Special edition: Outbreak of hepatitis A in men who have sex with men in 2017

December 2017

Featuring

• Outbreak reports from England, France, Germany, Israel and the Netherlands
• and more...

www.eurosurveillance.org
## Special Edition: Outbreak of Hepatitis A in Men Who Have Sex With Men in 2017

### Rapid Communications

<table>
<thead>
<tr>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatitis A outbreak in HIV-infected MSM and in PrEP-using MSM despite a high level of immunity, Lyon, France, January to June 2017</td>
<td>2</td>
</tr>
<tr>
<td>Charre C et al.</td>
<td></td>
</tr>
<tr>
<td>Ongoing hepatitis A among men who have sex with men (MSM) linked to outbreaks in Europe in Tel Aviv area, Israel, December 2016 – June 2017</td>
<td>6</td>
</tr>
<tr>
<td>Mor O et al.</td>
<td></td>
</tr>
<tr>
<td>Hepatitis A outbreak among men who have sex with men (MSM) predominantly linked with the EuroPride, the Netherlands, July 2016 to February 2017</td>
<td>10</td>
</tr>
<tr>
<td>Freidl G et al.</td>
<td></td>
</tr>
<tr>
<td>Ongoing outbreaks of hepatitis A among men who have sex with men (MSM), Berlin, November 2016 to January 2017 – linked to other German cities and European countries</td>
<td>15</td>
</tr>
<tr>
<td>Werber D et al.</td>
<td></td>
</tr>
<tr>
<td>Outbreak of hepatitis A associated with men who have sex with men (MSM), England, July 2016 to January 2017</td>
<td>20</td>
</tr>
<tr>
<td>Beebeejaun K et al.</td>
<td></td>
</tr>
</tbody>
</table>
Since 2016, an increase in the number of hepatitis A cases affecting mainly men who have sex with men (MSM) has been reported in low endemic countries in Europe. We calculated the attack rate in Lyon, France, in populations considered at high-risk: HIV-infected MSM and HIV-negative MSM receiving HIV pre-exposure prophylaxis (PrEP). In these populations, high level of immunity did not prevent the outbreak, indicating that vaccination should be reinforced, particularly in younger individuals.

Several outbreaks of acute hepatitis A among men who have sex with men (MSM) have been recently reported in different European countries [1-4]. Since the end of 2016, an important increase in the number of acute hepatitis A cases in MSM has been also notified in France through the national mandatory reporting system [5]. The aim of this study was to evaluate the proportion of hepatitis A virus (HAV)-susceptible individuals and the attack rate of acute hepatitis A in HIV-infected MSM and in HIV-negative MSM receiving HIV pre-exposure prophylaxis (PrEP). In these populations, high level of immunity did not prevent the outbreak, indicating that vaccination should be reinforced, particularly in younger individuals.

Case definition and cohort description
The infectious diseases department of the Hospices Civils de Lyon follows ca 3,800 HIV-infected patients per year, representing 94% of HIV-infected patients followed in the Rhône department. Additionally, 415 MSM who used PrEP in the Rhône department were followed in the infectious diseases department during the study period. All cases of acute hepatitis A diagnosed in the Hospices Civils de Lyon virology laboratory between 1 January and 30 June 2017 were included. Diagnosis was based on the detection of serum HAV-specific IgM antibodies (ADVIA Centaur HAV assays, Siemens, Canada) along with elevated liver enzymes. HAV sequencing from IgM-positive samples was performed by the HAV national reference centre in Villejuif, France, as previously reported [6].

All 2,023 HIV-infected MSM and 415 PrEP users followed during the period were enrolled. Demographics (age, HIV status, PrEP use), HAV and hepatitis B virus (HBV) serological status, previous history of HAV infection and HAV vaccination history were retrieved from the clinical database and are compiled in the Table. The proportion of HAV-susceptible patients was determined based on medical, serological and vaccination history. Criteria for HAV immunity were: (i) past documented acute hepatitis A or (ii) past positive test for HAV total antibodies or (iii) administration of at least one dose of hepatitis A vaccine before January 2017.
of the attack rate, since the denominator for this population is unknown. The study was approved by the local ethics committee.

Description of the outbreak

From 1 January 2017 to 30 June 2017, 46 cases of acute hepatitis A were diagnosed in the laboratory (Figure 1), among whom 34 occurred between May and June. Two cases occurred in children under 15 years old. Among 44 adult cases, 38 were men (sex ratio M/F: 6.3); 33 were MSM, including 17 HIV-negative (among whom three were PrEP users) and 16 HIV-infected. Two cases in HIV-infected MSM who did not live in the Rhône department were excluded from the attack rate analysis. In all but one case occurring in MSM, sequencing identified one of the three epidemic strains circulating among MSM in many European countries [2-4]: 1a_VRD_521_2016 (UK/Spain; 18/33), 1a_RIVM_HAV16–090 (EuroPride; 12/33), and 1a_V16–25801 (2/33) (Table).

