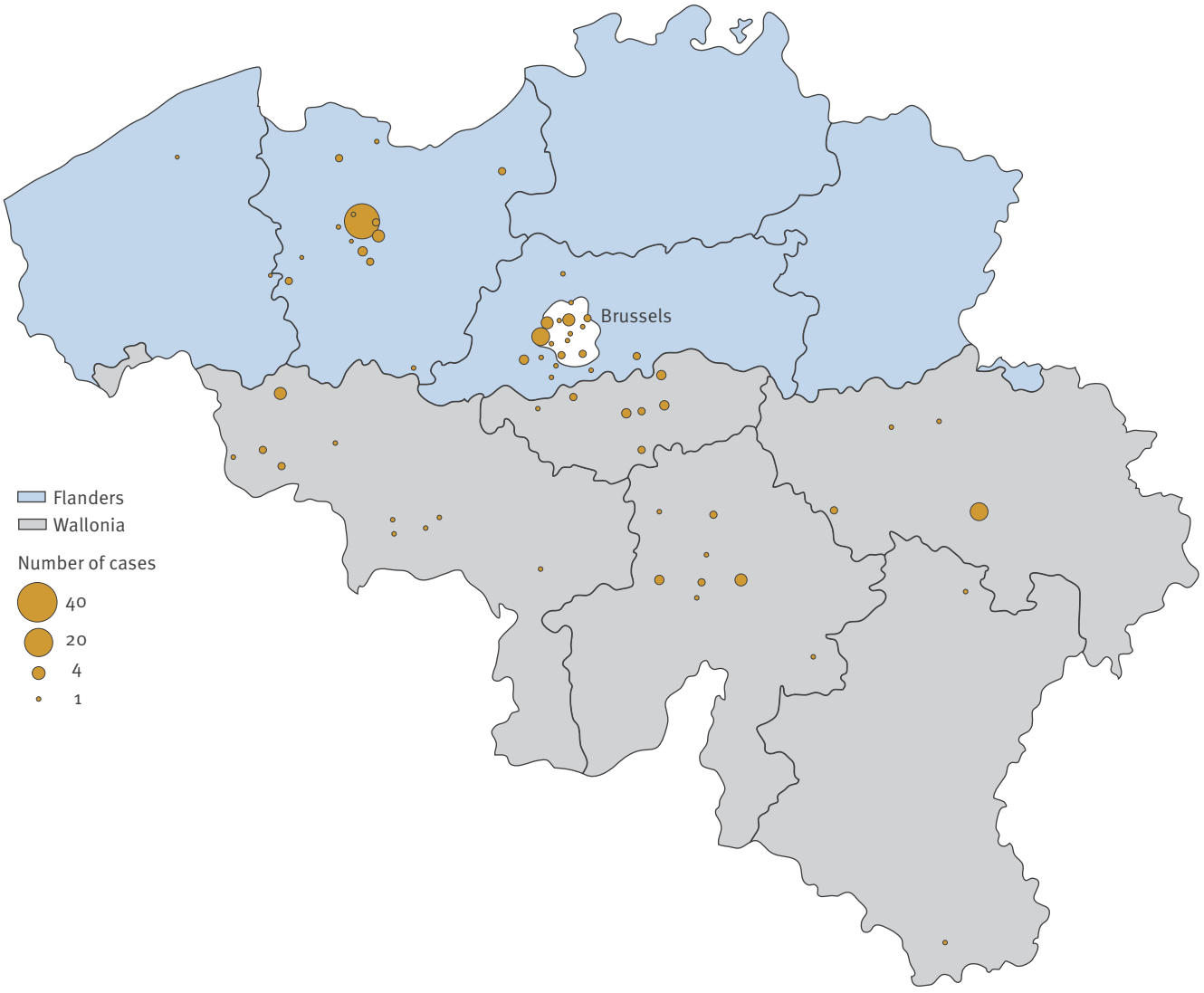
MMR: measles-mumps-rubella.

[a] Vaccine coverage as reported by the French-speaking and Flemish-speaking communities.

Source: [6-8].

Figure 1

Geographical distribution of measles cases in Belgium, January–March 2011 (n=151)



The internal lines represent the provinces. The dots represent the number of cases by municipality.

Source: Scientific Institute of Public Health, Brussels, Belgium. Preliminary data.

Details of cases

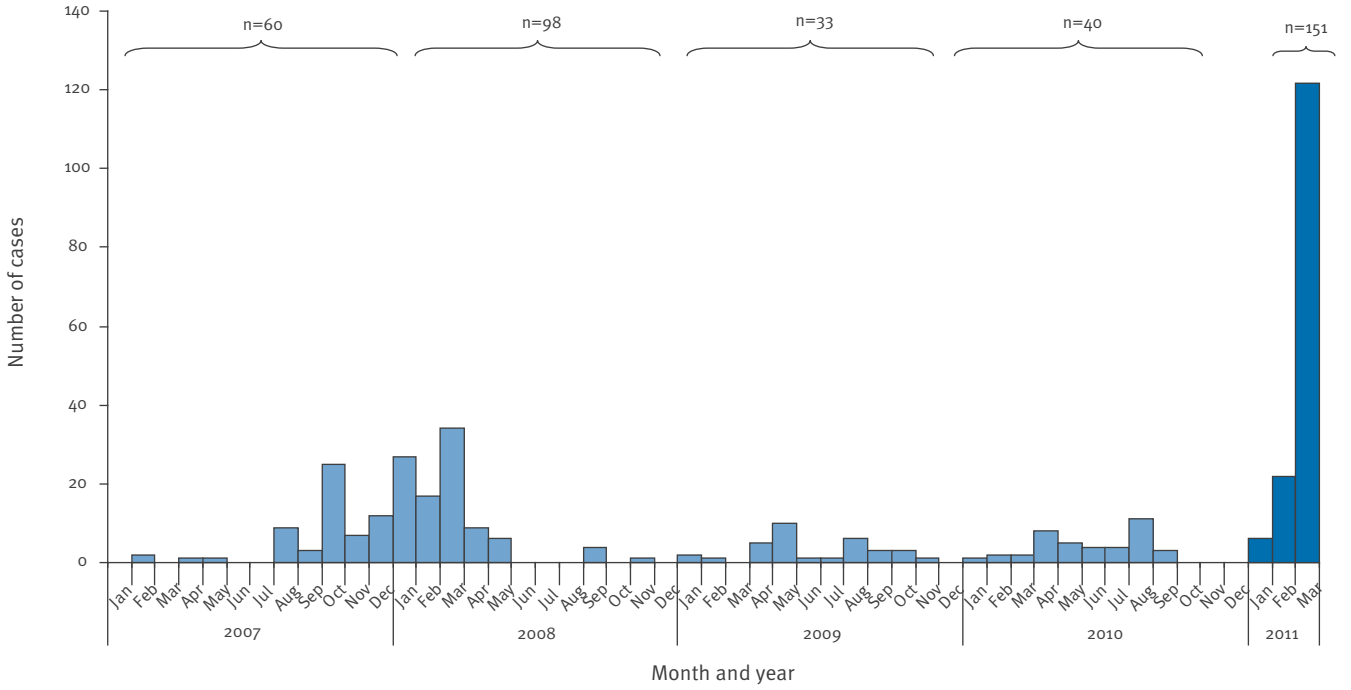
Of the 155 Belgian cases identified between January and 14 April 2011, 147 had known date of birth and date of symptom onset. Their median age was nine years (range: 0–20 years). The median age of the cases not belonging to the outbreak in anthroposophical schools (n=99) was 12 years (range: 0–49 years). One third of all the cases were aged 15 years or older (Figure 3).

Among the 12 cases aged less than one year, eight were laboratory confirmed. Four cases were younger than nine months.

Vaccination status was known for 103 cases (66%). Of these, 90 had not been vaccinated with MMR vaccine. Of the 13 vaccinated cases, all had received one dose

Figure 2

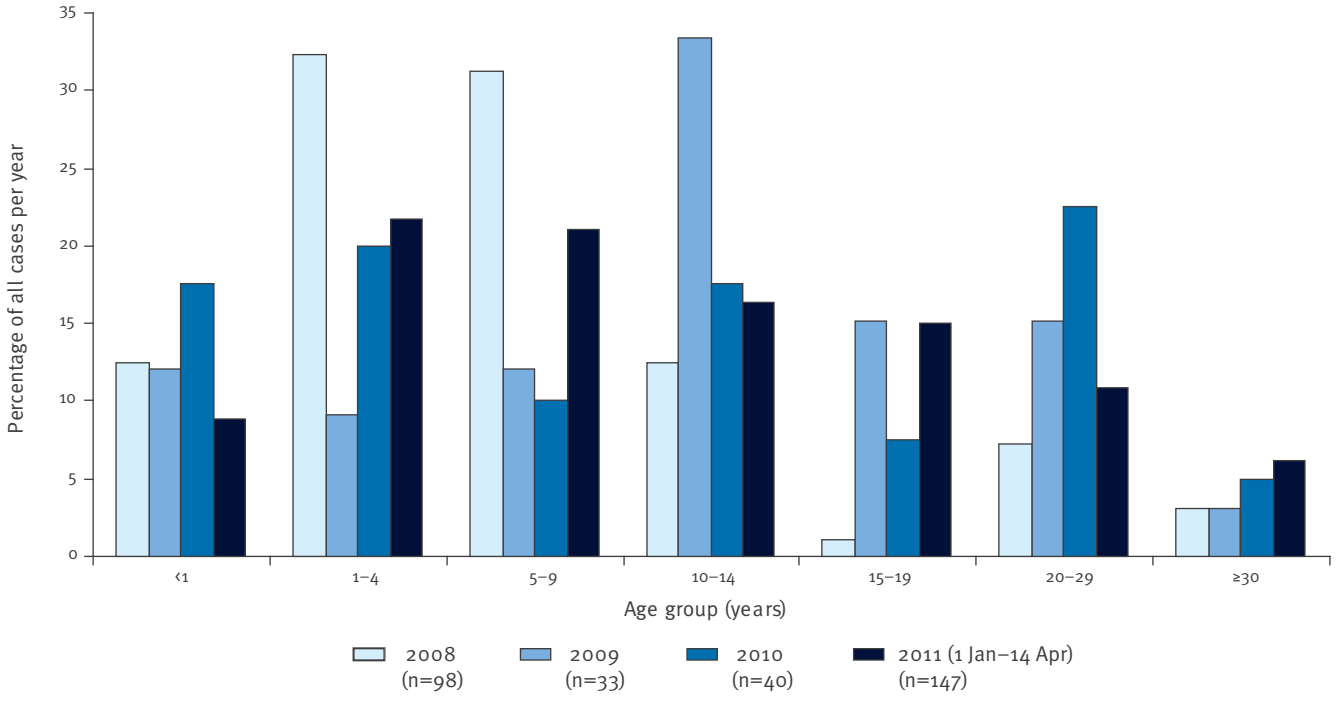
Reported measles cases, by month of symptom onset, Belgium, January 2007–March 2011



Source: Scientific Institute of Public Health, Brussels, Belgium. Preliminary data.

