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# Ongoing African measles virus genotype outbreak in Tel Aviv district since April, Israel, 2012

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**A measles outbreak is affecting the Tel Aviv district, Israel, since April 2012. As of 10 September, 99 cases were confirmed, including 63 (64%) migrants of Eritrean and Sudanese origin. All genotyped cases had the African B3 genotype*. The mean age of migrant and non-migrant cases was 6.0±9.6 and 30.2±24.2 years, respectively (p<0.001). The majority of both migrant and non-migrant cases was unvaccinated. This is the second African measles B3 genotype outbreak within the World Health Organization European region in 2012.**

During the spring and summer of 2012, a large outbreak of measles affecting 99 cases as of 10 September 2012, emerged in the Tel Aviv district area. We describe the methods and findings of the epidemiological investigation that was conducted by the Tel Aviv District Health Office.

## Background

Measles is a highly contagious vaccine-preventable viral disease, easily-transmissible by airborne route. The required herd immunity level for transmission interruption is 95% for two doses of a measles-containing vaccine [1].

Measles re-emerged in Israel in the past decade with several large recurrent outbreaks of genotypes D4 and D8 mainly in infants living within communities that had very low vaccination rates for age (<5%) such as some ultra-orthodox Jewish communities in Jerusalem [2-5]. In one of these outbreaks, the index cases were British visitors who had contracted the illness in the United Kingdom (UK) [3,5]. Measles is a mandatorily notifiable disease in Israel by law since 1948. Cases are notified to the district health offices from community and hospital healthcare authorities and are nationally channelled to the Division of Epidemiology of the Ministry of Health. The two-dose vaccination schedule, introduced in 1994, foresees one dose of measles-mumps-rubella (MMR) vaccine at 12 months of age and a second dose at the first grade (around 6 years of age) [2]. The vaccine coverage for the first MMR dose in Tel Aviv district was 96% in 2009.

## Case definition

The national case definition is based on laboratory confirmation (i.e. positive serologic test for immunoglobulin M antibody or polymerase chain reaction (PCR)) or on characteristic measles clinical symptoms (i.e. fever, rash, coryza) with an epidemiological link to a laboratory-confirmed case [2]. The case definition is similar to the current, 2010, United States (US) Centers for Disease Control and Prevention case definition for a confirmed case [6].

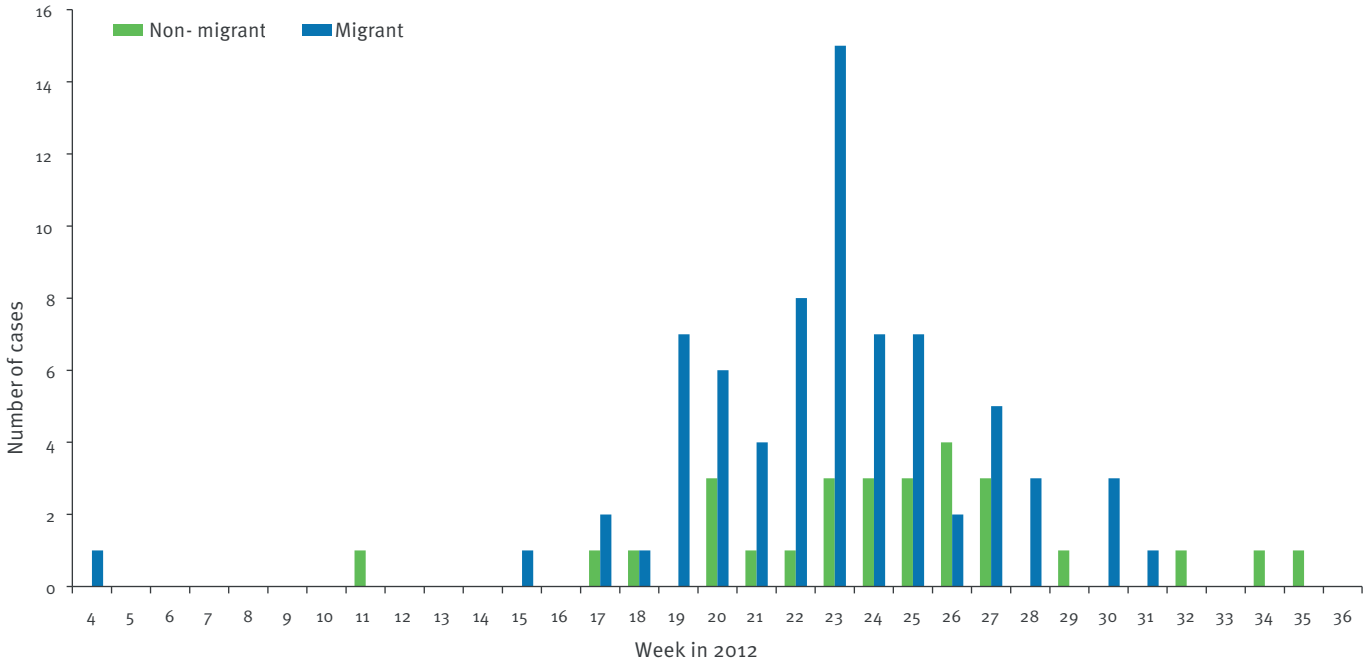
## Outbreak description

For the outbreak investigation, data were extracted from the District Health Office files. Migrant status was defined as not having an Israeli identification card number. The migrant population includes asylum-seekers, refugees, and labour-workers; excluding tourists. Frequencies and percentages were calculated for categorical variables and mean with standard deviation for age. Student's t test was applied to measure the significance of mean age difference between non-migrant and migrant cases. The chi-squared test for sex variable and Fisher's exact test for vaccine coverage variable were used for measuring the significance of the variables' distribution between non-migrant and migrant patients. All p value calculations were 2-tailed and were considered statistically significant if their value was ≤0.05. The statistical analyses were performed with IBM SPSS version 19.0 (Chicago, Illinois, USA).

A total of 101 confirmed cases were notified in the Tel Aviv district between 1 January and 10 September 2012 (Figure 1), with the latest notified confirmed case having had onset of illness on 28 August 2012. Of these, 73 (72%) were migrants. Up to 12 April 2012, only two confirmed measles cases had been identified, but the numbers subsequently increased reaching 99 confirmed cases as of 10 September 2012. The peak of the

**Figure 1**

Confirmed measles cases[a] by week of onset of illness and migrant status, January–September 2012, Tel Aviv district, Israel (n=101)




Week 4 begins on 23 January.

[a] Confirmed measles cases include laboratory-confirmed cases and clinical cases epidemiologically linked to laboratory-confirmed cases.

measles transmission period was observed in week 23, between 4 and 10 June 2012, with a total of 18 confirmed cases (15 in migrants, three in non-migrants).

Of the 101 cases, 49 (49%) were migrants of Eritrean origin and 15 (15%) were migrants of Sudanese origin. Of the 73 total migrant cases, 55 (75%) were males vs. 10 of 28 (36%) of the non-migrant cases ($p<0.001$) (Table).

Mean age of migrant and non-migrant cases was 6.0±9.6 and 30.2±24.2 years, respectively ($p<0.001$). The majority 57 (78%) of the migrant cases were below three years of age, whereas 10 of 28 (36%) of the non-migrant cases were in this age group (Figure 2).

Among cases between one and six years of age, two of a total of seven migrants and two of a total of 21 non-migrants had respectively received one dose of measles-containing vaccine ($p=0.25$). None of the eligible cases, migrants and non-migrants alike, had two vaccine doses as appropriate for age six years and above.

## Viral genotyping

The molecular characterisation of the current outbreak's measles virus was based on a fragment of 450 nucleotides (nt) of the conserved region of the nucleoprotein (N) gene and was in concordance with World Health Organization (WHO) standardised protocols [7]. The genotype revealed in all genotyped samples of laboratory-confirmed cases was the B3 genotype, which is predominant in Africa*.

## Outbreak control measures

A number of epidemiological measures were taken in order to control the outbreak. Contact tracing was conducted and post-exposure prophylaxis up to 72 hours from exposure, was given in the form of MMR vaccine, for all susceptible (i.e. not-vaccinated for age) contacts aged six months and above, of any case, particularly for those in kindergartens, hospitals, and community healthcare centres. Early MMR vaccine administration was also offered free of charge, from nine months of age, in addition to the routine first MMR (MMR1) dose at 12 months of age, for all migrant infants (i.e. asylum seekers) visiting the Maternal and Child Health Centres in residential areas with viral transmission activity. An active outreach for routine MMR1 vaccination of migrant infants and kindergarten children took place in the Maternal and Child Health Centres located in residential areas with viral transmission activity. As a result, approximately 1,000 contacts older than six months of age and susceptible migrant infants older than nine months of age were vaccinated with one MMR vaccine dose. Moreover, all district Maternal and Child Health Centres were actively advised to in particular routinely

**Table**

Characteristics of confirmed measles cases, by migrant status, Tel Aviv district, Israel, January–September 2012 (n=101)[a]

| Characteristic | Migrant (N=73) | Non-migrant (N=28) | p value |
|---|---|---|---|
| Age, mean years ± standard deviation | 6.0±9.6 | 30.2±24.2 | <0.001 |
| Males n (%) | 55 (75) | 10 (36) | <0.001 |
| Place of family origin | | | |
| Eritrea n (%) | 49 (67) | 0 (0) | NA |
| Sudan n (%) | 15 (20) | 0 (0) | NA |
| Israel n (%) | 0 (0) | 28 (100) | NA |
| Proportion of vaccinated with one dose of measles-containing vaccine among measles cases aged 1–6 years | 2/21 | 2/7 | 0.25 |

NA: not applicable.

[a] Confirmed measles cases include laboratory-confirmed cases and clinical cases epidemiologically linked to laboratory-confirmed cases. The majority (n=99) of the 101 confirmed cases occurred between April and August 2012.

vaccinate all infants with MMR1 vaccine at 12 months of age, without significant delay. Finally, active guidance was provided to all district hospitals and selected community healthcare centres to validate MMR vaccine status and further vaccinate (if indicated) susceptible healthcare employees.