HIV-infected MSM were significantly older than PrEP users (p<0.001). Among those with information available, the proportion of HAV-susceptible patients was not significantly different between groups (HIV-infected MSM: 26.6%, PrEP users: 24.9%, p=0.48). The attack rate irrespective of age was similar in HIV-infected MSM (best case scenario: 2%; worst case scenario: 3.8%) and in PrEP users (best case scenario: 2.7%; worst case scenario: 3%; Table). HAV susceptibility in patients with a known immune status was higher in patients aged 18–30 years, both among PrEP users (36%) and in HIV-infected MSM (47%) and decreased with age. The best and worst case scenario gave results that were close, except for the older HIV-infected group, in which a greater number of unknown status led to an increase in susceptibility in the best case scenario (Figure 2). The attack rate in HIV-infected MSM was highest in those aged 18–30 years (best case scenario: 5.2%; worst case scenario: 6.3%) and decreased with age to reach 0% in those aged 60 years or more.

Discussion

In high-income countries the prevalence of anti-HAV antibodies in the general population is usually low (<50% by the age of 30 years) [7] Therefore, the high proportion of susceptible individuals among adults...
could theoretically allow transmission, but usually hygiene measures limit the circulation of the virus and the risk of acquiring infection remains low. However, if HAV is introduced in groups at particular high-risk of transmission, outbreaks may occur according to level of immunity. Due to faeco-oral transmission during sexual activities, in particular bucco-anal, digital-anal, digital-rectal, and genito-oral activities following anal sex, MSM are at a high risk of HAV transmission. Moreover, as HAV transmission from sharing needles has also been described [8], intravenous injection of recreational drugs along with anal intercourse (also known as slamming) may increase the risk of HAV transmission in some groups of MSM. For these reasons, anti-HAV vaccination is routinely recommended in France in HIV-infected MSM and PrEP users [9], contributing to a high level of immunity compared with the general population. For example, in a recent survey, 78% of adults aged 20–29 years were susceptible to HAV, as opposed to 31% of HIV-infected MSM and 29% of PrEP users in the present study [10]. Nevertheless, this high level of immunity did not prevent HAV outbreak in the present study.

Between 1 January 2017 and 30 June 2017, 57 cases of acute hepatitis A were notified through the mandatory reporting system in the Rhône department. Among these 57 cases, 46 were diagnosed in our laboratory, suggesting a satisfying representativeness of the cases analysed here for the overall outbreak in the department. As previously reported, the outbreak described here affected mainly MSM with a similar attack rate in HIV-positive MSM and PrEP users, suggesting a comparable transmissibility in both groups considered at high risk of transmission.

One limitation of the study is that HAV immune status remained unknown in 17.9% of HIV-infected MSM and in 2.2% of PrEP users. However, in the best case scenario sensitivity analysis attack rates were high, confirming that both populations were engaged in at-risk sexual behaviour, as previously described [11,12]. Another limitation is that HAV immune status was not systematically confirmed serologically. Moreover, a single dose of hepatitis A vaccine may not be sufficient to provide immunity in a HIV-positive patients [13]. However, during the study period, no case of acute hepatitis A was reported in our centre among patients who received a single dose of vaccine.

Predictions from a modelling study suggested that population immunity must exceed 70% to prevent future person-to-person transmission of hepatitis A virus among MSM [14]. According to this model, the
immunity level in the study population should have conferred protection against HAV outbreaks. However, HAV-susceptibility was much higher in younger individuals, which is likely to explain the higher attack rate observed before 40 years of age. Additionally, differences in risk practices among age groups may also have influenced transmission of the virus and the attack rate.

As immunity threshold of 70% seems to be insufficient to prevent HAV outbreaks, it should be adjusted considering behavioural characteristics, socio-demographic characteristics, and different age structures. Promotion of HAV vaccination should be reinforced, especially in young MSM who are at high risk of HAV transmission.

Members of the HAV Lyon Study Group


Conflict of interest

None declared.

Authors’ contributions

Caroline Charre, Christophe Ramière, Caroline Scholtès performed laboratory diagnostics.

Anne-Marie Roque Afonso performed sequencing data analysis.

Christian Chidiac, Fabien Zoulim, Matthieu Godinot, Joseph Koffi, Jean-Michel Livrozet, Laurent Cotte provided clinical care.

Caroline Charre, Christophe Ramière, Laurent Cotte analysed the data and drafted the manuscript.

All authors reviewed the manuscript before submission.

Members of the HAV study group contributed to the acquisition of the clinical or biological data, revised the work, and approved the submitted version.