Figure 3

Reported measles cases with known date of birth, by age group, Belgium, 1 January 2008–14 April 2011



Source: Scientific Institute of Public Health, Brussels, Belgium. Preliminary data.

of MMR vaccine (Figure 4), but sometimes this could not be verified on the vaccination chart. No recently vaccinated measles case was reported. In the cases older than one year, and thus old enough to be vaccinated, the main reasons for non-vaccination were their parents' anthroposophical beliefs (55%), anti-vaccination counselling of the paediatrician resulting in parental refusal (26%) or vaccination could not be carried out due to circumstances such as illness or travelling (13%).

Complications

Hospitalisation was required for 19 patients. Seven cases were diagnosed with pulmonary complications: in one infant, this was followed by septic shock. One case of encephalitis occurred in a man in his late thirties. No deaths were reported.

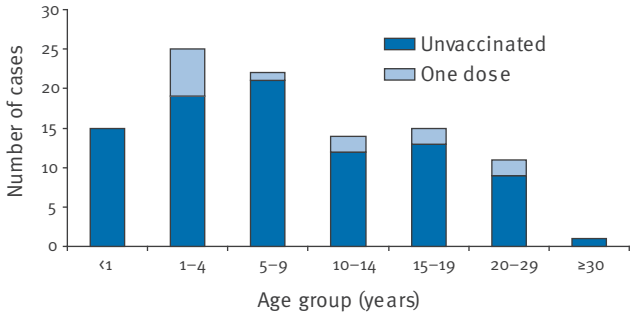
Laboratory results

More than two thirds (n=108) of the cases reported as of 14 April 2011 have been confirmed, either by detecting measles virus-specific IgM antibodies or viral RNA by reverse transcription-PCR (67 cases) or by an epidemiological link with a laboratory-confirmed case (41 cases). Preliminary results from the National Reference Laboratory showed that all viruses had genotype D4. However, two different subvariants of D4 were distinguished. The first subvariant strain MVs/Ghent. BEL/09.11/1/[D4], isolated during the outbreak in Ghent, is clearly related to MVs/Hamburg.DEU/03.09/[D4]. A second subvariant strain, MVs/Brussels. BEL/08.11/[D4], detected in Wallonia, is indistinguishable from strains reported by reference laboratories in France (MVs/Paris.FRA/18.10/[D4]).

D4-Hamburg is a new strain of measles virus imported from London, United Kingdom, to Hamburg, Germany, in December 2008 [10]. D4-Hamburg has been present in Europe for more than two years and has led to more than 25,000 cases in 12 countries. Its spread was mainly but not exclusively associated with travelling Roma.

Figure 4

Known vaccination status of measles-mumps-rubella vaccine of measles cases by age group, Belgium, 1 January–14 April 2011, preliminary data (n=103)



Source: Scientific Institute of Public Health, Brussels, Belgium. Preliminary data.

Control measures

Several control measures were implemented by local health authorities, according to the guidelines of the public health surveillance of the regions. Vaccination campaigns were organised in the anthroposophic schools in Ghent. Targeted information to health professionals and schools were sent. The national committee for the elimination of measles and rubella issued a press release, gave interviews on television and published articles in the press to inform the general public about the outbreaks and the need to be vaccinated. The main recommendations are for people to undergo vaccination according to the national immunisation schedule and to propose post-exposure vaccination, depending on age, time since exposure and existence of underlying diseases.

Discussion

Although measles incidence rate in 2009 was low, at 4 per 1,000,000 population, it did not meet the measles virus elimination indicator of less than one measles case per 1,000,000 population [5]. This suggests that progress has been made in Belgium towards elimination, but the current measles resurgence is not unexpected, given the insufficient vaccination coverage of MMR vaccine in Belgium in the past, allowing for silent accumulation of susceptible individuals. Current coverage, as reported by the French-speaking and Flemish-speaking communities, at 18–24 months of age with at least one dose is 92.4% in Wallonia and 96.6% in Flanders [6-8].

During outbreak investigations, several cases were identified who had not been notified to the local health authorities. This suggests that data available through the routine notification system underestimate measles incidence. Failure to notify such cases can be explained by no medical consultation for secondary cases in the same family plus insufficient knowledge or low motivation of some doctors regarding the notification procedure. The fact that measles only became mandatorily notifiable in 2009 for all the Belgian territory may also contribute to the underreporting.

The existence of groups with low measles vaccine coverage due to opposition to vaccination for religious or philosophical reasons or fear of side effects has been identified as one of the major barriers to achieve measles elimination in Europe [11]. In Belgium, anthroposophical schools, in which most of the children are unvaccinated, are mainly located in Flanders; only few are in Brussels and Wallonia. Other groups were affected by measles virus in Brussels and Wallonia – for example. a Roma community and families opposed to vaccination due to fear of side effects. Patients attending medical practices in which attention is not paid to their vaccination status, presumably due to reluctance or negligence, can also play a role in low vaccination coverage.

This resurgence of measles in Belgium highlights the need to improve and maintain high vaccination

coverage, along with disease surveillance and outbreak-control capabilities. Our findings also draw attention to the need to sensitise health professionals and raise their awareness of the issues through medical education. Convincing parents and health professionals reluctant to vaccinate children with MMR vaccine will be a challenge. Case investigation of every single measles case is a prerequisite to achieving the goal of measles elimination by 2015, planned by the World Health Organization Regional Office for Europe [12].

Acknowledgements

The authors would like to thank all GPs and paediatricians of PediSurv, our colleagues from the local public health surveillances and the members of the national committee for the elimination of measles and rubella in Belgium.

References

1. Lernout T, Kissling E, Hutse V, De Schrijver K, Top G. An outbreak of measles in orthodox Jewish communities in Antwerp, Belgium, 2007-2008: different reasons for accumulation of susceptibles. Euro Surveill. 2009;14(2):pii=19087. Available from: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19087
2. Sabbe M, Lernout T, Dupont Y, Quoilin S. The Belgian Paediatric Surveillance Unit "PediSurv": more than counting cases. Pediatr Infect Dis J. 2009;28(60):e73..
3. Sabbe M. Hue D. Elimination of measles and rubella in Belgium. Action plan 2009-2010. Report No.:D/2009/2505/008. Brussels: Institute of Public Health; 2009.
4. Hutse V, Van Hecke K, De Bruyn R , Samu O, Lernout T, Muyembe JJ, et al. Oral fluid for the serological and molecular diagnosis of measles. Int J Infect Dis. 2010;14(11):e991-7.
5. World Health Organization (WHO) Regional Office for Europe. Eliminating measles and rubella and preventing congenital rubella infection: WHO European Region strategic plan 2005-2010. Copenhagen: WHO Regional Office for Europe; 2005. Available from: http://www.euro.who.int/__data/assets/pdf_file/0008/79028/E87772.pdf
6. Hoppenbrouwers K, Vandermeulen C, Roelants M, Boonen M, Van Damme P, Theeten H, et al. Studie van de vaccinatiegraad bij jonge kinderen en adolescenten in Vlaanderen in 2008. 2009. Vaccine coverage survey in young children and adolescents in Flanders 2008. 2009 [Accessed 21 Apr 2011]. Flemish. Available from: http://www.google.co.uk/url?sa=t&source=web&cd=2&ved=0CBwQFjAB&url=http%3A%2F%2Fwww.zorg-en-gezondheid.be%2FWorkArea%2Flinkit.aspx%3FLinkIdentifier%3Did%26ItemID%3D22784&ei=EXKwTc-iIovUsga04pT4Cw&usg=AFQjCNHuyAcVSADPcKNH4F8mfh_eogg3vA
7. Robert E, Swennen B. Onderzoek naar de vaccinatietoestand van kinderen van 18 tot 24 maanden in het Brussels Hoofdstedelijk Gewest, december 2006. [Vaccine coverage study in chidren of 18 to 24 months in Brussels, December 2006]. ULB, Ecole de Santé Publique. [Accessed 21 Apr 2011]. Flemish. Available from: http://www.observatbru.be/documents/graphics/rapports-externes/onderzoek-naar-de-vaccinatietoestand-van-kinderen-van-18-tot-24-maanden-in-het-brussels-hoofdstedelijk-gewest.pdf
8. Robert E, Swennen B. Enquête de couverture vaccinale des enfants de 18 à 24 mois en communauté française (Bruxelles excepté). Novembre 2009. PROVAC-ULB; 2010. Vaccine coverage survey in children of 18 to 24 months in the French community (except Brussels). November 2009. PROVAC-ULB, Ecole de Santé Publique - ULB; 2010. [Accessed 21 Apr 2011]. French. Available from: http://www.sante.cfwb.be/fileadmin/sites/dgs/upload/dgs_super_editor/dgs_editor/documents/Publications/vacc/2009_CVac_nourrissons.pdf
9. Institut de veille sanitaire (InVs). Epidémie de rougeole en France. Données de déclaration obligatoire en 2010 et données provisoires pour début 2011. [Measles outbreak in France. Data from mandatory reporting in 2010 and preliminary data for 2011]. Paris: InVs. [Accessed 21 Apr 2011]. [French]. Available from: http://www.invs.sante.fr/surveillance/rougeole/Point_rougeole_220311.pdf
10. Mankertz A, Mihneva Z, Gold H, Baumgarte S, Baillot A, Helble R, et al. Spread of measles virus D4-Hamburg in Europe, 2008 - 2010. Emerg Infect Dis. Forthcoming.
11. Martin R, Deshevoi S, Buddha N, Jankovic D. Approaching measles and rubella elimination in the European region--need to sustain the gains. Euro Surveill. 2009;14(50):pii=19449. Available from: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19449
12. World Health Organization (WHO). Regional Committee for Europe. Sixtieth session. Resolution. Renewed commitment to elimination of measles and rubella and prevention of congenital rubella syndrome by 2015 and Sustained support for polio-free status in the WHO European Region. EUR/RC60/R12 . 16 September 2010. Available from: http://www.who.int/immunization/sage/3_Resolution_EURO_RC60_eRes12.pdf

Imported extensively drug-resistant Mycobacterium tuberculosis Beijing genotype, Marseilles, France, 2011

S Cohen-Bacrie[1,2], I Ben Kahla[1,2], E Botelho-Nevers[2,3], M Million[2,3], P Parola[2,3], P Brouqui[2,3], M Drancourt (michel.drancourt@univmed.fr)[1,2]

1. Fédération de Microbiologie Clinique, Assistance Publique des Hôpitaux de Marseille, Institut Hospitalier Universitaire POLMIT (University Hospital Institute for Infectious Diseases), Marseille, France
2. Unité de Recherche sur les Maladies Infectieuses et Tropicales Emergentes, CNRS-UMR 6236, IRD 198, IFR 48, Faculté de Médecine, Université de la Méditerranée (University of the Mediterranean), Marseille, France
3. Service de Maladies Infectieuses et Tropicales, Hôpital Nord, Assistance Publique des Hôpitaux de Marseille, Institut Hospitalier Universitaire POLMIT (University Hospital Institute for Infectious Diseases), Marseille, France

Citation style for this article:
Cohen-Bacrie S, Ben Kahla I, Botelho-Nevers E, Million M, Parola P, Brouqui P, Drancourt M. Imported extensively drug-resistant Mycobacterium tuberculosis Beijing genotype, Marseilles, France, 2011. Euro Surveill. 2011;16(16):pii=19846. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19846

Article published on 21 April 2011

Multidrug- (MDR) and extensively drug-resistant (XDR) tuberculosis (TB) are reported to gradually spread across European countries with low TB prevalence including France. Some isolates may even accumulate traits of resistance in addition to the XDR profile, as a result of therapeutic mismanagement. We report here the first case of XDR TB in Marseilles and discuss the potential effectiveness of sulfamide treatment in such cases.