## Discussion

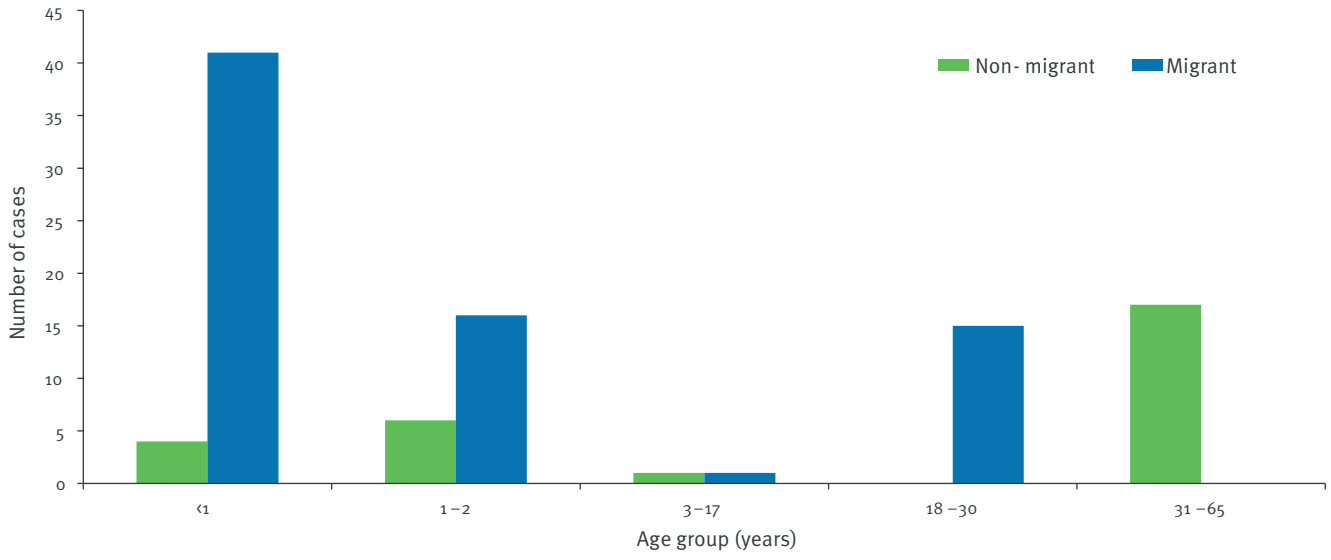
We report an ongoing outbreak of measles in the Tel Aviv district area, mainly affecting unvaccinated children below three years of age of migrants of Eritrean and Sudanese origin.

In 2011, the number of measles cases was reported to be rising in both the WHO European region [8] and the US [9] where an increase in measles importations from endemic countries was observed.

In contrast to the D4 and D8 genotypes detected in outbreaks of the past decade in Israel [2-5], the B3 genotype of this outbreak is endemic in Sub-Saharan Africa and its variants are increasingly being identified across Europe since 2005 [10]. In Israel, there was only one known case of importation to date of the B3 genotype by a returning traveller from Angola in 2011

**Figure 2**

Confirmed measles cases by age group and migrant status, January–September 2012, Tel Aviv district, Israel (n=101)[a]




[a] Confirmed measles cases include laboratory-confirmed cases and clinical cases epidemiologically linked to laboratory-confirmed cases. The majority (n=99) of the 101 confirmed cases occurred between April and August 2012.

(unpublished data). Within the WHO European region, a large measles outbreak with similar epidemiological characteristics to the one reported here (e.g. affecting mainly young age groups and extremely low vaccine coverage), as well as with a predominant B3 genotype, occurred in the United Kingdom (UK) in 2012 [11]. A large number of measles cases of the B3 genotype was also reported in Spain in 2011 [7,8].

The recent higher number of measles cases and outbreaks with B3 measles genotype in countries of the WHO European region and the one described here are possibly fuelled by migration of population with low vaccine coverage from measles-endemic regions, such as Africa. In this region, the average coverage with the first dose of measles vaccine has improved between 2000 and 2010 from 56% to 76% but is still one of the lowest in the world [12]. Alternatively to a direct importation from Africa, the current measles virus outbreak's genotype could as well have been imported from Europe [7,8,11]. In a previous measles outbreak in 2007–08 in Israel, the first three cases were visitors from London, UK, where they had had contact with measles patients [3,5].

Measures to control measles' outbreaks are generally expensive so preventing both domestic and imported measles provides a more cost-efficient solution [13]. For example, the direct cost for the public health response to a single case of imported measles in the US was recently estimated at approximately 25,000 US dollars [14]. The cost to control a small outbreak of eight patients in an asylum-seekers' shelter in Germany in 2010 was estimated to be of 90,000 Euro [15]. The obvious health benefits to the population of avoiding illness should encourage the formulation of specifically-tailored mass vaccination plans of migrant populations for vaccine-preventable diseases such as measles.

## Conclusions

The outbreak reported here is the second African measles B3 genotype outbreak within the WHO European region in 2012. Mass vaccination plans, primarily reaching out to migrants, should be implemented in order to achieve higher vaccination coverage and a progress toward control of measles in the region.

## * Authors' correction:

At the request of the authors, the sentence 'As of 10 September, 99 cases with B3 genotype were confirmed, including 63 (64%) migrants of Eritrean and Sudanese origin.' was changed to 'As of 10 September, 99 cases were confirmed, including 63 (64%) migrants of Eritrean and Sudanese origin. All genotyped cases had the African B3 genotype.' and the sentence 'The genotype revealed in all confirmed cases was the B3 genotype, which is predominant in Africa.' was changed to 'The genotype revealed in all genotyped samples of laboratory-confirmed cases was the B3 genotype, which is predominant in Africa.'. These changes were made on 17 September 2012.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## References


1. Measles vaccines: WHO position paper. Wkly Epidemiol Rec. 2009;84(35):349-60.
2. Anis E, Grotto I, Moerman L, Warshavsky B, Slater PE, Lev B, et al. Measles in a highly vaccinated society: the 2007-08 outbreak in Israel. J Infect. 2009;59(4):252-8.
3. Stein-Zamir C, Abramson N, Shoob H, Zentner G. An outbreak of measles in an ultra-orthodox Jewish community in Jerusalem, Israel, 2007--an in-depth report. Euro Surveill. 2008;13(8). pii: 8045. Available from: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=8045
4. Stein-Zamir C, Zentner G, Abramson N, Shoob H, Aboudy Y, Shulman L, et al. Measles outbreaks affecting children in Jewish ultra-orthodox communities in Jerusalem. Epidemiol Infect. 2008;136(2):207-14.
5. Stein-Zamir C, Shoob H, Abramson N, Zentner G. Who are the children at risk? Lessons learned from measles outbreaks. Epidemiol Infect. 2012;140(9):1578-88.
6. Centers for Disease Control and Prevention (CDC). Measles (Rubeola) 2010 Case Definition. In: Case Definitions for Infectious Conditions Under Public Health Surveillance. Atlanta: CDC. [Accessed 21 Aug 2012]. Available from: http://www.cdc.gov/osels/ph_surveillance/nndss/casedef/measles_2010.htm
7. Measles virus nomenclature update: 2012. Wkly Epidemiol Rec. 2012;87(9):73-81.
8. Increased transmission and outbreaks of measles, European Region, 2011. Wkly Epidemiol Rec. 2011;86(49):559-64.
9. Centers for Disease Control and Prevention (CDC). Measles - United States, 2011. MMWR Morb Mortal Wkly Rep. 2012;61(15):253-7.
10. Kremer JR, Brown KE, Jin L, Santibanez S, Shulga SV, Aboudy Y, et al. High genetic diversity of measles virus, World Health Organization European Region, 2005-2006. Emerg Infect Dis. 2008;14(1):107-14.
11. Vivancos R, Keenan A, Farmer S, Atkinson J, Coffey E, Dardamissis E, et al. An ongoing large outbreak of measles in Merseyside, England, January to June 2012. Euro Surveill. 2012;17(29). pii: 20226. Available from: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=20226
12. Simons E, Ferrari M, Fricks J, Wannemuehler K, Anand A, Burton A, et al. Assessment of the 2010 global measles mortality reduction goal: results from a model of surveillance data. Lancet. 2012;379(9832):2173-8.
13. Takahashi K, Ohkusa Y, Kim JY. The economic disease burden of measles in Japan and a benefit cost analysis of vaccination, a retrospective study. BMC Health Serv Res. 2011;11:254.
14. Coleman MS, Garbat-Welch L, Burke H, Weinberg M, Humbaugh K, Tindall A, et al. Direct costs of a single case of refugee-imported measles in Kentucky. Vaccine. 2012;30(2):317-21.
15. Takla A, Barth A, Siedler A, Stöcker P, Wichmann O, Deleré Y. Measles outbreak in an asylum-seekers' shelter in Germany: comparison of the implemented with a hypothetical containment strategy. Epidemiol Infect. 2012;140(9):1589-98.

# An outbreak of Legionnaires' disease associated with a display spa pool in retail premises, Stoke-on-Trent, United Kingdom, July 2012

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**Twenty-one confirmed cases of Legionnaires' disease (*Legionella pneumophila* serogroup 1) were identified in the Stoke-on-Trent area of England with onsets since 2 July 2012. Sequence-based typing results are available for nine cases; all are a unique type (ST1268). Initial interviews highlighted a number of possible environmental sources. Inspection of premises of interest revealed an operating spa pool on display, from which the outbreak strain was identified. All cases had visited the retail premise with this spa pool.**

On 20 July 2012, public health authorities in the West Midlands, England, were notified of two confirmed cases of Legionnaires' disease (LD) in Stoke-on-Trent residents admitted to the local hospital in the previous week. Initial interviews identified no possible shared exposures, and indicated that neither patient had travelled abroad or in the United Kingdom (UK) during their incubation periods. A review of previous notifications identified two earlier cases resident in this area, one in May and one in June 2012; both had spent part of their incubation periods abroad.

The local Health Protection Unit notified local enforcement agencies and convened an outbreak control team on 23 July 2012 to coordinate investigations, control measures, and public communications, as well as the response by local agencies. This paper describes the preliminary findings of this investigation and summarises data available at 14 August 2012.