References


License and copyright

This is an open-access article distributed under the terms of the Creative Commons Attribution (CC BY 4.0) Licence. You may share and adapt the material, but must give appropriate credit to the source, provide a link to the licence, and indicate if changes were made.

This article is copyright of the authors, 2017.
Between December 2016 and June 2017, 19 Hepatitis A virus (HAV)-positive cases, 17 of which were among men who have sex with men (MSM) were identified in the Tel Aviv area. Seven of the 15 sewage samples collected between January and June 2017 were also HAV-positive. All sequences clustered with two of the three strains identified in the current European HAV outbreak. We demonstrate that despite an efficient vaccination programme, HAV can still be transmitted to an unvaccinated high-risk population.

An ongoing hepatitis A outbreak involving 15 European countries with the first case identified in June 2016 in the United Kingdom (UK) [1], was recently reported [2]. By June 2017, 1,173 hepatitis A virus (HAV) infections mainly among men who have sex with men (MSM) were notified. In December 2016, when the first hepatitis A cases in Tel Aviv district were diagnosed, the local public health authority was notified and an ongoing virological, epidemiological and environmental surveillance has commenced. Here we report the current findings of 1 June 2017.

Identification of hepatitis A virus 1a in clinical and environmental samples

Hepatitis A is a notifiable disease in Israel and only 17 sporadic cases were reported between March 2013 and December 2016 in the Tel Aviv district, when the first case of the current hepatitis A outbreak was identified in a hospitalised man. A case was defined as a report of an individual who had been in the Tel Aviv health district (covering the Tel Aviv metropolitan region) with a clinical presentation of abrupt onset of hepatitis (fatigue, nausea, anorexia, abnormal liver function tests) and laboratory confirmed anti-HAV (immunoglobulin M, IgM positivity) serology. By June 2017, 19 cases of HAV infection confirmed by serology were notified to the Tel Aviv district health office (Figure 1). Seventeen cases were men, aged 22 to 41 years, who self-identified as MSM. One was a woman with a travel history to India during the incubation period. Of the 15 MSM, three had travelled to Europe, and one to the United States (US) in the two months before symptom onset. Fifteen infections were also confirmed by RT-PCR and sequencing: eight MSM were infected by the HAV 1a_ RIVM_HAV16–90 (EUROPRIDE) and six by the HAV 1a_ VRD_521_2016 (UK/SPAIN) strain; the woman was infected with an HAV 1b_India strain. The Table shows the characteristics of the patients, none of whom were vaccinated.

To support the outbreak investigation, the presence of HAV sequences was assessed in sewage samples (n = 23) collected between August 2016 and June 2017 as part of the routine polio surveillance programme [3] from three facilities located in the Tel Aviv area.

All sewage samples collected between August and the end of December 2016 were HAV- negative. Seven of the fifteen samples (3/7 from the Shafdan, the sewage treatment plant of Tel Aviv, and 4/4 samples from a southern Tel Aviv pipeline), collected between January and June 2017, were found to be HAV-positive.

Phylogenetic analysis of clinical and sewage HAV-positive samples showed that all sequences from the current outbreak among MSM in Israel and the seven positive sewage samples, clustered with either RIVM_ HAV16–90 (EUROPRIDE) or VRD_521_2016 (UK/SPAIN)
isolates identified in the 2016–2017 European HAV outbreak [1,4,5].

Three MSM were infected with the VRD_521_2016 (UK/SPAIN) strain and epidemiologically-linked to the same non-household venue. Moreover, sequencing results were available for three of four MSM who reported travelling in the 2 months before symptoms onset. One of them, identified with the VRD_521_2016 (UK/SPAIN) strain in December 2016 (week 52), was most likely infected in Berlin. Another adult MSM, harbouring the RIVM_HAV16–90 (EUROPRIDE) strain and diagnosed in May 2017 (week 18), reported a stay in Poland during the incubation period. The third MSM, diagnosed in late May (week 22), presented with acute hepatitis two weeks after returning from New York and carried the VRD_521_2016 (UK/SPAIN) strain. All other cases had not travelled abroad and were infected in Israel.

HAV isolates from sewage also clustered with both HAV strains implicated in the ongoing European outbreak. In two of the sewage samples (9,794 and 9,773), both strains could be identified together. HAV sequences from past outbreaks in Tel Aviv formed a separate cluster with HAV 1b sequences (Figure 1, 2).