Extensively drug-resistant (XDR) *Mycobacterium tuberculosis* strains are defined as resistant to isoniazid and rifampicin (multidrug-resistant, MDR) and at least to one fluoroquinolone and one of the following antibiotics: amikacin, capreomycin or kanamycin [1]. Hence, treatment options become very restricted, further complicating the management of cases and constituting a potential public health threat calling for particular vigilance [2]. By the end of 2010, 68 countries including 19 of the 27 countries in the European Union had reported at least one XDR-TB case [1]. XDR-TB is an emerging issue in Europe, illustrated by the present report of the first case infected with an XDR *M. tuberculosis* strain detected in Marseilles.

Case report

A 63-year-old Russian woman originating from the Republic of Dagestan was admitted on 11 January 2011 to our Departement for Infectious Diseases and Tropical Medicine in Marseille, France. The patient had a medical history of pulmonary tuberculosis (TB) first diagnosed in 2008 in Russia. She reported having undergone three sequential lines of anti-tuberculosis treatments including a combination of isoniazid, rifampicin, pyrazinamide, ofloxacin and kanamycin, but could not provide any further details. At the time of her arrival in France on 21 December 2010, she was treated by levofloxacine alone and spent three weeks in her daughter's home before being admitted to our department for persistent febrile cough and a major weight loss. At the time of her admission, the physical examination found a body-mass index of 17 and diffuse rhonchi. Chest radiography and computed tomography scan highlighted multiple excavated lesions and infiltrates of both upper lobes of the lungs. The first sputum and stool specimens (a non-invasive specimen replacing gastric fluid) processed in our laboratory [3] on 13 January 2011 exhibited ›100 acid-fast bacilli per power field after Ziehl-Neelsen staining.

Molecular anlayses

Subsequent molecular identification by 16S-23S intergenic spacer-based real-time PCR [4] and the GeneXpert system (Cepheid, Toulouse, France) [5] detected the presence of *M. tuberculosis* complex (MTC) DNA and drug resistance to rifampicin. Multispacer sequence typing (MST) specified an MST4 profile [6] and the pyrosequencing analysis of the Rv0927c gene and the Rv0927c-pstS3 intergenic region showed a Beijing genotype [7]. A bacterial growth was detected after 14 days of automated liquid culture (BD Bactec MGIT 960, Sparks, Maryland); further culture in the presence of drugs confirmed resistance to first-line anti-tuberculosis drugs including isoniazid, rifampicin, streptomycin, ethambutol, pyrazinamide, and further to kanamycin. The minimum inhibitory concentration (MIC) of trimethoprim-sulfamethoxazole (TMP-SMX) was determined by the dilution method using the Bactec MGIT supplemented medium tubes, in the presence of a growth control. After a five-day incubation period, no bacterial growth was detected at concentrations of TMP-SMX ≥1.6/8.3 µg/ml. Sequencing showed the -15C/T and S315T mutation in the *inhA* regulatory region and in the *katG* gene, which confirmed high level resistance to isoniazid and associated resistance to ethionamide, the D516Y mutation in the rifampicin resistance-determining region of the *rpoB* gene, the K43R mutation in the *rpsL* gene (resistance to streptomycin) and the G to A substitution at position 119 resulting in a nonsense mutation in the *pncA* gene (locus associated with

resistance to pyrazinamide). While no mutation was found in the *gyrB* gene, we detected two mutations D94G and S95Y in the *gyrA* gene known to cause fluoroquinolone resistance. No additional mutation was found in the 526 bp partial sequence of the *embB* gene (including the 306 codons associated with ethambutol resistance) or in the *rrs* gene (locus associated with resistance to aminoglycosides).

Treatment

Based on these laboratory results, the treatment regimen was switched to the combination of ethambutol, linezolid, para-aminosalicylic acid, cycloserin, amikacin and TMP-SMX. At the time of publication of the present report, the patient is still under treatment with this antibiotic combination and a clinical improvement has been observed so far including apyrexia. Additionally, two sputum specimens collected eight weeks after initiation of this antibiotic combination treatment showed, for the first time, no acid-fast bacilli after Ziehl staining and direct microscopic examination.

Discussion

The 1 % prevalence of resistant TB observed in Marseilles has been unexpectedly low so far, even compared to the prevalence reported at national level in France [8]. Our mycobacteriology reference laboratory routinely collects respiratory tract specimens from all four tertiary care hospitals of Marseilles covering a population of approximately 1 million. Between 1 January 2001 and 1 January 2011, 18,778 respiratory tract samples yielded a low prevalence of 384 *M. tuberculosis* isolates (2%), including a very low prevalence of five MDR isolates and no XDR isolate. In France, between 38 and 60 MDR TB cases were reported annually from 2001 through 2009 [8]. The first XDR TB case was detected in 2002, one to two cases were reported annually from 2003 through 2008 and four cases in 2009 (amounting to 8% of the MDR cases) [8].

The isolate reported here had accumulated several phenotypic and molecular traits of resistance in addition to the XDR profile. Such a highly resistance pattern may have resulted from a multistep process combining both primary and secondary resistance. The patient had been treated in Russia, a country ranking third for the prevalence of resistant tuberculosis [9]. The acquisition of additional resistances may have been secondarily facilitated by the sequential lines of anti-tuberculosis treatments. The resulting resistance pattern inherently limited the choice of anti-tuberculosis drugs available for treating the patient, leading to the initiation of long-term potentially harmful intravenous therapy.

The lack of active anti-tuberculosis drugs has recently led to a renewed interest in neglected molecules such as TMP-SMX [10], a combination known to be particularly effective for the treatment of pulmonary infections such as pneumocystosis. Currently, no standardised method based on clinical correlation studies has been validated to determine the susceptibility of *M. tuberculosis* strains to sulfamides. Based on a daily oral dose of 960 mg/4,800 mg TMP/SMX prescribed to eight non-tuberculosis patients in our hospital, we observed a mean serum concentration of 4.4/81.5 µg/ml, nearly 10 times higher than the MIC of the *M. tuberculosis* isolate described here. TMP-SMX might be considered as an alternative, cheap and overall well tolerated second-line antibiotic to treat highly resistant pulmonary tuberculosis, warranting further investigations.

Acknowledgements

We are grateful to the members of EuroTravNet, the European Centre for Disease Prevention and Control (ECDC) Collaborative Network for Travel and Tropical Medicine (www.eurotravnet.eu) for helpful comments.

Patient consent

The patient had given written informed consent to the publication of this report.

References

1. World Health Organization (WHO). Multidrug and extensively drug-resistant TB (M/XDR-TB): 2010 global report on surveillance and response. Geneva: WHO. [Accessed March 2011]. Available from: http://whqlibdoc.who.int/publications/2010/9789241599191_eng.pdf.
2. Kim HR, Hwang SS, Kim HJ, Lee SM, Yoo CG, Kim YW, et al. Impact of extensive drug resistance on treatment outcomes in non-HIV-infected patients with multidrug-resistant tuberculosis. Clin Infect Dis. 2007;45(10):1290-5.
3. El Khechine A, Henry M, Raoult D, Drancourt M. Detection of Mycobacterium tuberculosis complex organisms in the stools of patients with pulmonary tuberculosis. Microbiology. 2009;155(Pt 7):2384-9.
4. Bruijnesteijn Van Coppenraet ES, Lindeboom JA, Prins JM, Peeters MF, Claas EC, Kuijper EJ. Real-time PCR assay using fine-needle aspirates and tissue biopsy specimens for rapid diagnosis of mycobacterial lymphadenitis in children. J Clin Microbiol. 2004;42(6):2644-50.
5. Boehme CC, Nabeta P, Hillemann D, Nicol MP, Shenai S, Krapp F, et al. Rapid molecular detection of tuberculosis and rifampin resistance. N Engl J Med. 2010;363(11):1005-15.
6. Djelouadji Z, Arnold C, Gharbia S, Raoult D, Drancourt M. Multispacer sequence typing for Mycobacterium tuberculosis genotyping. PLoS One. 2008;3(6):e2433.
7. Djelouadji Z, Henry M, Bachtarzi A, Foselle N, Raoult D, Drancourt M. Pyrosequencing identification of Mycobacterium tuberculosis W-Beijing. BMC Res Notes. 2009;2:239.
8. Centre National de Référence des Mycobactéries et de la Résistance des Mycobactéries aux Antituberculeux (CNR-MYRMA). Rapport d'activité pour l'année 2009 [Activity Report for 2009]. Paris: CNR-MYRMA. Mar 2010. French. Available from: http://cnrmyctb.free.fr/IMG/pdf/CNR_MyRMA_Rapport2009.pdf.
9. Gandhi NR, Nunn P, Dheda K, Schaaf HS, Zignol M, van Soolingen D, et al. Multidrug-resistant and extensively drug-resistant tuberculosis: a threat to global control of tuberculosis. Lancet. 2010;375(9728):1830-43.
10. Forgacs P, Wengenack NL, Hall L, Zimmerman SK, Silverman ML, Roberts GD. Tuberculosis and trimethoprim-sulfamethoxazole. Antimicrob Agents Chemother. 2009;53(11):4789-93

Contamination of the cold water distribution system of health care facilities by *Legionella pneumophila*: Do we know the true dimension?