## Investigation

The reporting hospital is the only acute care facility serving the residents of Stoke-on-Trent and surrounding districts, a population of approximately 500,000. Active case finding involved close liaison with the microbiology department and medical staff at the hospital, referral of pneumonia cases by hospital clinicians for microbiological testing, and encouraging respiratory sample collection on *L. pneumophila* urinary antigen-positive patients where possible. Regular letters were sent to all general practitioners (GPs) in the local area asking for vigilance in detecting potential cases, all surrounding hospitals and laboratories were informed to be vigilant and report associated cases, all Health Protection Units across England were briefed, and all national Legionella case reports reviewed.

## Case definitions

A confirmed case was defined in accordance with the definitions from the European Centre for Disease Prevention and Control (ECDC) as a person with clinical or radiological evidence of pneumonia and laboratory confirmation by culture of *Legionella pneumophila*, by detection of *L. pneumophila* urinary antigen or by seroconversion against *L. pneumophila* serogroup (sgp)1 [1], and with both an onset date after 30 June 2012 and a history of living in or visiting the Stoke-on-Trent area in the 14 days before onset.

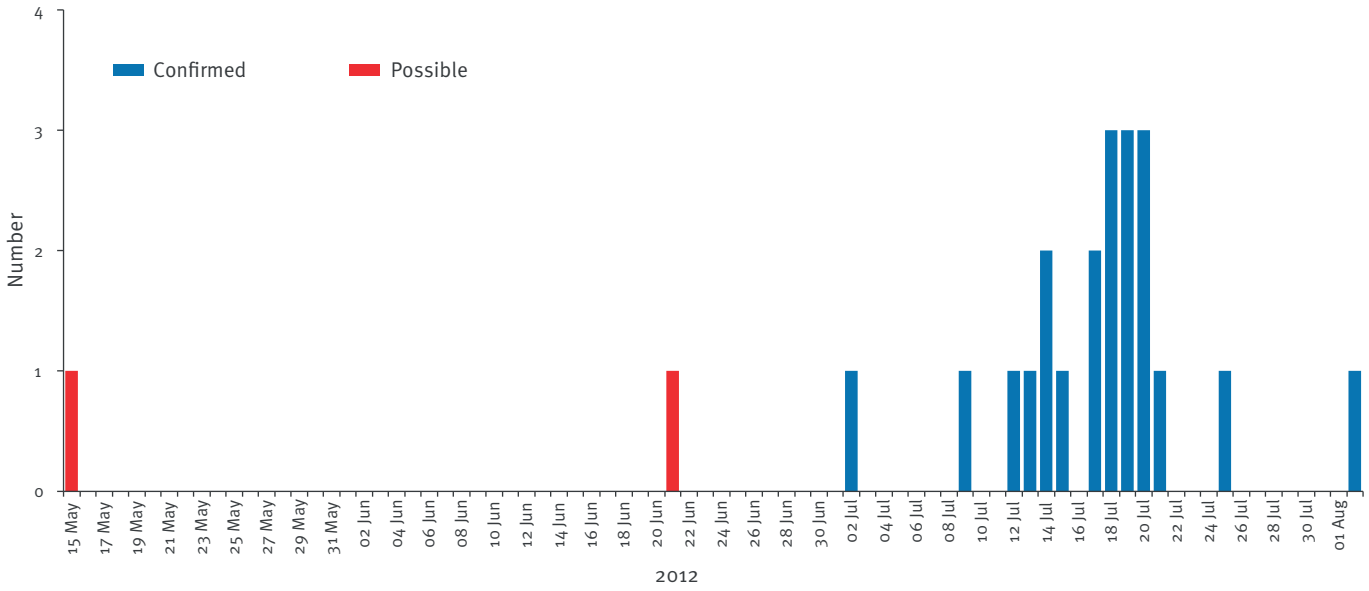
A possible case met the same definition, but with an onset date from 2 May 2012.

## Epidemiological investigation

All detected cases were interviewed with a standard questionnaire within one day of notification, covering details of clinical risk factors, where they lived, worked and visited over the 14 days before becoming ill, including movement routes and visits to or nearby water systems with the potential to be a source of exposure. When cases reported a potential risk site (e.g. a car wash) or any site was mentioned by more than one case, all other cases were re-questioned to determine if they had also visited there.

**Figure**

Legionnaires' disease cases, by date of onset and case status, Stoke-on-Trent area, May-August 2012 (n=23)




## Preliminary results

As of 14 August 2012, 21 confirmed cases have been identified. Two possible cases with earlier onset have also been re-investigated. All cases live in and around Stoke-on-Trent. The median age of cases is 64 years (range 48–79 years) and 14 of 21 are male. Most cases had existing underlying medical conditions and all were admitted to hospital, where two died. A review of risk factors for disease onset in cases is underway.

All the cases have onset dates from 2 July to 2 August 2012.The epidemic curve (Figure) shows a peak onset (12/21 cases) between 17 and 21July, with the majority of those 12 cases occurring from 18 to 20 July (9 cases).

## Microbiology of case samples

All cases were positive for *L. pneumophila* sgp 1 urinary antigen [2]. Sputum samples were obtained from 11 cases, and direct DNA-sequence based typing (SBT) [3] of the nine *L. pneumophila* PCR-positive sputum samples identified the same strain (a previously unrecognised sequence type designated ST1268); SBT was not attempted on the two PCR-negative samples. In six cases legionellae have been cultured and the infecting strain confirmed as *L. pneumophila* sgp1, mAb subgroup 'Benidorm', ST1268.

## Environmental investigation

All six active registered cooling towers in Stoke-on-Trent were contacted by Health and Safety Executive (HSE) and local authority (LA) inspectors over the weekend 21–22 July to confirm adherence with the nationally approved code of practice for the control of Legionella bacteria in water systems and institute control measures if indicated [4]. Two towers in adjacent districts were included later. Towers were inspected and water samples and swabs of biofilm were taken, although for five of the Stoke-on-Trent towers, this was after initial control measures had been implemented by the owners. All cooling towers were negative by L .pneumophila PCR except one of the towers with poor epidemiological fit to the outbreak, which was positive for *L. pneumophila* sgp1ST62, but not the outbreak strain. This was subsequently confirmed by culture of *L. pneumophila* sgp1, mAb subgroup 'Allentown/France', ST62. All other towers were found to be culture-negative.

Case interviews identified overlapping locations and local travel routes pointing to an area of south Stoke-on-Trent for further environmental investigation and assessment of potential water sources. This area was systematically investigated by the HSE and LA, and more than 30 sites (including light industry, engineering works, retail, car washers, dry cleaners, and public fountains) were assessed. Five sites containing water systems with the potential to be a source were inspected and sampled. All samples from these sites were negative in PCR and culture.

Three retail sites common to more than three cases were identified: all 21 cases reported visiting one particular retailer (A), 20 of them definitely within the incubation period for the organism, 14 visited another retailer (B) and 10 visited a third (C). Assessment of these three sites found two to have potential sources of exposure: an operating display spa pool (site A) and garden fountains/water features (site B), all of which were drained and disconnected. Samples from site B were negative in PCR and culture. A swab sample (water samples were not available) from the spa pool

identified the outbreak strain (ST1268) by PCR and direct SBT. Attempts were made to culture *L. pneumophila* from swab sample concentrates, but have to date not been successful. Maintenance and the use of biocides during the five months the spa pool was operating and on display prior to decommissioning on 24 July are being investigated in detail. On 30 July 2012, seven days after convening the outbreak control team, the media were briefed that the spa pool was the probable source of the outbreak.

## Discussion and conclusions

The epidemic curve and the molecular typing results were highly suggestive of a common source for this outbreak. The use of rapid and detailed investigation techniques confirmed that all cases had visited the indoor retail premises with the display spa pool, and the same, previously unrecognised, strain has been found in all cases tested and in the spa pool. This strain has not been found in any other site tested and no other site had such a strong epidemiological link to all cases. Operating spa pools on display in indoor spaces, even if not used for bathing, have been shown to be the cause of previous outbreaks [5-16]. Although the possibility of ongoing exposure from other sources cannot yet be completely ruled out, the epidemic curve is consistent with the source having been removed on 24 July (the date the spa pool was drained), and no further cases have been identified with disease onset after 2 August.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### References