M Arvand (mardjan.arvand@hlpug.hessen.de)[1], K Jungkind[2], A Hack[1]
1. Hesse State Health Office, Centre for Health Protection, Dillenburg, Germany
2. Communal Health Office of the Wetteraukreis, Friedberg, Germany

Citation style for this article:
Arvand M, Jungkind K, Hack A. Contamination of the cold water distribution system of health care facilities by Legionella pneumophila: Do we know the true dimension?. Euro Surveill. 2011;16(16):pii=19844. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19844

Article published on 21 April 2011

German water guidelines do not recommend routine assessment of cold water for *Legionella* in healthcare facilities, except if the water temperature at distal sites exceeds 25 °C. This study evaluates *Legionella* contamination in cold and warm water supplies of healthcare facilities in Hesse, Germany, and analyses the relationship between cold water temperature and *Legionella* contamination. Samples were collected from four facilities, with cases of healthcare-associated Legionnaires´ disease or notable contamination of their water supply. Fifty-nine samples were from central lines and 625 from distal sites, comprising 316 cold and 309 warm water samples. *Legionella* was isolated from central lines in two facilities and from distal sites in four facilities. 17% of all central and 32% of all distal samples were contaminated. At distal sites, cold water samples were more frequently contaminated with *Legionella* (40% vs 23%, p <0.001) and with higher concentrations of *Legionella* (≥1,000 colony-forming unit/100 ml) (16% vs 6%, p<0.001) than warm water samples. There was no clear correlation between the cold water temperature at sampling time and the contamination rate. 35% of cold water samples under 20 °C at collection were contaminated. Our data highlight the importance of assessing the cold water supply of healthcare facilities for *Legionella* in the context of an intensified analysis.

Introduction

Legionnaires´ disease (LD) is an important cause of hospital-acquired pneumonia [1]. Potable water was recognised as the major environmental source of healthcare-associated LD (hca-LD) in the early 1980s [1]. After this discovery, almost all cases of hca-LD have been linked to potable water [2-5]. For example, in the United Kingdom, 19 of 20 hospital LD outbreaks from 1980 to 1992 could be attributed to the water distribution system (WDS) [6]. Microaspiration is the major mode of transmission of hca-LD [7]. Because the clinical manifestations are non-specific, and specialised laboratory testing is required, LD is easily underdiagnosed [1,8].

Routine testing for *Legionella* of environmental water samples by culture has emerged as an effective strategy for prevention of hca-LD. Guidelines mandating routine monitoring of *Legionella* contamination of the WDS in hospitals and other healthcare facilities have been implemented in many European countries, including Spain, France, the United Kingdom, and Germany [1,9]. In contrast, the Centers for Disease Control and Prevention (CDC) recommends environmental cultures only when cases of hca-LD are discovered [10], an approach which remains controversial, taking into account that a specific diagnostic for LD is not routinely performed in many laboratories. For example, in the United States of America (USA) only 19% of the hospitals that participated in the CDC National Nosocomial Surveillance System did routinely provide *Legionella* testing of patients at high risk for developing hca-LD [11]. In Germany, the Federal Environment Agency (Umweltbundesamt) and the German National Public Health Institute (Robert Koch Institute) recommend periodical analysis of the WDS of hospitals, nursing homes and other healthcare facilities [12]. If a moderate to high level contamination is detected, i.e. at *Legionella* concentration of ≥1,000 colony-forming unit (cfu)/100 ml, an intensified analysis with additional sampling points according to the guidelines of the German Technical and Scientific Association for Gas and Water (DVGW) is recommended [12,13].

Legionella can grow and amplify at temperatures between 25 °C and 45 °C with an optimum between 32 °C and 42 °C. *Legionella pneumophila* is able to withstand temperatures of 50 °C for several hours, but does not multiply at temperatures below 20 °C [9]. Therefore, keeping water temperature outside the range for *Legionella*, i.e. ≥55 °C and <20 °C is an effective prevention and control measure for both warm and cold water systems. In Germany, which has a temperate climate, the temperature of cold water at entry to a building is usually below 20 °C. The German guidelines do not recommend routine assessment of cold water for *Legionella* contamination. In the context of intensified analysis, assessment of cold water is rec-

ommended if the water temperature at the distal site exceeds 25 °C [12].

The Hesse State Health Office (HSHO) is a federal institution in charge of surveillance, prevention, and control of LD in Hesse, a state with six million inhabitants located in west-central Germany. The diagnostic laboratories of HSHO offer a broad spectrum of chemical and microbiological analysis for water samples. Our institution is usually consulted by the communal health authorities when cases of hca-LD are detected in a healthcare facility or if routine environmental cultures reveal a notable contamination by *Legionella* species. We here present the results of the evaluation of the WDS of four healthcare facilities, which had contacted us for assistance to control and prevent *Legionella* contamination of their WDS. Two cases of hca-LD had been diagnosed in one facility, an acute care hospital with a solid organ transplantation unit, whereas a moderate to high *Legionella* contamination had been detected upon routine assessment in the other facilities, which included a rehabilitation centre and two nursing homes. A multidisciplinary team was sent to each facility in order to determine the extent of contamination of the WDS, to assess the contamination of cold and warm WDS independently and to investigate a possible correlation between the water temperature at sampling time and the extent of *Legionella* contamination.

Methods

Healthcare facilities

The healthcare facilities included in this study consisted of an acute care hospital specialised in thoracic surgery and solid organ transplantation (260 beds), a rehabilitation centre with cardiologic, orthopaedic and psychosomatic departments (183 beds), a nursing home for physically disabled individuals (47 beds), and a nursing home for elderly people (220 beds). These facilities had been requested by the Communal Health Office to conduct intensified *Legionella* monitoring because high *Legionella* concentrations had been detected during periodical assessment and/or cases of hca-LP had been reported. Each facility was visited by a team of specialists of the Communal Health Office and the HSHO several times (four to six times) between March 2009 and August 2010. The results presented in this study are derived from the analysis of samples that were obtained at the first visit of our team to the facilities between March 2009 and February 2010.

Sampling procedure

Sampling points were selected by the team of specialists in cooperation with the technical teams of the facilities to obtain a comprehensive sample of cold and warm water for intensified analysis, in accordance with the recommendations of DVGW [13]. Fifty-nine samples were obtained from central lines (cold and hot-water tanks, return lines) of all facilities, including facility A (one warm sample), facility B (four cold samples), facility C (24 warm, 25 cold samples), and facility D (three warm, two cold samples). Six hundred and twenty-five samples were obtained from distal sites (467 showerheads, 155 taps, one pond and two spring fountains) of the facilities, comprising facility A (10 warm, 12 cold samples), facility B (15 warm, 16 cold samples), facility C (252 warm, 256 cold samples), and facility D (32 warm, 32 cold samples). Cold and warm water were generally sampled in parallel at distal sites. The temperature was documented and samples of approximately 200 ml were collected at central sites after discarding 3 L of cold or 3 L of warm water, and at distal sites after discarding 3 L of cold or 5 L of warm water, according to recommendations of the Federal Environment Agency [12]. It is noteworthy that the latter sampling method differs slightly from the European guidelines, which recommend samples of one litre in volume to be collected immediately after the opening of the water outlet [14].

Laboratory investigation

Legionella culture was performed on GVPC agar (Oxoid) according to recommendations of the Federal Environment Agency [15]. Two aliquots of 0.5 ml water were inoculated directly to GVPC agar and 100 ml was filtered through a 0.45 µm cellulose-nitrate membrane. The filter was overlaid with 20 ml 0.2 M HCl-KCl [pH 2.2] and incubated for 4–5 min. The buffer was discarded, the filter was rinsed with 10 ml sterile water and placed on GVPC agar. The cultures were incubated at 37 °C in a humidified atmosphere and examined after three, five, seven and 10 days. The detection limit of our method was one cfu/100 ml.

Table 1

Legionella contamination rate in cold and warm water samples obtained from four healthcare facilities, Hesse, Germany, March 2009–February 2010 (n=684)

Sample collection site	Sample type	*Legionella* positive n (%)	*Legionella* negative n (%)	Total n
Central line	**All**	**10 (17)**	**49 (83)**	**59**
	Cold water	1 (3)	30 (97)	**31**
	Warm water	9 (32)	19 (68)	**28**
Distal	**All**	**197 (32)**	**428 (68)**	**625**
	Cold water	125 (40)	191 (60)	**316**
	Warm water	72 (23)	237 (77)	**309**

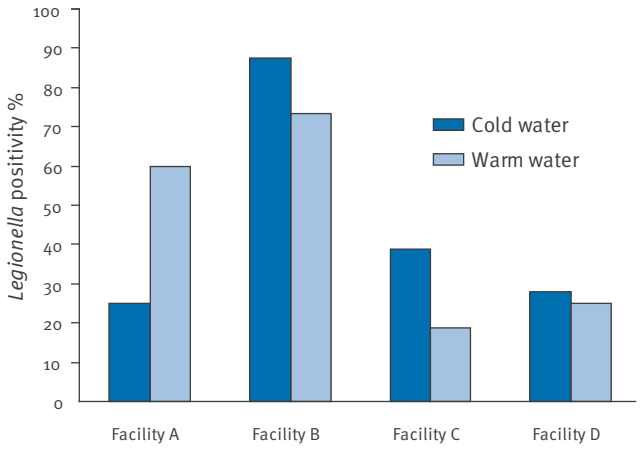
Identification was conducted by performing subcultures of at least three colonies per sample on BCYE agar (Oxoid) and sheep-blood agar. *Legionella* isolates grew on BCYE agar but not on sheep-blood agar. Serotyping was performed with a latex agglutination kit (*Legionella* Latex Test, Oxoid), which allows the identification of *Legionella pneumophila* serogroup 1, *L. pneumophila* serogroups 2-14, and non-pneumophila *Legionella* species.

Statistical analysis

Statistical analysis was performed with Stata, Version 11.1, 2009 (StataCorp LP, Texas, USA). Chi square test or Fisher exact test were used for analyzing qualitative data. Results were considered statistically significant when the P value was ‹0.05.

Figure 1

Legionella contamination in cold and warm water collected at distal sampling sites in four healthcare facilities, Hesse, Germany, between March 2009 and February 2010 (n= 625)



Results

Contamination rate in cold and warm water

Fifty-nine samples were collected at central lines, including 28 warm (temperature range: 46–75 °C) and 31 cold (temperature range: 7–14 °C) water samples. A total of 10 of 59 central samples were contaminated, comprising nine of 28 warm and one of 31 cold water samples (Table 1). Hence, among the central samples, warm water was more frequently contaminated with *Legionella* than cold water (p‹0.001).

Six hundred and twenty-five distal samples were analysed, including 309 warm (temperature range: 32–70 °C) and 316 cold (temperature range: 7–29 °C) water samples. A total of 197 of 625 (32%) distal samples were contaminated. *Legionella* was detected in 125 of 316 (40%) cold water samples and 72 of 309 (23%) warm water samples (Table 1). Thus, among the distal samples, cold water was more frequently contaminated with *Legionella* than warm water (p‹0.001).

We next evaluated the results at the level of individual facilities. The temperature of cold and warm water differed slightly between the facilities. At distal sites, cold water temperatures of 8–25 °C (facility A), 9–24 °C (facility B), 7–28 °C (facility C), and 13–29 °C (facility D) and warm water temperatures of 40–64 °C (facility A), 36–65 °C (facility B), 32–70 °C (facility C), and 50–66 °C (facility D) were measured at sampling time. *Legionella*

Table 2

Legionella contamination in distal cold and warm water samples collected in four healthcare facilities, Hesse, Germany, March 2009–February 2010 (n=625)

	Cold water			Warm water		
Healthcare facility	Total	*Legionella* positive	*Legionella* ≥1,000 cfu/100 ml	Total	*Legionella* positive	*Legionella* ≥1,000 cfu/100 ml
Facility A (n=22)	**12**	3	0	**10**	6	0
Facility B (n=31)	**16**	14	8	**15**	11	5
Facility C (n=508)	**256**	99	37	**252**	47	15
Facility D (n=64)	**32**	9	4	**32**	8	0

Table 3

Legionella concentration and temperature range of cold and warm water collected at distal sites in four healthcare facilities, Hesse, Germany, March 2009–February 2010 (n= 625)

Legionella concentration (cfu/100 ml)	Cold water			Warm water			P value[a]
	Temperature range (°C)	n	%	Temperature range (°C)	n	%	
‹1	7–28	191	60	38–70	237	77	‹0.001
1–99	8–25	13	4	39–65	18	6	0.361
100–999	11–27	63	20	37–64	34	11	0.003
≥1,000	11–29	49	16	32–62	20	6	‹0.001
Total	**7–29**	**316**	**100**	**32–70**	**309**	**100**	

[a] The P values were calculated by comparing the proportion of cold water samples displaying a distinct *Legionella* concentration among all cold water samples with the proportion of warm water samples with the similar *Legionella* concentration among all warm water samples.

contamination was detected in distal cold and warm water of all facilities. The overall positivity rate was nine of 22 (41%), 25 of 31 (81%), 146 of 508 (29%), and 17 of 64 (27%) in distal water of the facilities A, B, C, and D, respectively. Remarkably, contamination was more frequently detected in cold water than in warm water in three facilities (Figure 1). The contamination rate of cold and warm water in the facilities A, B, C, and D were 25% versus 60%, 88% versus 73%, 39 versus 19%, and 28 versus 25%, respectively (Table 2).

Figure 2

Relationship between the temperature of distal water at sampling time and *Legionella* contamination, Hesse, Germany, March 2009–February 2010 (n= 625)

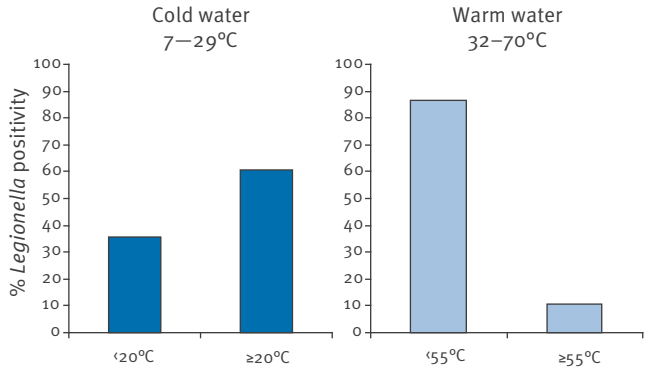
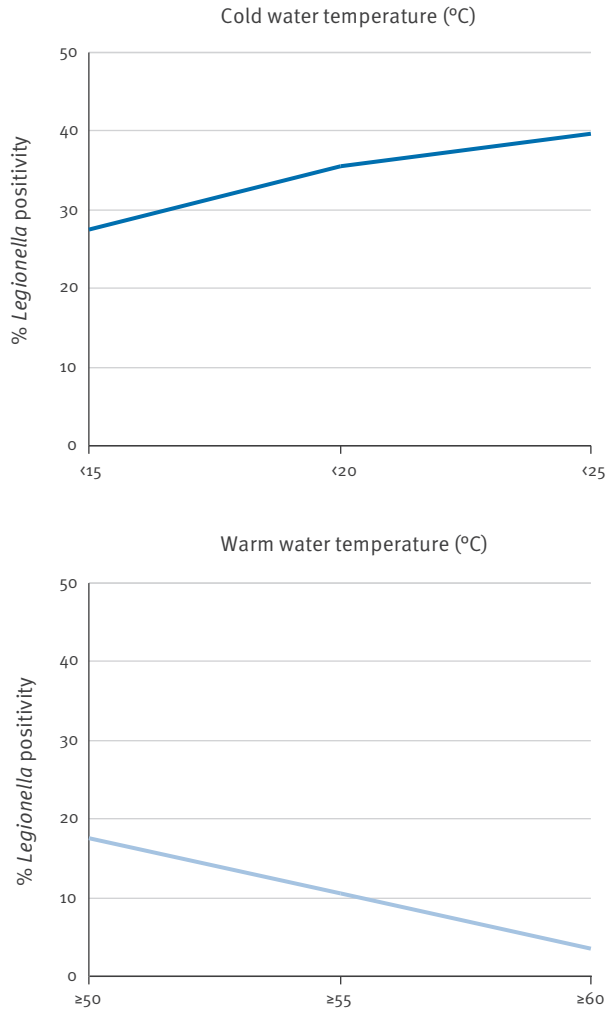


Figure 3

Relationship between contamination rate of distal water and the threshold temperature for cold and warm water, Hesse, Germany, March 2009–February 2010 (n= 625)



Legionella species and serogroups detected

Serological differentiation of the *Legionella* isolates from the WDS revealed *L. pneumophila* serogroup 1 in facility A, C, and D, *L. pneumophila* serogroup 2-14 in facility B, and non-pneumophila *Legionella spp.* in facility A and C. *L. pneumophila* serogroup 1 was also isolated from the bronchoalveolar lavage fluid of the index patient with hca-LD in facility C. The *L. pneumophila* isolates obtained from the patient and the water supply displayed the same geno- and serotype, as determined by multilocus sequence typing (MLST) and monoclonal antibody serotyping, which were performed at the *Legionella* Reference Laboratory, University of Dresden, Germany.

Legionella concentration in cold and warm water

Of 316 distal cold water samples analysed, 60% were tested negative for *Legionella*, 4% revealed minimal contamination (colony count 1–99 cfu/100 ml), 20% moderate contamination (100–999 cfu/100 ml) and 16% high contamination (≥1,000 cfu/100 ml). Of 309 distal warm water samples analysed, 77% were negative, 6% displayed minimal contamination, 11% moderate contamination, and 6% high contamination (Table 3). In detail, a total of 69 samples comprising 49 cold and 20 warm water samples revealed a high *Legionella* concentration (≥1,000 cfu/100 ml). Thirty three of 49 (67%) highly contaminated cold water samples displayed a temperature of ‹20 °C at collection time, whereas three of 20 (15%) highly contaminated warm water samples displayed a temperature of ≥55 °C at sampling time. Together, cold water samples were more frequently contaminated with higher *Legionella* concentrations compared to warm water samples. The difference between cold and warm water was significant in all categories except for minimal contamination (Table 3).

We next evaluated the prevalence of high *Legionella* concentrations, i.e. ≥1,000 cfu/100 ml, in cold and warm water of different facilities. As shown in Table 2, a high grade contamination was detected in three of four facilities. Cold water samples were more frequently contaminated with high *Legionella* concentrations than warm water samples in three of four facilities (Table 2).

Relationship between temperature and *Legionella* contamination

We next examined the relationship between the temperature of distal water at sampling time and *Legionella* contamination. Cold and warm water samples were assigned to four groups, cold water ‹20 °C, cold water ≥20 °C, warm water ‹55 °C, and warm water ≥55 °C and the contamination rate was calculated for each group. The positivity rate was 94 of 265 (35%), 31 of 51 (61%), 45 of 52 (87%), and 27 of 257 (11%) in the latter groups, respectively (Figure 2). It is noteworthy that 35% of

cold water samples that displayed an optimal temperature in terms of *Legionella* prevention at sampling time, that is <20 °C, were contaminated. In contrast, only 11% of warm water samples that displayed an optimal temperature in terms of *Legionella* prevention, that is ≥55 °C, were contaminated. Outside the temperature range of *Legionella* growth, there was significantly less contamination in warm water than contamination in cold water ($p<0.001$).

We further examined whether we may find a threshold temperature that would allow a reliable discrimination between contaminated and non-contaminated distal water. The threshold temperatures of 15 °C, 20 °C and 25 °C were tested for cold water, and 50 °C, 55 °C, and 60 °C for warm water. The contamination rate of samples beyond the selected temperature was calculated separately. As shown in Figure 3, 43 of 156 (28%) of water samples that were below 15 °C at sampling time, which is below the lower limit (20 °C) of the range of *Legionella* growth, were contaminated by *Legionella*. This suggests that measuring cold water temperature at sampling does not allow the defining of a reliable temperature threshold, below which cold water would be considered free from *Legionella* contamination.

Discussion

We here present the results of assessment of the water supplies of four healthcare facilities in Germany. The investigation was initiated because cases of hca-LD were diagnosed in one facility (Facility C) or because periodical analysis had suggested a severe contamination of the WDS with *Legionella* (facilities A, B, and D). The contamination rate of distal water samples was 41%, 81%, 29% and 27% in the four facilities examined. The very high rate in some cases (81%) was not entirely unexpected in light of the circumstances that had led to the enrolment of the facilities in this study.

We found higher contamination rates and higher *Legionella* concentrations in cold water samples than in warm water samples collected from distal sites in three facilities (Figure 1, Table 2). Legionellosis has been traditionally associated with inadequately heated warm water [1]. There is a common belief that only the warm water supply may serve as a source of infection. Nonetheless, previous studies have shown that the cold water supply of healthcare facilities may be heavily contaminated with *Legionella* species [16]. Other investigators have reported cases of hca-LD that were attributed to contamination of the cold water supply. Hoebe et al. [17] reported two cases of fatal LD in a rehabilitation centre linked to the cold water supply. Johansson et al. [18] described a case of hca-LD in Sweden that was clearly linked to the cold WDS. Graman et al. [19] reported a case of hca-LD that was traced back to a contaminated ice machine. Our data show that the cold water supply of healthcare facilities may be even more heavily contaminated by *Legionella* species than the warm water supply. We found *Legionella* concentrations of up to 10,000 cfu/100 ml in distal cold water samples (data not shown). Different factors may have contributed to this interesting phenomenon. It is possible that a thermal disinfection of warm WDS was performed shortly prior to our visit to the facility. This could have resulted in a temporal suppression of *Legionella* in the warm water supply. Another possible explanation is a "warming-up" of cold water, which may occur after long intervals of stasis or when the cold and warm water pipes are closely fitted in the same shaft and run together over a long distance without appropriate insulation. The warming-up effect may not be detectable at the time of sampling, which is usually during daytime on a weekday. In the latter case, hot water flushing of warm water tubes may even have a paradoxical effect on contamination of the cold WDS by aggravating the warming-up effect.