1. Official Journal of the European Union 18.6.2008 L 159/65. COMMISSION DECISION of 28 April 2008 amending Decision 2002/253/EC laying down case definitions for reporting communicable diseases to the Community network under Decision No 2119/98/EC of the European Parliament and of the Council (reference number C(2008) 1589) 2008/427/EC. Available from: http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?
2. Birtles RJ, Harrison TG, Samuel D, Taylor AG. Evaluation of urinary antigen ELISA for diagnosing Legionella pneumophila serogroup 1 infection. J Clin Pathol. 1990;43(8):685-90
3. Mentasti M, Fry NK, Afshar B, Palepou-Foxley C, Naik FC, Harrison TG. Application of Legionella pneumophila specific quantitative real-time PCR combined with direct amplification and sequence-based typing in the diagnosis and epidemiological investigation of Legionnaires' disease. Eur J Clin Microbiol Infect Dis. 2012;31(8):2017-28.
4. Health and Safety Executive (HSE). Legionnaires' disease. The control of Legionella bacteria in water systems. Approved Code of Practice.and Guidance. London: HSE; 2000. Available from: http://www.hse.gov.uk/pubns/priced/l8.pdf
5. Centers for Disease Control and Prevention. Legionnaires' disease associated with a whirlpool spa display--Virginia, September-October, 1996. MMWR Morb Mortal Wkly Rep. 1997;46(4):83-6.
6. De Schrijver K, van Bouwel E, Mortelmans L, van Rossom P, De Beukelaer T, Vael C, et al. An outbreak of Legionnaire's disease among visitors to a fair in Belgium, 1999. Euro Surveill. 2000;5(11):pii=7. Available from: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=7
7. Benkel DH, McClure EM, Woolard D, Rullan JV, Miller GB Jr, Jenkins SR, et al. Outbreak of Legionnaires' disease associated with a display whirlpool spa. Int J Epidemiol. 2000;29(6):1092-8.
8. Campese C, Roche D, Clément C, Fierobe F, Jarraud S, de Waelle P, et al. Cluster of Legionnaires´ disease associated with a public whirlpool spa, France, April – May 2010. Euro Surveill. 2010;15(26):pii=19602. Available from: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19602
9. McEvoy M, Batchelor N, Hamilton G, MacDonald A, Faiers M, Sills A, et al. A cluster of cases of legionnaires' disease associated with exposure to a spa pool on display. Commun Dis Public Health. 2000;3(1):43-5.
10. Ruscoe Q, Hill S, Blackmore T, McLean M. An outbreak of Legionella pneumophila suspected to be associated with spa pools on display at a retail store in New Zealand. N Z Med J. 2006;119(1243):U2253.
11. Jernigan DB, Hofmann J, Cetron MS, Genese CA, Nuorti JP, Fields BS, et al. Outbreak of Legionnaires' disease among cruise ship passengers exposed to a contaminated whirlpool spa. Lancet. 1996;347(9000):494-9.
12. Redd SC, Lin FY, Fields BS, Biscoe J, Plikaytis BB, Powers P, et al. A rural outbreak of Legionnaires' disease linked to visiting a retail store. Am J Public Health. 1990;80(4):431-4.
13. Den Boer JW, Yzerman EP, Schellekens J, Lettinga KD, Boshuizen HC, Van Steenbergen, et al. A large outbreak of Legionnaires'disease at a flower show, the Netherlands, 1999. Emerg Infect Dis. 2002;8(1):37-43.
14. Kura F, Amemura-Maekawa J, Yagita K, Endo T, Ikeno M, Tsuji H, et al. Outbreak of Legionnaires' disease on a cruise ship linked to spa-bath filter stones contaminated with Legionella pneumophila serogroup 5. Epidemiol Infect. 2006;134(2):385-91.
15. Foster K, Gorton R, Waller J. Outbreak of legionellosis associated with a spa pool, United Kingdom. Euro Surveill. 2006;11(38):pii=3053. Available from: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=3053
16. Alsibai S, Bilo de Bernardi P, Janin C, Che D, Investigation team, Lee JV. Outbreak of legionellosis suspected to be related to a whirlpool spa display, September 2006, Lorquin, France. Euro Surveill. 2006;11(41):pii=3063. Available from: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=3063

# Prevalence of *Salmonella* enterica serovar 4,[5],12:i:- in England and Wales, 2010

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Difficulties in accurately identifying serovar 4,[5],12:i:- as monophasic variants of *Salmonella* enterica serovar Typhimurium mean there is confusion in the reporting of serovars Typhimurium and 4,[5],12:i:-. To gain insight into the prevalence and diversity of these monophasic variants in England and Wales, screening for *fljB*, *hin* and the serovar 4,[5],12:i:- DT193-associated genomic island was conducted on 609 *S. enterica* isolates designated as definitive phage type (DT) 193, and 142 isolates serologically-defined as monophasic variants of serovar Typhimurium but belonging to phage types other than DT193. All latter 142 isolates were subtyped by multilocus variable-number tandem repeat analysis (MLVA). MLVA was also applied to 70 DT193 serologically-defined monophasic variant isolates. Results indicate that serovar 4,[5],12:i:- accounted for 108 of 209 (52%) of DT193 isolates with available serological data and 99 of 142 (70%) monophasic variant isolates belonging to other phage types. Of 609 DT193 isolates, 463 (76%) lacked *fljB* and *hin*. Moreover, genetically-related isolates of DTs 120, 191, 191a, 195, phage types U311 and U323, and reacts but does not conform (RDNC) and untypable (UT) strains were also lacking either *hin* and/or *fljB*. Of note, the serovar 4,[5],12:i:- DT193-associated genomic island was identified in not only 458 of 463 (99%) monophasic DT193 isolates, but also 25 of 139 (18%) biphasic DT193 isolates and 56 of 76 (74%) monophasic variants of other phage types. Accurate monitoring of the emergence of serovar 4,[5],12:i:- isolates is important to ascertain the public health impact of these strains; since 2012 the Health Protection Agency's *Salmonella* Reference Unit has therefore begun determining full antigenic structures of all presumptive O:4 isolates in addition to routinely performing phage typing for identification of variants of serovar Typhimurium.

## Introduction

*Salmonella enterica* serovar 4,[5],12:i:- strains failing to express the *fljB*-encoded phase-2 flagellar antigen have been increasingly isolated from food animals and humans in the European Union (EU) over the last two decades [1]. Such strains were rarely identified before the mid-1990s but according to Enter-Net data, serovar 4,[5],12:i:- was the fourth most common serovar isolated from humans in the EU in 2006 [2]. Nevertheless, as these strains cannot be fully typed by conventional serotyping, it is likely that serovar 4,[5],12:i:- is underreported, principally due to difficulties in differentiating it from serovar Typhimurium, with which it shares antigenic and genotypic similarities [3,4]. According to the Kauffmann-White scheme the two serovars share the same O-antigens and phase 1 H-antigen, but serovar 4,[5],12:i:- lacks expression of the phase 2 flagellar antigen and is therefore considered a monophasic variant of Typhimurium. Problems with the procedure of flagellar phase inversion, which can be time-consuming and technically demanding, and lack of standardisation on how many times phase inversion should be repeated to be confident that an isolate is monophasic may result in misclassification of these two serovars. This process may also be complicated by serovar Typhimurium strains in which serological detection of the phase-2 flagellar antigen is inconsistent [5].

Most isolates of serovar 4,[5],12:i:- can be designated as a recognised phage type using the phage typing scheme of Anderson et al. [6]. In busy reference laboratories where phage typing is used in lieu of full serotyping to identify strains of serovar Typhimurium this may result in misclassification of monophasic isolates as serovar Typhimurium [7]. Several phage types have been associated with recent emergence of monophasic Typhimurium strains [7]. Serovar 4,[5],12:i:- belonging to phage type U302 and expressing mainly resistance to ampicillin, chloramphenicol, gentamicin, streptomycin, sulfamethoxazole, tetracyclines and trimethoprim (R-type ACGSSuTTm) emerged in humans and pig or pork products in Spain in the late 1990s to subsequently become the fourth most common serovar identified between 1998 and 2000 [8]. In the last ten years serovar 4,[5],12:i:- definitive phage type (DT) 193, and to a lesser extent DT120, expressing resistance to ampicillin, streptomycin, sulphonamides and tetracycline (R-type ASSuT) have rapidly emerged within several European countries in humans [7,9,10,11]. Infections have been linked mainly to pigs and pork products, and occasionally to other food animals. More recently, England and Wales has seen the emergence of serovar

4,[5],12:i:- belonging to previously undefined phage type DT191a associated with frozen reptile feeder mice imported from the United States [12]. As well as belonging to a new phage type, these isolates were unable to utilise dulcitol and expressed resistance to tetracyclines only (R-type T) as has been previously reported in serovar 4,[5],12:i:- isolates from North and South America [13,14]. Recently a novel genomic island was identified in multidrug-resistant serovar 4,[5],12:i:- DT193 from several European countries, which is being further investigated with respect to virulence properties and metabolic functions to determine whether its acquisition may have contributed to the rapid emergence of this strain [15].

*Salmonella* strains submitted by primary diagnostic laboratories to the Health Protection Agency's (HPA) *Salmonella* Reference Unit (SRU) with a preliminary identification as serovar Typhimurium are only phage typed and not routinely subjected to further serological examination unless the phage typing results are inconclusive. Conversely, isolates of serovar 4,[5],12:i:- were not routinely phage typed until July 2010. In order to gain a clearer picture of the prevalence and diversity of serovar 4,[5],12:i:- strains isolated in England and Wales during January–December 2010, all *S. enterica* isolates designated as phage type DT193, and all isolates that were determined to be monophasic variants of phage types other than DT193 on the basis of the Kauffmann-White scheme were screened by polymerase chain reaction (PCR) for the presence of *fljB* (encoding the phase-2 flagellar antigen) and *hin* (facilitates inversion of a promoter element to regulate flagellar phase inversion). In addition, PCR was used to screen for the presence of the serovar 4,[5],12:i:- DT193-associated genomic island [15]. Multilocus variable-number tandem repeat analysis (MLVA) was applied to all serologically-defined monophasic variant isolates of phage types other than DT193 and a subset of DT193 monophasic variants.

## Methods

### Bacterial isolates

The study panel consisted of all *S. enterica* isolates (n=609) designated as phage type DT193 submitted to the HPA between January–December 2010 for which antigenic structures were readily available for 209 isolates. Of these, the phase-2 flagellar antigen was serologically-detected in 88 isolates: two of serovar 1,4,12:i:1,2, nine of serovar 1,4,5,12:i:1,2, 15 of 4,12:i:1,2 and 62 of 4,5,12:i:1,2. The phase-2 flagellar antigen was not serologically detected in the 121 remaining isolates: two were serovar 1,4,5,12:i:-, 11 were 4,12:i:- and 108 were 4,5,12:i:-.

Also included in this study were all isolates (n=142) determined to be serologically monophasic (i.e. exhibiting antigenic structures 1,4,12:i:- (n=5), 1,4,5,12:i:- (n=12), 4,12:i:- (n=26) or 4,5,12:i:- (n=99)) but belonging to phage types other than DT193 between January–December 2010.

Isolates were submitted to the HPA SRU and originated from human clinical specimens (n=624), animals (n=40), food products (n=26), animal feed (n=8), environmental isolates (n=3) and an unknown source (n=50).

### Strain characterisation

Serology was performed according to the Kauffmann-White scheme and phage typing performed in accordance with HPA protocols [6,16]. Isolates that did not react with any of the typing phages were screened using a PCR targeting the malic acid dehydrogenase (mdh) gene of serovar Typhimurium [17]. PCRs targeting *fljB* and *hin* were performed as previously described [5].