Analysis of the temperature of distal samples revealed that only 16 of 316 (5%) cold water samples displayed a temperature of 25 °C or more at sampling time, which is the threshold temperature recommended by the German water guidelines for assessment of cold water [12]. We therefore tested other threshold temperatures. We found that 94 of 265 (35%) and 43 of 156 (28%) of the distal cold water samples that displayed a temperature of <20 °C and <15 °C at sampling time were contaminated (Figure 3). Taken together, our data show that high *Legionella* concentrations may be found in cold water samples displaying a temperature of as low as 11 °C at sampling time, whereas no or very low *Legionella* concentrations may be associated with cold water temperatures of up to 28 °C at sampling time (Table 3). Hence, our data suggest that there is no reliable correlation between the temperature of cold water at sampling time and the extent of *Legionella* contamination. A possible explanation for this incoherence is that the temperature at sampling time, which is usually a busy time on a working day, is not representative of the temperatures that the sampled water has undergone prior to sampling.

After release of the results of our investigation, the infection control precautions were reassessed in all facilities and additional decontamination measures and prevention strategies were initiated for the warm and cold WDS. The results of the intervention activities were controlled by follow-up investigation.

In conclusion, our data suggest that the cold water supply of healthcare facilities may be heavily contaminated with *Legionella* species. We did not find a reliable correlation between cold water temperature at sampling time and *Legionella* contamination rate or concentration. If we had restricted our analysis to cold water samples that displayed at least 25 °C at sampling time, we would have missed many cases of severe contamination. Our results highlight the importance of assessment of cold water in the context of intensified analysis of the water supply of healthcare facilities.

Acknowledgements

We would like to thank the technical team of the Hygiene and Infection Control laboratory of the HSHO for excellent technical assistance and Jens Fitzenberger for statistical support.

References

1. Sabria M, Yu VL. Hospital-acquired legionellosis: solutions for a preventable infection. Lancet Infect Dis. 2002;2(6):368-73.
2. Garcia-Nunez M, Sopena N, Ragull S, Pedro-Botet ML, Morera J, Sabria M. Persistence of Legionella in hospital water supplies and nosocomial Legionnaires' disease. FEMS Immunol Med Microbiol. 2008;52(2):202-6.
3. Ozerol IH, Bayraktar M, Cizmeci Z, Durmaz R, Akbas E, Yildirim Z, et al. Legionnaire's disease: a nosocomial outbreak in Turkey. J Hosp Infect. 2006;62(1):50-7.
4. Sabria M, Garcia-Nunez M, Pedro-Botet ML, Sopena N, Gimeno JM, Reynaga E, et al. Presence and chromosomal subtyping of Legionella species in potable water systems in 20 hospitals of Catalonia, Spain. Infect Control Hosp Epidemiol. 2001;22(11):673-6.
5. Kohler JR, Maiwald M, Luck PC, Helbig JH, Hingst V, Sonntag HG. Detecting legionellosis by unselected culture of respiratory tract secretions and developing links to hospital water strains. J Hosp Infect. 1999;41(4):301-11.
6. Joseph CA, Watson JM, Harrison TG, Bartlett CL. Nosocomial Legionnaires' disease in England and Wales, 1980-92. Epidemiol Infect. 1994;112(2):329-45.
7. Blatt SP, Parkinson MD, Pace E, Hoffman P, Dolan D, Lauderdale P, et al. Nosocomial Legionnaires' disease: aspiration as a primary mode of disease acquisition. Am J Med. 1993;95(1):16-22.
8. von Baum H, Ewig S, Marre R, Suttorp N, Gonschior S, Welte T, et al. Community-acquired Legionella pneumonia: new insights from the German competence network for community acquired pneumonia. Clin Infect Dis. 2008;46(9):1356-64.
9. World Health Organization (WHO). Legionella and the prevention of legionellosis. Geneva:WHO; 2007. Available from: http://www.who.int/water_sanitation_health/emerging/legionella.pdf
10. Tablan OC, Anderson LJ, Besser R, Bridges C, Hajjeh R. Guidelines for preventing health-care-associated pneumonia, 2003: recommendations of CDC and the Healthcare Infection Control Practices Advisory Committee. MMWR Recomm Rep. 2004;53(RR-3):1-36.
11. Fiore AE, Butler JC, Emori TG, Gaynes RP. A survey of methods used to detect nosocomial legionellosis among participants in the National Nosocomial Infections Surveillance System. Infect Control Hosp Epidemiol. 1999;20(6):412-6.
12. Umweltbundesamt. Periodische Untersuchung auf Legionellen in zentralen Erwärmungsanlagen der Hausinstallation nach § 3 Nr. 2 Buchstabe c TrinkwV 2001, aus denen Wasser für die Öffentlichkeit bereitgestellt wird [Periodical analysis for Legionella in water heating and distributions systems]. Bundesgesundheitsbl. 2006;7:697-700. German.
13. Deutsche Vereinigung des Gas- und Wasserfaches e.V. (DVGW). Bonn: Trinkwassererwärmungs- und Trinkwasserleitungsanlagen; Technische Maßnahmen zur Verminderung des Legionellenwachstums [Association of gas and water technologies, Technical meausures to prevent Legionella contamination of water distribution systems]. DVGW Arbeitsblatt W 551, Ausgabe 4/2004. German.
14. Joseph C, Lee J, Van Wijngaarden J, Drasar V, Castellani Pastoris M. European Working Group for Legionella Infections. European Guidelines for Control and Prevention of Travel Associated Legionnaires' Disease. London: Public Health Laboratory Service; 2002. Available from: http://www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1274093149925.
15. Umweltbundesamt. Nachweis von Legionellen in Trinkwasser und Badebeckenwasser Empfehlung des Umweltbundesamtes nach Anhörung der Trink- und Badewasserkommission des Umweltbundesamtes. [Detection of Legionella in drinking water and bathing water]. Bundesgesundheitsbl. 2000;43:911-5. German.
16. Wagenvoort JH, Sijstermans ML. From legionnaire to guerrilla combatant: suppression of Legionella pneumophila in a hospital cold water supply. J Hosp Infect. 2004;58(2):162-3.
17. Hoebe CJ, Cluitmans JJ, Wagenvoort JH. Two fatal cases of nosocomial Legionella pneumophila pneumonia associated with a contaminated cold water supply. Eur J Clin Microbiol Infect Dis. 1998;17(10):740.
18. Johansson PJ, Andersson K, Wiebe T, Schalen C, Bernander S. Nosocomial transmission of Legionella pneumophila to a child from a hospital's cold-water supply. Scand J Infect Dis. 2006;38(11-12):1023-7.
19. Graman PS, Quinlan GA, Rank JA. Nosocomial legionellosis traced to a contaminated ice machine. Infect Control Hosp Epidemiol. 1997;18(9):637-40.

European Risk Assessment Guidance for Infectious Diseases transmitted on Aircraft – the RAGIDA project

K Leitmeyer (katrin.leitmeyer@ecdc.europa.eu)[1]
1. European Centre for Disease Prevention and Control (ECDC), Stockholm, Sweden

Citation style for this article:
Leitmeyer K. European Risk Assessment Guidance for Infectious Diseases transmitted on Aircraft – the RAGIDA project. Euro Surveill. 2011;16(16):pii=19845. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19845

Article published on 21 April 2011

In order to assist national public health authorities in the European Union to assess the risks associated with the transmission of infectious agents on board aircrafts, the European Centre for Disease Prevention and Control initiated in 2007 the RAGIDA project (Risk Assessment Guidance for Infectious Diseases transmitted on Aircraft). RAGIDA consists of two parts: the production of a systematic review and a series of disease-specific guidance documents. The systematic review covered over 3,700 peer-reviewed articles and grey literature for the following diseases: tuberculosis, influenza, severe acute respiratory syndrome (SARS), invasive meningococcal disease, measles, rubella, diphtheria, Ebola and Marburg haemorrhagic fevers, Lassa fever, smallpox and anthrax. In addition, general guidelines on risk assessment and management from international aviation boards and national and international public health agencies were systematically searched. Experts were interviewed on case-based events by standardised questionnaires. Disease-specific guidance documents on tuberculosis, SARS, meningococcal infections, measles, rubella, Ebola and Marburg haemorrhagic fevers, Lassa fever, smallpox and anthrax were the result of consultations of disease-specific expert panels. Factors that influence the risk assessment of infectious disease transmission on board aircrafts and decision making for contact tracing are outlined.

Background

With increasing numbers of passengers travelling internationally by air the potential risk of introduction and spread of infectious diseases by travellers increases. In 2009, the global airport traffic reported 4.796 x 10^9 passengers arriving and departing from 1,354 airports located in 171 countries worldwide, with passengers on international flights accounting for 42 percent [1]. Almost 800 million passengers are carried on national/international flights annually within the European Union (EU) alone [2].

The outbreak of SARS in 2003 and pandemic influenza A(H1N1) in 2009 illustrated how infectious diseases can suddenly appear, spread, and threaten the health, economy and social lives of citizens even in countries that are not or not yet affected by the epidemic itself. When passengers and/or crew members become exposed to an infectious or potentially infectious person during a flight, early recognition of disease and coordinated risk assessment among the affected countries is needed to initiate appropriate public health response without unnecessarily alarming the public and disrupting air traffic.

There are legal obligations for the member states of the World Health Organization (WHO) to report events of public health concern in accordance with the International Health Regulations (IHR) [3] and for the Member States of the EU to provide information to the Community Network in accordance to the Decision No 2119/98/EC [4]. However, very limited international guidance exists for the public health management of infectious diseases related to air travel, both aboard aircrafts and at airports [5]. Existing international guidance, e.g. the WHO international guidelines for the control of tuberculosis [6], does not necessarily reflect the epidemiologic situation in the individual EU Member States, while the national guidelines, e.g. for meningococcal diseases [7], are frequently inconsistent.

In order to assist national public health authorities in EU Member States in the evaluation of risks related to the transmission of various infectious agents on board aircrafts and to help in the decision on the most appropriate, operationally possible public health measures for containment, e.g. on whether or not to contact-trace air travellers and crew in case of exposure, the European Centre for Disease Prevention and Control (ECDC) initiated in 2007 the project Risk Assessment Guidance for Infectious Diseases transmitted on Aircraft (RAGIDA) [8].