### Susceptibility testing

Susceptibility to a panel of 18 antimicrobials was determined by a breakpoint method in Isosensitest agar (Oxoid, Basingstoke, UK). The final plate concentrations (µg/mL) used routinely by the HPA on the basis of long-term studies were: ampicillin (A; 8), chloramphenicol (C; 8), gentamicin (G; 4), kanamycin (K; 16), neomycin (Ne; 8), streptomycin (S; 16), sulphonamides (Su; 64), tetracycline (T; 8), trimethoprim (Tm; 2), furazolidone (Fu; 8), nalidixic acid (Nx; 16), ciprofloxacin ((low-level (Cpl); 0.125); (high-level (Cp); 1)), amikacin (Ak; 4), cephalexin (Cx; 16), cephradine (Cr; 16), cefuroxime (Cf; 16), ceftriaxone (Cn; 1) and cefotaxime (Ct; 1).

### Detection of serovar 4,[5],12:i:- DT193-associated genomic island

Multiplex PCR to discriminate between free, prophage-containing and island-carrying forms of the thrW tRNA locus was performed using previously described primers [15].

### Multilocus variable-number tandem repeat analysis subtyping

A total of 212 isolates defined as serologically monophasic were subjected to MLVA according to a previously described protocol [18]. This comprised the 142 monophasic variant isolates of phage types other than DT193 (of which 99 (70%) were serovar 4,[5],12:i:-) and 70 randomly selected monophasic variants of DT193 (of which 63 (90%) were serovar 4,[5],12:i:-). Multilocus variable-number tandem repeat analysis profiles were assigned based on the fragment size amplified from each locus, with 'NA' used to denote a locus not present [19]. Standard minimum spanning trees generated in the Bionumerics software package (version 6.1; Applied Maths, Sint-Martens-Latem, Belgium) using the single and double locus variance priority rules were used to visualise the relationships between isolates. Clonal complexes were created based on maximum neighbour distance of changes at one locus and a minimum of five MLVA profiles per complex.

## Results

### Phage typing

The serologically-determined monophasic isolates (n=142) belonged to phage types DT120 (n=44; of which 29 (66%) were serovar 4,[5]12:i:-), DT191a (n=33; of which 31 (94%) were serovar 4,[5]12:i:-), U323 (n=12; of which all were serovar 4,[5]12:i:-), reacts but does not conform (RDNC) (n=9; of which 4 (44%) were serovar 4,[5]12:i:-), U311 (n=7; of which 3 (43%) were serovar 4,[5]12:i:-) and between one to five isolates each of DT7, DT97, DT135, DT191, DT195, DT208, U302 (of which 6 of 16 (38%) were serovar 4,[5],12:i:-). A further 21 isolates were untypable (UT); all of which were positive for mdh, therefore variants of serovar Typhimurium (of which 14 (67%) were serovar 4,[5],12:i:-).

### Detection of *fljB* and *hin* by polymerase chain reaction

Overall, 463 (76%) of 609 DT193 isolates were PCR-negative for both *fljB* and *hin* (*fljB*-/*hin*-). A further four isolates were positive for *fljB* only (*fljB*+/*hin*-) and three isolates were positive for *hin* only (*fljB*-/*hin*+). Serological detection of the phase-2 flagellar antigen largely agreed with detection of *fljB* by PCR, with only eight of 209 isolates where the phase-2 flagellar antigen was reportedly detected in isolates that were *fljB*-/*hin*-. Conversely, there were three isolates where the phase-2 flagellar antigen was not detected in isolates that were positive for both *fljB* and *hin* (*fljB*+/*hin*+).

Seventy-six (54%) of the 142 monophasic isolates of other phage types were *fljB*-/*hin*-. Of these, 33 were DT120, 18 were UT, 12 were U323, six were U311, five were DT195 and one isolate each of DT97 and U302. A further 35 isolates were *fljB*-/*hin*+, of which 28 were DT191a, four isolates of RDNC and three isolates of DT191, and seven isolates were *fljB*+/*hin*-, of which six were DT120. The twenty-four isolates that were *fljB*+/*hin*+ belonged to a variety of phage types (DT7, DT120, DT135, DT191, DT191a, DT208, RDNC and UT).

### Source of monophasic (*fljB*-/*hin*-) isolates

Three hundred and ninety-nine of the 463 (86%) DT193 *fljB*-/*hin*- isolates were from humans, with the remainder isolated from animal feed (n=5), a cat (n=1), cattle (n=7), lamb meat (n=1), pigs (n=12), pork meat products (n=12) and an unknown source (n=26). The travel history section was completed for only 153 of the 399 (38%) submission forms. A recent history of travel abroad was reported for 43 of 153 (28%) patients, with travel to the African continent, Asian continent, Cambodia, Egypt, Greece, Hungary, Iraq, Italy, Japan, Mexico, Norway, Qatar and Turkey (each 1 patient), France and Vietnam (each 3 patients), Spain (5 patients) and Thailand (17 patients); the remaining 110 patients did not travel abroad prior to acquiring Salmonella.

Fifty-seven of 76 (75%) *fljB*-/*hin*- monophasic isolates of other phage types were from humans, with the remainder isolated from cattle (n=1), pigs (n=5), pork meat products (n=6) and an unknown source (n=7). A travel history was provided for only 15 of 76 patients, with recent travel to Malta, Portugal and Spain (each 1 patient) reported; the remaining 12 patients did not travel abroad prior to acquiring Salmonella.

### Susceptibility testing

Among the 609 DT193 isolates, 364 (60%) expressed resistance to ampicillin, streptomycin, sulphonamides and tetracyclines (R-type ASSuT) only; among 463 *fljB*-/*hin*- DT193 isolates 332 (72%) were R-type ASSuT. Other common resistance profiles among *fljB*-/*hin*- DT193 isolates were resistance to ampicillin, streptomycin and sulphonamides (R-type ASSu) in 50 (11%) isolates and resistance to tetracyclines only (R-type T) in 19 (4%) isolates. Eleven isolates (2%) were fully sensitive to all antimicrobials in the test panel.

Among the 142 monophasic isolates of other phage types the most common resistance profiles were R-type ASSuT (15 isolates of DT120, 11 untypable (UT) isolates, six isolates of U311, four isolates of U323 and one each of DT7, DT195 and U302) and resistance to tetracyclines only (25 isolates of DT191a, four of DT120, three each of DT191 and U323, two of RDNC and one UT). Twenty-eight isolates (20%) were fully sensitive to all antimicrobials in the test panel, of which 13 isolates were DT120, five were DT191a, four were RDNC, two each of DT191 and DT208, and one each of DT135 and U323.

### Occupancy of the thrW site

Among the 463 *fljB*-/*hin*- DT193 isolates, 284 (61%) produced two respective amplicons of 1,128 base pairs (bp) and 903 bp spanning the thrW site between genes proA and STM0325 and indicative of presence of the serovar 4,[5],12:i:- DT193-associated genomic island (Table 1). A further 174 (38%) produced a single amplicon of 903 bp. The island was also present in nine *fljB*+/*hin*+ isolates, and a further 16 *fljB*+/*hin*+ and one *fljB*-/*hin*+ isolate produced a single 903 bp amplicon.

Thirty-eight (50%) of *fljB*-/*hin*- isolates of other phage types than DT193 produced amplicons indicative of presence of the island (Table 1); these isolates belonged to DT120, UT, U323 and DT195. A further 18 (24%) *fljB*-/*hin*- isolates belonging to DT120 and U323 produced a 903 bp amplicon only. The island was also present in five DT120 *fljB*+/*hin*-, two *fljB*+/*hin*+ isolates belonging to DT120 and RDNC, and one DT120 *fljB*+/*hin*+ isolate produced a single 903 bp amplicon.

### Multilocus variable-number tandem repeat analysis subtyping

A total of 212 isolates, which consisted of 70 randomly selected DT193 serologically-defined monophasic isolates and all serologically-defined monophasic isolates of other phage types were subjected to MLVA subtyping. Fragment analysis identified 51 different profiles, within which two clonal complexes could be identified: clonal complex-1 (CC1) consisting of 29 profiles (155

**Table 1**

Occupancy of the *thrW* site in *Salmonella enterica* serovar Typhimurium DT193 and monophasic variants belonging to DT193 and other phage types, England and Wales, 2010 (n=751 isolates)

| Results of PCRs targeting *fljB/hin* | Phage type | Results of multiplex PCR targeting the *thrW* site Amplicon sizes (in base pairs)[a] | | | | Number of isolates |
|---|---|---|---|---|---|---|
| | | 1,128 | 903 | 663 | 432 | |
| *fljB–/hin–* | DT193 | + | + | – | – | 284 |
| | | – | + | – | – | 174 |
| | | – | – | + | – | 3 |
| | | – | – | – | + | 1 |
| | | – | – | – | – | 1 |
| *fljB–/hin+* | DT193 | – | + | – | – | 1 |
| | | – | – | – | + | 2 |
| *fljB+/hin–* | DT193 | – | – | + | – | 4 |
| *fljB+/hin+* | DT193 | + | + | – | – | 9 |
| | | – | + | – | – | 16 |
| | | – | – | + | – | 96 |
| | | – | – | – | + | 12 |
| | | – | – | – | – | 6 |
| *fljB–/hin–* | Other than DT193 | + | + | – | – | 38 |
| | | – | + | – | – | 18 |
| | | – | – | + | – | 12 |
| | | – | – | – | + | 2 |
| | | – | – | – | – | 6 |
| *fljB–/hin+* | Other than DT193 | – | – | – | + | 35 |
| *fljB+/hin–* | Other than DT193 | + | + | – | – | 5 |
| | | – | – | + | – | 1 |
| | | – | – | – | + | 1 |
| *fljB+/hin+* | Other than DT193 | + | + | – | – | 2 |
| | | – | + | – | – | 1 |
| | | – | – | + | – | 4 |
| | | – | – | – | + | 16 |
| | | – | – | – | – | 1 |

DT: definitive phage type; PCR: polymerase chain reaction.

A '+' indicates 'presence' while a '-' indicates 'absence' of an amplicon of given size.