The RAGIDA project consists of two parts: (i) a systematic review of the literature of documented past events of infectious disease transmission on aircrafts, guidance documents and expert interviews assessing case-based information on events (produced by the Robert Koch Institute, Germany in response to an ECDC open call for tender OJ/2007/06/20- PROC/2007/009) [8], and (ii) a series of disease-specific guidance documents

produced by external disease-specific expert panels [9] on which this article will mainly focus. This guidance does not address contacts at the airport or occurring during transit.

Methods

Part I: Systematic review and expert interviews

In the first part of the RAGIDA project a systematic review of over 3,700 peer-reviewed articles and grey literature was performed for the following 12 infectious diseases: tuberculosis, influenza, SARS, invasive meningococcal disease, measles, rubella, diphtheria, Ebola and Marburg haemorrhagic fevers, Lassa fever, smallpox and anthrax. The aim was to evaluate the exact circumstances that led to the transmission of these infectious diseases on board aircrafts. For peer-reviewed publications, PubMed and the database of the German Institute of Medical Documentation and Information (DIMDI) were searched, using the following two combinations of search terms: (aircraft OR airplane OR flight OR flight crew OR air travel OR airline OR air passenger) AND (epidemiology OR microbiology OR transmission), (aircraft OR airplane OR flight OR flight crew OR air travel OR airline OR air passenger) AND (infectious).

Grey literature was searched in ProMed using the search terms 'airline OR air travel OR air passenger'. In addition, general guidelines on risk assessment and management were systematically searched from international aviation boards, the Airport Council International (ACI), International Air Transport Association (IATA) and International Civil Aviation Organisation (ICAO) and several national and international public health agencies such as the WHO, the United States Centers for Disease Control and Prevention, Health Canada, the Health Protection Agency in the United Kingdom and the Robert Koch Institute in Germany. Standardised questionnaires were used to interview an international group of experts to collect case-based information on events.

Contacts were defined as persons with relevant exposure to an infectious or potentially infectious index case. The credibility of an exposure was assessed by referring to event-specific factors such as pathogen, infectiousness of the index case, infectious period, availability of information on on-board exposure, possible alternative exposures, and risk factors for infection. The evidence of on-board transmission was assessed for each event according to a set of established criteria. These criteria took into account the validity and relevance of diagnostic tests (index case(s)/contacts), the validity and relevance of information for exposures or alternative exposures of contacts, and the susceptibility of contacts. Evidence for transmission was graded into four categories: high, probable, possible and none. If no transmission was concluded, the level of evidence for non-transmission was assessed using the proportion of the successfully traced contacts among all susceptible contacts on board the flight. The evidence was assessed as low if the proportion was smaller than 35%; medium if the proportion was between 35% and 75%, and high if the proportion was larger than 75%.

Part II: Disease-specific guidance

Within the second part of the RAGIDA project, the production of a series of operational guidance documents for assisting in the evaluation of risk for transmission of diseases was initiated. In June 2009, ECDC convened the first RAGIDA disease-specific expert meeting that focused on tuberculosis, SARS and invasive meningococcal infections. In 2010 a second meeting followed that concentrated on measles, rubella, Ebola and Marburg haemorrhagic fevers, Lassa fever, smallpox and anthrax.

For both meetings, small, multidisciplinary disease-specific expert panels were established. The participants were selected to include representatives of national public health authorities, particularly those with experience in the investigation and follow-up of incidents involving infectious diseases in travellers, European and international experts for the disease(s) under investigation, experts in microbiology and mathematic modelling, and representatives of the ECDC, the European Commission and the WHO International Health Regulations Coordination Programme. No conflicts of interest were declared by any of the participants.

Evidence obtained included the review of the published literature by disease related to air travel, the review of data on air travellers obtained from national public health authorities (from RAGIDA part I), and expert opinions from the members of the expert panel. Experts discussed basic elements of the Scottish Intercollegiate Guidelines Network (SIGN) approach for developing guidelines [10] and reviewed the evidence base taking into account the available scientific evidence for disease transmission as well as other relevant aspects such as disease severity, the potential for public health intervention, and availability of treatment.

Each disease-specific chapter contains a short literature review, outlines an approach for contact tracing including an algorithm and a template for questions and answers.

Results

Part I: Systematic review and expert interviews

The available information published in peer-reviewed journals was very limited for most of the diseases for which only a few on-board transmission events were described, limiting the power for evidence-based decision making. With the exception of tuberculosis no international guidance for contact tracing was identified [7,11,12]. A detailed report of this first part of the project has been published [8].

Part II: Disease-specific guidance

Overall the expert panels agreed that for each of the diseases contact tracing should be recommended only after careful risk assessment. Contact tracing was considered as reasonable if the probability of an infectious disease causing a secondary infection and/or further spread in the population was high in conjunction with an assessment that the impact on human health in terms of an adverse outcome (the scale of harm caused by the infectious threat in terms of morbidity and mortality) was also high. Several additional factors were identified that influence the decision making regarding contact tracing.

Factors that affect the probability of disease transmission on board aircrafts

The probability that a certain infectious disease is transmitted on board an aircraft depends on characteristics of the causative agent and the host, and on environmental factors. These include:

- infectivity of the index case during the flight in the symptomatic or pre-symptomatic stage, taking into account epidemiological attributes such as Ro, period of shedding, infectiousness period, mode of transmission, as well as signs and symptoms of disease;
- susceptibility of the passengers, considering their level of natural immunity and vaccination status;
- effectiveness of exposure, depending on proximity to the index case, duration of exposure as well as the technical specifications of the airplane and the quality of the cabin air.

Factors that affect the impact on human health

The impact on human health, the scale of harm that a certain infectious disease causes in terms of morbidity and mortality, depends on characteristics of the pathogen and the host, and on the available means for detection and intervention. The relevant factors include:

- pathogen-specific attributes for disease manifestation such as virulence, resistance pattern and case fatality;
- underlying condition associated with severity, considering compromised immune system, comorbidity or pregnancy;
- means for detection and possibilities for diagnosis, taking into account the availability and reliability of diagnostic tests;
- effectiveness of intervention, e.g. availability of prophylaxis and/or treatment.

Factors that influence the decision on contact tracing

In addition to the probability of transmission and the impact on human health, there are several additional factors that influence the decision making regarding contact tracing, such as:

- susceptibility of the passengers for the disease, taking into account the level of natural immunity and the vaccine coverage in the population of the countries of origin and destination;
- the maximum incubation period, i.e. the time period during which it is possible to intervene with public health measures; contact tracing at a later time could be initiated for scientific purposes;
- ethical aspects, e.g. whether treatment is available or whether containment and/or mitigation measures are acceptable for the contacts;
- means for response, i.e. the public health actions taken after identification of infected individuals, the options that can be offered to the infected individuals identified by contact tracing;
- alternative actions instead of contact tracing such as risk communication including leaflets for passengers of the flight and information on airports;
- media coverage and public attention;
- political sensitivities in the involved countries;
- available resources.

Discussion

In a globalised world, the risk for transmission and spread of infectious diseases through travel and trade needs to be addressed. In terms of passenger numbers, Europe has four of the eleven airports receiving the highest passenger numbers worldwide: London, Paris, Frankfurt and Madrid. Each of them receive more than 50 million passengers a year (with the larger proportion of passengers on international flights) [1,2], some of whom are likely to have or incubate infectious diseases. Airline cabins, as confined spaces, may provide an environment for disease transmission. There is some evidence from studies examining microbial contaminants in cabin air, that suggest air quality in an airline cabin is better than in most buildings [13-15] and most other means of public transportation (e.g. buses, trains, subways). Most modern airplanes operate a ventilation system with laminar air flow with exchange rates of 20 air exchanges per hours during cruising. Before re-entering the cabin, the air is filtered through a set of high-efficiency particulate air (HEPA) filters, which remove at least 99.97% of airborne particles between 0.1 and 0.3 µm in diameter and 100% of particles larger than 0.3 µm in diameter. However, when an aircraft is parked at the gate with the engines off for more than 30 minutes with passengers on board, adequate cabin ventilation should be ensured [16].

According to the IHR which legally bind 194 States worldwide, events of disease transmission among passengers on international flights require notification to the WHO [3]. Member States of the EU must further provide information on such cases through the appropriate designated structures and/or authorities in a timely manner to allow an effective joint response of the affected countries [4].

Assessing the risk of transmission of infectious diseases on board an aircraft is not always easy and often has to rely on individual expert opinion. The available

evidence is limited and assessing the publicly available evidence retrieved from the literature/grey literature is challenging. For most of the infectious diseases only a small number of studies are available on a limited number of events. The majority of the studies are observational, lack an appropriate control group and do not control for biases. In most of the reported studies the proportion of passengers (contacts) successfully traced and followed up is small, and for diseases with a long incubation period such as tuberculosis, asymptomatic passengers are often not followed up long enough to document seroconversion. For diseases with a high proportion of asymptomatic or mild cases or with an atypical presentation, cases are less likely to be detected because diagnostic tests are less likely to be performed. In addition, studies not showing transmission or disease outcome are less likely to be published (publication bias).

The decision on public health action and contact tracing has to be made fast and is influenced by several factors that differ between countries, such as the available resources, the purpose of contact tracing, its feasibility and the perception of the risk of the disease when evidence is lacking or when media attention or political pressure is high. Contact tracing requires significant resources in terms of manpower, money, and time. The amount of resources needed further depends on the objective of the tracing, e.g. whether it is done to initiate disease containment measures, disease mitigation measures, to delay the spread of the disease or to eradicate the disease. Only a limited number of studies are available on the cost-effectiveness of contact tracing in this regard. In the case of tuberculosis several studies indicate that the costs are high and the outcome is poor [17,18]. It must also be considered that adequate contact tracing in resource-poor countries may come at the expense of other more effective health measures [18]. Contact tracing is often complicated when passenger information is lacking. Aircraft manifests are not standardised across airlines and passenger lists are rarely kept for more than 48 hours. Legal matters and data protection issues could hamper the exchange of information between countries and organisations. Communication and coordination between the different national authorities can be complex and the proportion of contacts that can be successfully traced is often rather small [19,20].

Finally the perception of a risk plays a crucial role in its assessment and the decision for contact tracing. Assessments are influenced not only by the societal environment in which events occur and decisions are being made, but also by politics and the economic situation in a country. An infectious disease assessed at low risk, for instance, can have a significant economic and political impact in a certain context.