[a] According to Trüpschuch et al. [15] amplicons of the multiplex PCR indicate three different occupancy possibilities: amplicons of 1,128bp and 903 bp for presence of the genomic island, 663 bp for prophage-occupied site and 432 bp for the free locus.

isolates) and clonal complex-2 (CC2) consisting of nine profiles (41 isolates) (Figure).

Ten MLVA profiles were shared by six or more isolates accounting for 66% of isolates (Table 2). All but one of these MLVA profiles was shared by more than one phage type (Figure, Table 2). Forty-three (98%) of 44 DT120 isolates and 67 (96%) of 70 DT193 isolates were located in CC1, whilst 29 (94%) of 31 DT191a isolates were located in CC2. All CC1 isolates failed to amplify the Typhimurium-specific virulence plasmid pSLT-bound locus STTR10, whereas all isolates in CC2 produced an amplicon.

Clonal complex 1 and CC2 also correlated well with *fljB*/*hin* PCR results and occupancy of the thrW site. One hundred and thirty-nine (90%) of CC1 isolates were *fljB*-/*hin*- and 34 (83%) of CC2 isolates were *fljB*-/*hin*+, although identical MLVA profiles were shared by *fljB*-/*hin*-, *fljB*+/*hin*+ and *fljB*+/*hin*- isolates in CC1, and by *fljB*-/*hin*+ and *fljB*+/*hin*+ isolates in CC2. All but one isolate harbouring the serovar 4,[5],12:i:- DT193-associated genomic island were located in CC1, regardless of phage type or *fljB*/*hin* PCR results.

## Discussion

Serotyping using the widely accepted Kauffmann-White scheme is central to the epidemiological classification of *Salmonella* strains and thus to surveillance studies, to identify trends in disease transmission, and for detection of outbreaks. Nevertheless, in recent years there has been a move towards development of

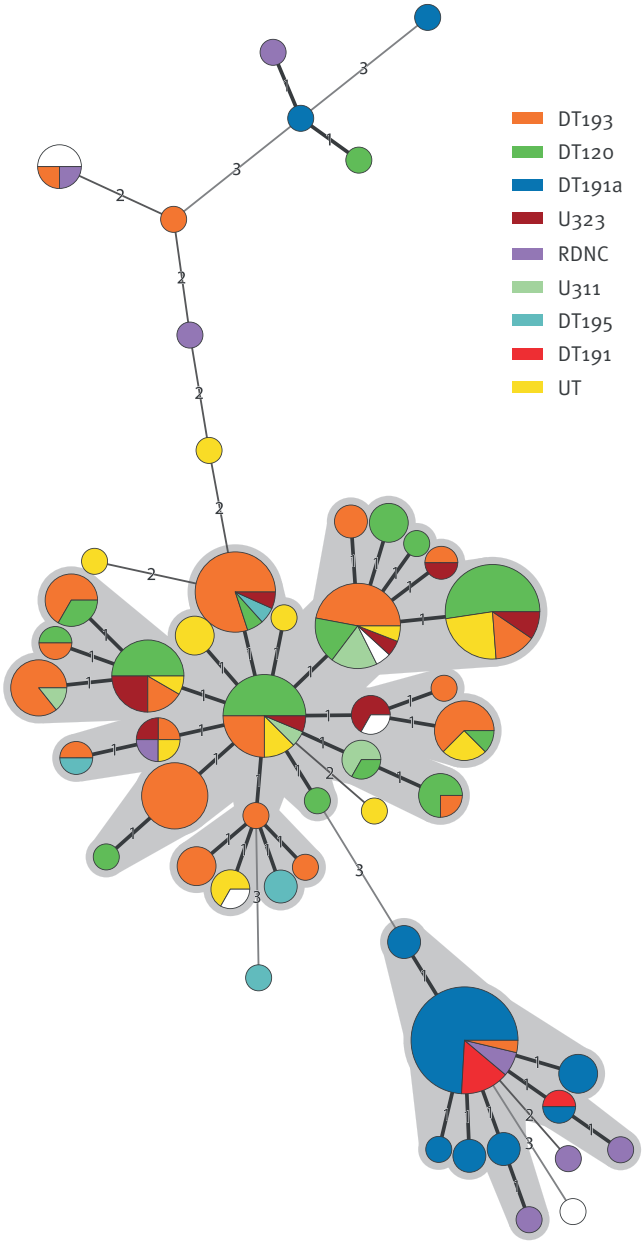
DNA-based techniques to replace or augment serological testing, and such methods may be used as a basis to define strains as serovar 4,[5],12:i:- or Typhimurium [20,21,22]. The range of mechanisms that can result in non-expression of the phase-2 flagellar antigen may mean that development of a reliable molecular serotyping scheme is complex. Lack of phase-2 flagellar antigen expression may be due to different mutations and deletions in *fljB*, fljA (encoding a repressor of the phase-1 flagellin gene fliC) and *hin* [5,23,24]. Alternatively, the invertible promoter that controls expression of *fljB* and fliC may become locked in one position, thereby allowing only expression of the fliC-encoded phase-1 flagellum [23]. This range of mechanisms that contribute to lack of *fljB* expression means that there can be discrepancies in detection of the phase-2 flagellum between conventional and molecular serology. The data presented here suggest that conventional serology is adequate for detection of serovar 4,[5],12:i:- DT193, as serological detection of the phase-2 flagellar antigen agreed with detection of *fljB* by PCR in 95% of isolates. Discrepancies between conventional and molecular serology were more apparent in monophasic isolates of other phage types, where 22% of monophasic isolates were *fljB*+ by PCR. This may become problematic if any of these strains persist and amplify to the same extent as serovar 4,[5],12:i:- DT193. Identification of not only *fljB*-/*hin*- monophasic isolates, but also *fljB*+/*hin*- and *fljB*-/*hin*+ isolates supports previous suggestions that serovar 4,[5],12:i:- represents multiple genotypes that have emerged independently from serovar Typhimurium [5,24].

Numbers of DT193 isolated in England and Wales have increased from 5.3% of all serovar Typhimurium in 2000 to 28% in 2010, with the number of DT193 R-type ASSuT increasing from 28% to 62% over the same time period (HPA Salmonella database, unpublished data). In this study 399 of 509 (78%) human DT193 isolates were found to be *fljB*-/*hin*- monophasic variants, thereby providing strong evidence that the emergence of serovar 4,[5],12:i:- DT193 is contributing to the increase in DT193 isolates from cases of human infection in England and Wales as previously suggested [7]. In addition, we identified multiple isolates of phage types U311, U323 and DT195. Monophasic isolates of serovar 4,[5],12:i:- U311 have previously been reported in Italy, France and Spain [7,25]. This is, however, the first time we have identified serovar 4,[5],12:i:- belonging to phage types U323 and DT195, thereby adding to the diversity of phage types already associated with this serovar [7].

Recently, an 18.4 kb novel genomic island was identified in 90% of serovar 4,[5],12:i:- DT193 isolated from humans between 2001 and 2008 in Germany and in similar isolates from Luxembourg, Austria, France, Italy and the Netherlands, therefore was proposed as an additional epidemiological marker for the serovar 4,[5],12:i:- DT193 clone emerging across Europe [15]. In this study only 61% of *fljB*-/*hin*- DT193 isolates produced two amplicons representative of carriage of

**Figure**

Minimum spanning tree of multilocus variable-number tandem repeat analysis of monophasic *Salmonella* Typhimurium isolates, England and Wales, 2010 (n=212 isolates)




DT: definitive phage type; MLVA: multilocus variable-number tandem repeat analysis; RDNC: reacts but does not conform; UT: untypable.

Node size is proportional to the number of strains with that MLVA profile. Wedges within nodes represent the proportion of isolates with that MLVA profile that belong to a specific phage type (only phage types shared by more than two isolates are indicated). Numbers on branches indicate the number of loci that vary between each MLVA profile. Grey shading indicates clonal complexes created based on maximum neighbour distance of changes at one locus and a minimum of five MLVA profiles per complex.

**Table 2**

Comparison of the ten most common MLVA profiles among *Salmonella* Typhimurium monophasic isolates with clonal complex and phage type, England and Wales, 2010 (n=139 isolates)

| MLVA profile | Number of isolates | Clonal complex | Phage type (number of isolates) |
|---|---|---|---|
| 2-11-5-8-0212 | 27 | CC2 | DT191 (4) |
| | | | DT191a (20) |
| | | | DT193 (1) |
| | | | RDNC (2) |
| 3-11-10-NA-0211 | 21 | CC1 | DT120 (11) |
| | | | DT193 (3) |
| | | | U323 (2) |
| | | | UT (5) |
| 3-11-9-NA-0211 | 17 | CC1 | DT120 (3) |
| | | | DT193 (8) |
| | | | U302 (1) |
| | | | U311 (3) |
| | | | U323 (1) |
| | | | UT (1) |
| 3-12-9-NA-0211 | 16 | CC1 | DT120 (8) |
| | | | DT193 (4) |
| | | | U311 (1) |
| | | | U323 (1) |
| | | | UT (2) |
| 3-13-9-NA-0211 | 15 | CC1 | DT120 (1) |
| | | | DT193 (12) |
| | | | DT195 (1) |
| | | | U323 (1) |
| 3-12-10-NA-0211 | 12 | CC1 | DT120 (6) |
| | | | DT193 (2) |
| | | | U323 (3) |
| | | | UT (1) |
| 3-10-9-NA-0211 | 10 | CC1 | DT193 (10) |
| 3-12-10-NA-0211 | 8 | CC1 | DT120 (6) |
| | | | DT193 (2) |
| | | | U323 (3) |
| | | | UT (1) |
| 3-13-10-NA-0211 | 7 | CC1 | DT193 (6) |
| | | | U311 (1) |
| 3-14-10-NA-0211 | 6 | CC1 | DT120 (2) |
| | | | DT193 (4) |

CC: clonal complex; DT: definitive phage type; MLVA: multiple locus variable-number tandem repeat analysis; NA: not amplified; RDNC: reacts but does not conform; UT: untypable.

the island. However, a further 38% produced a single amplicon of 903 bp, suggesting mutation or deletion occurring either upstream of the inserted island or in the 5' end of the island itself (leading to a 'partial island'), or within the primer binding sites. In a random selection of six isolates producing only the 903bp band, five isolates supported amplification of the 1,128bp band when tested in a monoplex PCR with a slightly lowered primer annealing temperature (data not shown). This suggests that for at least some isolates, the absence of the 1,128bp band when testing using the multiplex PCR is due to mutation(s) within the primer binding site(s). In addition, the complete or 'partial island' was identified in 25 *fljB*+/*hin*+ DT193 isolates and nearly three quarters of monophasic isolates belonging DT120, UT, U323 and DT195. Given that all but one isolate harbouring the genomic island clustered together in CC1 regardless of antigenic structure and phage type, and assuming that all 17 open reading frames (ORFs) that make up the genomic island are present in these strains, these *fljB*+/*hin*+ DT193 isolates may be progenitors of the *fljB*-/*hin*- DT193 isolates. In turn, these may have changed phage type by plasmid loss or acquisition, lysogenic conversion or alterations in lipopolysaccharide to account for the presence of the genomic island in genetically related monophasic isolates of other phage types. Trüpschuch et al. hypothesised that uptake of the island occurred in two or more steps [15]; if this is the case it seems unlikely that the genomic island would have been acquired through multiple independent genetic events.

Monophasic variants of serovar Typhimurium have already caused substantial outbreaks in several countries and continue to pose a public health risk [10,11,13,26]. Reliable detection of monophasic variants of serovar Typhimurium is important to ascertain the impact the emergence of these strains is having on the food chain and the number of human infections, and to monitor control efforts. Legislation of the EU has now been redrafted to include serovar 4,[5],12:i:- in actions taken to detect and control Salmonella serovars of public health significance in laying hens (Commission Regulation (EU) No. 517/2011). In order to more accurately identify these isolates, the HPA SRU has been determining the full antigenic structure of all presumptive O:4 isolates since the beginning of 2012 in addition to performing phage typing for identification of serovar Typhimurium and its variants. Isolates will be passaged through single strength Craigie's tubes, followed by double strength Craigie's tubes if a negative result is obtained after the first attempt at flagellar phase inversion. At present molecular methods will not be applied due to the large number of isolates received in the laboratory, but new molecular methods for identification of serovar Typhimurium and its variants will be assessed as they become available.

## References


1. European Food Safety Authority (EFSA) Panel on Biological Hazards (BIOHAZ). Scientific Opinion on monitoring and assessment of the public health risk of "Salmonella Typhimurium-like" strains. EFSA Journal. 2010;8(10):1826. http://www.efsa.europa.eu/en/scdocs/doc/1826.pdf
2. European Food Safety Authority. The community summary report on trends and sources of zoonoses, zoonotic agents, antimicrobial resistance and foodborne outbreaks in the European Union in 2006. EFSA Journal. 2007;130. Available from: http://www.efsa.europa.eu/en/scdocs/scdoc/130r.htm
3. Echeita MA, Herrera S, Usera MA. Atypical, fljB-negative Salmonella enterica subsp. enterica strain of serovar 4,5,12:i:- appears to be a monophasic variant of serovar Typhimurium. J Clin Microbiol. 2001;39(8):2981-3.
4. Dionisi AM, Graziani C, Lucarelli C, Filetici E, Villa L, Owczarek S et al. Molecular characterization of multidrug-resistant strains of Salmonella enterica serotype Typhimurium and Monophasic variant (S. 4,[5],12:i:-) isolated from human infections in Italy. Foodborne Pathog Dis. 2009;6(6):711-7.
5. Soyer Y, Moreno SA, Davis MA, Maurer J, McDonough PL, Schoonmaker-Bopp DJ et al. Salmonella 4,5,12:i:-: an emerging Salmonella serotype that represents multiple distinct clones. J Clin Microbiol. 2009;47(11):3546-56.
6. Anderson ES, Ward LR, Saxe MJ, de Sa JD. Bacteriophage-typing designations of Salmonella typhimurium. J Hyg (Lond). 1977;78(2):297-300.
7. Hopkins KL, Kirchner M, Guerra B, Granier SA, Lucarelli C, Porrero MC et al. Multiresistant Salmonella enterica serovar 4,[5],12:i:- in Europe: a new pandemic strain? Euro Surveill. 2010;15(22):pii=19580. Available from: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19580
8. Echeita MA, Aladueña A, Cruchaga S, Usera MA. Emergence and spread of an atypical Salmonella enterica subsp. enterica serotype 4,5,12:i:- strain in Spain. J Clin Microbiol. 1999;37(10):3425.
9. Hauser E, Tietze E, Helmuth R, Junker E, Blank K, Prager R et al. Pork contaminated with Salmonella enterica serovar 4,[5],12:i:-, an emerging health risk for humans. Appl Environ Microbiol. 2010;76(14):4601-10.
10. Bone A, Noel H, Le Hello S, Pihier N, Danan C, Raguenaud ME et al. Nationwide outbreak of Salmonella enterica serotype 4,12:i:- infections in France, linked to dried pork sausage, March-May 2010. Euro Surveill. 2010;15 (24): pii=19592. Available from: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19592
11. Mossong J, Marques P, Ragimbeau C, Huberty-Krau P, Losch S, Meyer G et al. Outbreaks of monophasic Salmonella enterica serovar 4,[5],12:i:- in Luxembourg, 2006. Euro Surveill. 2007;12(6): pii=719. Available from: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=719
12. Harker KS, Lane C, de Pinna E, Adak GK. An outbreak of Salmonella Typhimurium DT191a associated with reptile feeder mice. Epidemiol Infect. 2011;139(8):1254-61.
13. Agasan A, Kornblum J, Williams G, Pratt CC, Fleckenstein P, Wong M et al. Profile of Salmonella enterica subsp. enterica (subspecies I) serotype 4,5,12:i:- strains causing food-borne infections in New York City. J Clin Microbiol. 2002;40(6):1924-9.
14. Tavechio AT, Ghilardi AC, Fernandes SA. "Multiplex PCR" identification of the atypical and monophasic Salmonella enterica subsp. enterica serotype 1,4,[5],12:i:- in São Paulo State, Brazil: frequency and antibiotic resistance patterns. Rev Inst Med Trop Sao Paulo. 2004;46(2):115-7.
15. Trüpschuch S, Laverde Gomez JA, Ediberidze I, Flieger A, Rabsch W. Characterisation of multidrug-resistant Salmonella Typhimurium 4,[5],12:i:- DT193 strains carrying a novel genomic island adjacent to the thrW tRNA locus. Int J Med Microbiol. 2010;300(5):279-88.
16. Bale JA, de Pinna EM, Threlfall EJ, Ward LR. Kauffmann-White Scheme - 2007: Salmonella Identification - Serotypes and Antigenic Formulae. London: Health Protection Agency; 2007.
17. Amavisit P, Boonyawiwat W, Bangtrakulnont A. Characterization of Salmonella enterica serovar Typhimurium and monophasic Salmonella serovar 1,4,[5],12:i:- isolates in Thailand. J Clin Microbiol. 2005;43(6):2736-40.
18. Lindstedt BA, Vardund T, Aas L, Kapperud G. Multiple-locus variable-number tandem-repeats analysis of Salmonella enterica subsp. enterica serovar Typhimurium using PCR multiplexing and multicolor capillary electrophoresis. J Microbiol Methods. 2004;59(2):163-72.
19. Larsson JT, Torpdahl M, Petersen RF, Sorensen G, Lindstedt BA, Nielsen EM. Development of a new nomenclature for Salmonella Typhimurium multilocus variable number of tandem repeats analysis (MLVA). Euro Surveill. 2009;14(15):pii=19174. Available from: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19174
20. Echeita MA, Herrera S, Garaizar J, Usera MA. Multiplex PCR-based detection and identification of the most common Salmonella second-phase flagellar antigens. Res Microbiol. 2002;153(2):107-13.
21. Tennant SM, Diallo S, Levy H, Livio S, Sow SO, Tapia M et al. Identification by PCR of non-typhoidal Salmonella enterica serovars associated with invasive infections among febrile patients in Mali. PLoS Negl Trop Dis. 2010;4:e621.
22. Barco L, Lettini AA, Ramon E, Longo A, Saccardin C, Pozza MC et al. A rapid and sensitive method to identify and differentiate Salmonella enterica serotype Typhimurium and Salmonella enterica serotype 4,[5],12:i:- by combining traditional serotyping and multiplex polymerase chain reaction. Foodborne Pathog Dis. 2011;8(6):741-3.
23. Zamperini K, Soni V, Waltman D, Sanchez S, Theriault EC, Bray J et al. Molecular characterization reveals Salmonella enterica serovar 4,[5],12:i:- from poultry is a variant Typhimurium serovar. Avian Dis. 2007;51(4):958-64.
24. Hopkins KL, Nair S, Kirchner M, Guerra B, Granier SA, Lucarelli C et al. Genetic variation in emerging multidrug-resistant Salmonella enterica 4,[5],12:i:- from seven European countries. 2nd ASM Conference on Antimicrobial Resistance in Zoonotic Bacteria and Foodborne Pathogens in Animals, Humans and the Environment; 2010 Jun 8-11; Toronto, Canada.
25. Lucarelli C, Dionisi AM, Filetici E, Owczarek S, Luzzi I, Villa L. Nucleotide sequence of the chromosomal region conferring multidrug resistance (R-type ASSuT) in Salmonella Typhimurium and monophasic Salmonella Typhimurium strains. J Antimicrob Chemother. 2012;67(1):111-4.
26. Peters T, Hopkins KL, Lane C, Nair S, Wain J, de Pinna E. Emergence and characterization of Salmonella enterica serovar Typhimurium phage type DT191a. J Clin Microbiol. 2010;48(9):3375-7.

# Importance of standardisation of HAI definitions in interpretation of international and/or multinational prevalence studies

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## To the editor:

A recent publication by Eilers et al. reported the Dutch experience of the prevalence and determinants associated with healthcare-associated infections (HAI) in long-term care facilities [1]. Ireland also participated in the European Centre for Disease Control coordinated healthcare-associated infections in long-term care facilities (HALT) point prevalence study in 2010. Eilers et al. reported that the prevalence of HAI in Irish long-term care facilities was 11.3%; however, this figure represents the proportion of residents that had either signs or symptoms of infection and/or were on antibiotics. The prevalence of infection in our study was 3.7% (using adapted McGeer definitions) or 2.4% (when strictly applying the McGeer definitions) [1–3].