Conclusions

Considering the lack of published data available on evaluating the risk of transmission of most infectious agents on board aircrafts, and taking into account the key factors that influence the decision making, the RAGIDA guidance provides a viable evidence-based tool for public health authorities determining triggers and making decisions on whether to undertake contact tracing in air travellers or crew. These guidance documents may be adapted to the local situation, national and international regulations or preparedness plans. To improve the evidence base for contact tracing and to conclude on the cost-effectiveness of this public health intervention, information on the outcome of disease events during air travel needs to be collected continuously as initiated by this project.

Acknowledgements

Participants for RAGIDA Part 1

Robert Koch Institute: Karl Schenkel, Rachel Amorosa, Inge Mücke, Valentina Dias-Ferrao, Michaela Diercke, Gérard Krause, Tim Eckmanns.

Interviewed experts: Preben Aavitsland, Franz Allerberger, Paulo M. Alves, Peter Andersen, Thomas Bettes, Dounia Bitar, Bonita Brodhun, Udo Buchholz, Silke Buda, Neville Byrne, Marty Cetron, Jacques Chemardin, Miguel Dávila Cornejo, Annette Dietrich, Suzanne Cotter, Susan Courage, Roel Coutinho, Agnes Csohan, Jean-Claude Desenclos, Jozef Dlhý, Anou Dreyfus, Sabine Erne, Anthony Evans, Christina Frank, David Gamper, Helen Giamarella, Miguel Mínguez Gonzalo, Rene Gottschalk, Walter Haas, Danielle Hansen-Koenig, Wiebke Hellenbrand, Pierrette Huberty-Krau, Ansa Jordaan, Irena Klavs, Jan Klika, Judith Koch, Henry Kong, Ichiro Kurane, Kuulo Kutsar, Irina Lucenko, Tomohiko Makino,Patrick Mathys, Karen Marineau, Tanya Melillo Fenech, Kore Molbak, Maria Jose Sierra Moros,Ion Morrison, Howard Njoo, Joan O'Donnell, Darina O'Flanagan, Rose Ong, Maria Teresa Avilez Paixao, Androula Pavli, Gabriele Poggensee, Jelena Rjabinina, Petri Ruutu, Daniel Sagebiehl, Stefania Salmaso, Kirsten Schubert, Anette Siedler, René Snacken, Gianfranco Spiteri, Klaus Stark, Robert Steffen, Arnaud Tarantola, Claude Thibeault, Thomas Tsang, Rolanda Valinteliene, Anneke van den Hoek, Cliff Webster, Brita Winje, Anne Witschi.

Participants for RAGIDA Part 2

Tuberculosis expert group: Ibrahim Abubakar (chair), Jacques Chemardin, Annick Darrieu-Merlou, José Figueroa, Peter Helbling, Jean-Paul Klein, Vladimir Prikazsky, Gerard De Vries.

SARS expert group: Philippe Barboza, Christian Drosten, Tim Eckmans (chair), Celine Gossner, Helge Hollmeyer, Masja Straetemans, Sylvie Van der Werf, Peter White.

Meningococcal disease expert group: Suzanne Cotter (chair), Ida Czumbel, Paolo D'Ancona, Wiebke Hellenbrand, Sigrid Heuberger, Isabelle Parent du Chatelet, Pawel Stefanoff, Lena de Vries.

Measles and rubella expert group: Kevin Brown, Donato Greco (chair), Susan Hahné, Peter Kreidl, Claude Muller, Mark Muscat, Darina O'Flanagan, Anette Siedler.

Viral haemorrhagic fevers expert group: Roberta Andraghetti, Ray Arthur, Andreas Gilsdorf, Stephan Günther, Michel van Herp, Katrin Leitmeyer, Dilys Morgan (chair), Aura Timen, Maggie Tomlinson.

Smallpox and anthrax expert group: Franz Allerberger (chair), Agoritsa Baka, Tim Brooks, Roland Grunow, Sabina Lyson, Vincenzo Puro, Sybille Rehmet, Anna Swiatecka, Alexander Theus.

References

1. Airports Council International (ACI). ACI Annual World Airport Traffic Report 2009. Montreal: ACI; July 2009. Available from: http://www.aci.aero/cda/aci_common/display/main/aci_content07_c.jsp?zn=aci&cp=1-6-43-3647^2003_666_2__
2. Eurostat. Europe in figures. Eurostat yearbook 2010. Luxembourg: Eurostat; 2010. Available from: http://epp.eurostat.ec.europa.eu/cache/ITY_OFFPUB/KS-CD-10-220/EN/KS-CD-10-220-EN.PDF
3. World Health Organization (WHO). International Health Regulations (2005). 2nd ed. Geneva: WHO; 2008. Available from: http://whqlibdoc.who.int/publications/2008/9789241580410_eng.pdf
4. European Commission. Decision No 2119/98/EC of the European Parliament and of the Council of 24 September 1998 setting up a network for the epidemiological surveillance and control of communicable diseases in the Community. Official Journal of the European Union. Luxembourg: Publications Office of the European Union; 3 Oct 1998. L 268. Available from: http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CELEX:31998D2119:EN:HTML
5. Gaber, W. Goetsch U, Diel R, Doerr HW, Gottschalk R. Screening for infectious diseases at international airports: the Frankfurt model. Aviat Space Environ Med. 2009;80(7):595-600.
6. Hoek, M, Hanquet G, Heuberger S, Stefanoff P, Zucs P, Ramsay M, et al. A European survey on public health policies for managing cases of meningococcal disease and their contacts. Euro Surveill. 2008;13(10):pii=8060. Available from: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=8060
7. World Health Organization (WHO). Tuberculosis and air travel: guidelines for prevention and control. 3rd ed. Geneva: WHO; 2008. Available from: http://www.who.int/tb/publications/2008/WHO_HTM_TB_2008.399_eng.pdf
8. European Centre for Disease Prevention and Control (ECDC). Risk assessment guidelines for infectious diseases transmitted on aircraft. Stockholm, ECDC: Jun 2009. Available from: http://www.ecdc.europa.eu/en/publications/publications/0906_ter_risk_assessment_guidelines_for_infectious_diseases_transmitted_on_aircraft.pdf
9. European Centre for Disease Prevention and Control (ECDC). Risk assessment guidelines for diseases transmitted on aircraft. Part 2: Operational guidelines for assisting in the evaluation of risk for transmission by disease. Stockholm, ECDC; Nov 2009. Available from: http://ecdc.europa.eu/en/publications/Publications/0911_GUI_Risk_Assessment_Guidelines_for_Diseases_Transmitted_on_Aircraft.pdf
10. Scottish Intercollegiate Guidelines Network (SIGN). SIGN 50: a guideline developer's handbook. Chapter 7: Forming guideline recommendations. Edinburgh: SIGN; Jan 2008. http://www.sign.ac.uk/pdf/sign50.pdf
11. World Health Organization (WHO). Tuberculosis and air travel: Guidelines for prevention and control. Geneva: WHO; 1998. Available from: http://www.emro.who.int/stb/media/pdf/98_256.pdf
12. World Health Organization (WHO). Tuberculosis and air travel: Guidelines for prevention and control. 2nd ed. Geneva: WHO; 2006. Available from: http://whqlibdoc.who.int/hq/2006/WHO_HTM_TB_2006.363_eng.pdf
13. Nagda NL, Koontz MD. Review of studies on flight attendant health and comfort in airliner cabins. Aviat Space Environ Med. 2003;74(2):101-9.
14. Dechow M, Sohn H, Steinhanses J. Concentrations of selected contaminants in cabin air of airbus aircrafts. Chemosphere. 1997;35(1-2):21-31.
15. Wick RL Jr, Irvine LA. The microbiological composition of airliner cabin air. Aviat Space Environ Med. 1995;66(3):220-4.
16. Mangili A, Gendreau MA. Transmission of infectious diseases during commercial air travel. Lancet. 2005;365(9463):989-96.
17. Vassiloyanakopoulos A, Spala G, Mavrou E, Hadjichristodoulou C. A case of tuberculosis on a long distance flight: the difficulties of the investigation. Euro Surveill. 1999;4(9):pii=83. Available from: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=83
18. McFarland JW, Hickman C, Osterholm M, MacDonald KL. Exposure to Mycobacterium tuberculosis during air travel. Lancet. 1993;342(8863):112-3.
19. Abubakar I. Tuberculosis and air travel: a systematic review and analysis of policy. Lancet Infect Dis. 2010;10(3): 176-83.
20. Kornylo-Duong K, Kim C, Cramer EH, Buff AM, Rodriguez-Howell D, Doyle J, et al. Three air travel-related contact investigations associated with infectious tuberculosis, 2007-2008. Travel Med Infect Dis. 2010;8(2):120-8.

Agreement on a pandemic influenza preparedness framework for the sharing of viruses and benefit sharing

Eurosurveillance editorial team (eurosurveillance@ecdc.europa.eu)[1]
1. European Centre for Disease Prevention and Control (ECDC), Stockholm, Sweden

Citation style for this article:
Eurosurveillance editorial team. Agreement on a pandemic influenza preparedness framework for the sharing of viruses and benefit sharing. Euro Surveill. 2011;16(16):pii=19847. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19847

Article published on 21 April 2011

On 16 April 2011, a working group of World Health Organization (WHO) member states agreed on a pandemic influenza preparedness framework [1]. It regulates the sharing of viruses within the WHO Laboratory Global Influenza Surveillance Network (GISN) [2] and the access to vaccines, antiviral drugs, diagnostic kits, and other benefits, in particular with regard to lower-income countries. It foresees mandatory regular contributions from industry partners.

The four-year negotiations by 193 WHO member states began in November 2007, at a time when concerns about the fair distribution of benefits impaired the timely global sharing of influenza sequences.

The agreed framework will be presented to the World Health Assembly in May 2011 for its consideration and approval. The agreement will strengthen global preparedness for potential future influenza pandemics.

More detailed background information and a comment on the implications of this achievement has been published by the European Centre for Disease Prevention and Control [3].

References

1. Pandemic influenza preparedness framework for the sharing of influenza viruses and access to vaccines and other benefits. Geneva: World Health Organization; 16 Apr 2011. Available from: http://www.who.int/csr/disease/influenza/pip_framework_16_april_2011.pdf
2. WHO Global Influenza Surveillance Network. Geneva: World Health Organisation. [Accessed 20 Apr 2011]. Available from: http://www.who.int/csr/disease/influenza/surveillance/en/
3. Pandemic Influenza Preparedness - Significant agreement on sharing of influenza viruses samples and benefit sharing at a global Open Ended Working Group (Geneva April 11th-16th). Stockholm: European Centre for Disease Prevention and Control; 20 Apr 2011. Available from: http://www.ecdc.europa.eu/en/activities/sciadvice/Lists/ECDC%20Reviews/ECDC_DispForm.aspx?List=512ff74f-77d4-4ad8-b6d6-bf0f23083f30&ID=1064#table