Eilers et al. defined infection as having a 'suspicion of infection', i.e. having at least one symptom or sign on the HALT score list. In our study 266 (6.4%) residents had signs or symptoms of infection and it is this figure that is perhaps more comparable than the 11.3% quoted.

The HALT study has provided, for the first time, many European countries (including Ireland) with baseline data on HAI prevalence and antimicrobial use in long-term care facilities. As long-term care facilities represent a heterogeneous group of healthcare facilities, with care ranging from social to medical, inter-facility comparisons without adjustment for case mix can be difficult. In Ireland, we have used the HALT results to draft national guidelines for antimicrobial prescribing in long-term care [4] and to inform preventative programmes at a local level. However, surveillance definitions for HAI in this setting are not yet standardised leading to difficulties when comparing international and/or multinational studies. The proposed HALT-2 study in 2013 may be an opportunity to address this deficit.

## References

1. Eilers R, Veldman-Ariesen MJ, Haenen A, van Benthem BH. Prevalence and determinants associated with healthcare-associated infections in long-term care facilities (HALT) in the Netherlands, May to June 2010. Euro Surveill. 2012;17(34):pii=20252. Available from: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=20252
2. Cotter M, Donlon S, Roche F, Byrne H, Fitzpatrick F. Healthcare-associated infection in Irish long-term care facilities: results from the First National Prevalence Study. J Hosp Infect. 2012;80(3): 212-6.
3. McGeer A, Campbell B, Emori TG, Hierholzer WJ, Jackson MM, Nicolle LE, et al. Definitions of infection for surveillance in long-term care facilities Am J Infect Control. 1991;19(1):1-7
4. HSE-Health Protection Surveillance Centre. Diagnosis & Management of Urinary Tract Infection in Long Term Care Residents › 65 years. Dublin:HPSC; 2011. Available from: http://www.hpsc.ie/hpsc/A-Z/MicrobiologyAntimicrobialResistance/InfectionControlandHAI/Guidelines/File,12929,en.pdf.

# Authors reply: Importance of standardisation of HAI definitions in interpretation of international and/or multinational prevalence studies

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## To the editor:

We would like to thank M Cotter et al. for their comments regarding the application of uniform definitions for infections in the nursing home setting. In our article we indeed used a 'suspicion of infection', i.e. having at least one symptom or sign on the healthcare-associated infections in long-term care facilities (HALT) score list. In this first European HALT study it was decided to register signs and symptoms of disease separately so that Mc Geer criteria might be applied afterwards. Previously, Rothan-Tondeur et al argued that it is time to revise the Mc Geer criteria [1].

It is important to have uniform definitions not only for prevalence studies such as the HALT study, but also for incidence studies of infectious diseases in nursing homes. In the Netherlands we have a sentinel surveillance network for infectious diseases in nursing homes (SNIV) in place since January 2009. Within this network, on a weekly basis and for each participating nursing home, an elderly care physician or nurse practitioner records the number of gastroenteritis, probable pneumonia and influenza-like illness and urinary tract infections based on clinical criteria. In 2009 we adopted clinical definitions used by general practitioners for surveillance of influenza-like illness and probable pneumonia, and guidelines for gastroenteritis used in research in nursing homes since 2007, for the SNIV network (Box).

After half a year of surveillance in 2009 we evaluated the above definitions used in the SNIV network and compared them to the McGeer criteria [2]. For this evaluation we interviewed eight elderly care physicians, who in the Netherlands are in charge of medical care to nursing home residents and are medical doctors specialised in providing medical care to the elderly [3]. The focus of the interviews was the way the elderly care physicians diagnose infectious disease in these residents and the experiences thus far participating in the SNIV nursing home network. We concluded that the clinical view of the respondents on the infectious diseases under surveillance in the SNIV network very much agreed with the clinical definitions as used for the surveillance.

We see it as a challenge for the HALT-2 study to gather the experiences of the different European countries with the application of surveillance definitions for infectious disease. With M Cotter et al. we hope that the HALT-2 study in 2013 addresses the deficit of uniform European definitions of infectious diseases in nursing homes. In particular, we find it important to consider the need to base future clinical criteria for surveillance definitions on ways in which physicians diagnose infectious disease in nursing homes.

## References

1. Rothan-Tondeur M, Piette F, Lejeune B, de Wazieres B, Gavazzi G. Infections in nursing homes: is it time to revise the McGeer criteria? J Am Geriatr Soc. 2010;58:199-201.
2. McGeer A, Campbell B, Emori TG, Hierholzer WJ, Jackson MM, Nicolle LE, et al. Definitions of infection for surveillance in long-term care facilities. Am J Inf Control. 1991; 19(1): 1-7.
3. Schols JM. Nursing home medicine in The Netherlands. Eur J Gen Pract. 2005;11(3–4:141-3.

## Box

Definitions used by the 'Sentinel surveillance network for infectious diseases in nursing homes', the Netherlands, since 2009

**Gastroenteritis**

The resident must have one of the following four conditions:

a) diarrhoea three or more episodes in 24h, deviating from normal for this person

b) diarrhoea and two of the following symptoms: fever, vomiting, nausea, stomach ache, abdominal cramps, blood or mucus in stool

c) vomiting and two of the following symptoms: fever, nausea, stomach ache, abdominal cramps, blood or mucus in stool

d) vomiting three of more episodes in 24h (without other symptoms and vomiting is not related to the use of medication).

**Influenza-like illness**

The resident must meet the following conditions:

a) an acute start of symptoms and

b) at least one of the following systemic symptoms: fever or febrile feeling, malaise, headache, myalgia and

c) at least one of the following three respiratory symptoms: cough, sore throat, shortness of breath.

**Probable pneumonia**

The resident must have a suspected infection of the low respiratory tract, probably pneumonia, and must have at least one of the following symptoms:

a) tachypnoea, malaise, confusion, shortness of breath, cough (productive or improductive), fever › 38°C or fever in the last 48 hours, pain in the chest (respiratory) and

b) with new focal (unilateral) abnormalities upon auscultation of the lungs

as they occur as change compared to the former situation and other likely diagnoses are excluded.

# Health requirements for pilgrims attending the Hajj in Mecca, Kingdom of Saudi Arabia, 24–29 October 2012

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Hajj is the annual pilgrimage to Mecca, the Kingdom of Saudi Arabia (KSA). The 2012 Hajj is expected to gather over two million Muslims from more than 180 countries across the globe between 24 and 29 October and is by far the largest mass gathering in the world. With the Hajj approaching, the Ministry of Health of Saudi Arabia has issued information in Arabic and English about health requirements and recommendations on its website [1].

A publication in the *Weekly Epidemiological Record* informs visitors in English and French of the full requirements for entry into Saudi Arabia and information is also available in English from The National Travel Health Network and Centre (NaTHNaC) website [2,3].

Special requirements for visitors to the Hajj concern vaccinations against meningococcal meningitis, polio and yellow fever.

Health authorities in countries of origin are required to provide information to pilgrims on infectious diseases symptoms, methods of transmission, complications and means of prevention. In an attempt to prevent the spread of foodborne infections Hajj performers are not allowed to bring fresh food to Saudi Arabia. Only properly canned or sealed food or food stored in containers with easy access for inspection is allowed in small quantities, sufficient for one person for the duration of his or her trip.

The KSA provides free healthcare to all visiting pilgrims during the Hajj, with the KSA Ministry of Health as one of the main contributors.

## References

1. Saudi Ministry of Health Requirements and Health Matters. Riyadh: Ministry of Hajj. Kingdom of Saudi Arabia. [Accessed 13 Sep 2012]. Available from: http://www.hajinformation.com/main/t20.htm
2. Health conditions for travellers to Saudi Arabia for the pilgrimage to Mecca (Hajj). Wkly Epidemiol Rec. 2012;87(30):277-80.
3. National Travel Health Network and Centre. Advice for Pilgrims for the Hajj and Umrah Season of 1433 (2012). London: Health protection Agency. [aCCESSED 13 sEP 2012]. Available from: http://www.nathnac.org/pro/factsheets/pdfs/Hajj_Umrah.pdf

# Updated version of ECDC guidance on human papillomavirus vaccines in Europe available

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The European Centre for Disease Prevention and Control (ECDC) published an update to its 2008 guidance on human papillomavirus (HPV) vaccines in Europe on 5 September 2012 [1]. The update follows the introduction of vaccination programmes in 19 European countries and new evidence from research studies over the past four years.

Randomised trials and observations from the field have demonstrated good safety profiles and efficacy against cervical cancer precursors for the vaccines. Despite this, and although most of these countries are providing the vaccine for free, vaccination rates are lower than expected.
The vaccination rates for those meeting the prescribed schedule of three doses in six months range from 17% to 84% for the reporting countries. Portugal (84%), the United Kingdom (80%) and Denmark (79%) were at the top of that range. Separate reports suggest that Sweden's vaccination coverage rate is also around 80% of their target group. The update considers among the deterring factors the high cost of the vaccines and the regime of three doses in six months.

Since the vaccine was authorised, the inclusion of HPV for boys in vaccination programmes is regularly debated. The ECDC guidance document recommends that public health initiatives should continue to focus on vaccinating girls. Routine HPV vaccination should target girls aged 10-14 years before the onset of sexual activity and should be administered in three doses within six months.

The update points to evidence that alternative vaccination schedules are not less effective than the currently recommended protocol of three doses. Further research is needed to confirm this but could have a great impact on costs and strategies for HPV vaccination programmes. The update does not recommend changing the current vaccination schedule at this point in time.

## References

1. European Centre for Disease Prevention and Control. Introduction of HPV vaccines in EU countries – an update. Stockholm: ECDC; 2012. Available from: www.ecdc.europa.eu/en/publications/Publications/20120905_GUI_HPV_vaccine_update.pdf