**Laboratory investigation**

Serum or plasma samples from acute hepatitis A cases positive for anti-HAV IgM were transferred to the national centre of HIV and viral hepatitis in the central virology laboratory of the Ministry of Health. Total nucleic acids were purified from 400 µL of plasma (or from 500 µL of filtered and concentrated sewage samples) and real-time PCR for HAV detection was performed as described previously [6]. PCR and sequencing primers of a 460-nt fragment located within the VP1/P2A region were chosen according to the HAVNET unified typing protocol [7]. Sequencing was performed on an ABI 3500 Genetic Analyzer (Applied Biosystems, Foster City, California, US) using an ABI PRISM BigDye Terminator Cycle Sequencing kit (Applied Biosystems). Raw sequence data was analysed corrected and trimmed to generate a 427-nt consensus sequence using Sequencher 5.4 (GeneCodes, Ann Arbor, Michigan, US). The resulting HAV sequences were aligned with the three distinct HAV 1a strains representing the current HAV MSM outbreak in Europe and with sequences from previously identified HAV infections in Israel. Phylogenetic analysis was conducted using a neighbour-joining algorithm in MEGA, version 6 [8], with 1,000 replicates for bootstrap testing.

**Discussion**

Hepatitis A virus infection causes a substantial number of viral hepatitis cases worldwide. It is an acute self-limiting illness, associated with fever, malaise, nausea, anorexia and jaundice, mainly transmitted via the faecal-oral route [9]. A two-dose universal toddler’s vaccination programme at 1.5 and 2 years of age, was initiated in Israel in 1999 and has led to an over 90% decline in incidence of the disease [10]. However, the programme cannot prevent HAV infection in high risk groups like MSM born in Israel before 1999.

Between March 2012 and March 2013, there was an outbreak in the Tel Aviv district with 75 cases of acute hepatitis, of which 73% were in non-vaccinated young men. HAV 1b was the predominant subtype identified in clinical as well as in sewage samples collected during the outbreak [6]. In the ongoing HAV outbreak occurring in the Tel Aviv district, in non-vaccinated, MSM in the age-group of 20-45 years, two of the three strains currently circulating in MSM in Europe were identified. They were detected in clinical samples from patients
and in samples collected from sewage facilities located in the Tel Aviv area. Interestingly, none of the sewage samples collected in the 5 months before the first HAV case was identified, were HAV-positive. We therefore assume that these strains did not circulate in Tel Aviv before December 2016. Moreover, a different HAV sub-type, HAV 1b, dominated in the 2012–13 outbreak that affected mainly non-vaccinated injecting drug users and not MSM. The identification of individuals that reported being infected while abroad also supports the conclusion that the current outbreak was imported to Israel by travelling MSM.

Anti-HAV vaccine is routinely recommended by the Israeli Ministry of Health to various risk groups, including MSM [11]. Following the identification of the first hepatitis A cases in MSM in Tel Aviv, we communicated about the outbreak through social media and offered free of charge vaccinations at all public health offices and sex clinics in Israel. Leaflets explaining HAV transmission and calling for anti-HAV vaccination were distributed at the venue where three infections occurred. Controlling the outbreak and protecting those who are not immune is complicated by undernotification as well as by possible asymptomatic HAV infection leading to continuous virus circulation. The abundance of HAV isolates in the environmental samples indicates that not all HAV cases have been identified.

In the past, molecular and phylogenetic analysis of HAV-positive cases in Israel was only done in specific cases. Following the 2012-13 outbreak, the need for a national diagnostic laboratory to support public health decisions on hepatitis A was emphasised. In June 2017, the viral hepatitis reference laboratory in the central virology laboratory of the Ministry of Health was formally established and an official requirement to send IgM-positive HAV samples for molecular confirmation put in place. Thus future outbreaks are expected to be better assessed. Our findings in the MSM population together with the current reports from Europe and recently also in North America [12] call for introduction of new methodologies aiming to increase vaccination coverage specifically within this risk group.

Acknowledgements

We would like to thank staff from the Tel Aviv Public Health Services and from the central virology laboratory involved in the investigation and management of the outbreak. We would also like to specially thank Jurgen Wenzel from the Regensburg University Medical Center, Germany, who provided us relevant in formation and sequences of HAV strains circulating in Europe.
Conflict of interest

None declared.

Authors’ contributions

All the authors contributed to the outbreak investigations described here, the presentation of information and reviewed and commented on the manuscript.

References


License and copyright

This is an open-access article distributed under the terms of the Creative Commons Attribution (CC BY 4.0) Licence. You may share and adapt the material, but must give appropriate credit to the source, provide a link to the licence, and indicate if changes were made.

This article is copyright of the authors, 2017.
Hepatitis A outbreak among men who have sex with men (MSM) predominantly linked with the EuroPride, the Netherlands, July 2016 to February 2017

GS Freidl ¹ ² , GJ Sonder ³ , LP Bovée ³ , IH Friesema ¹ , GG van Rijckevorsel ⁴ , WL Ruijs ⁴ , F van Schie ³ , EC Siedenburg ³ , J Yang ⁵ , H Vennema ⁶
1. Centre for Infectious Diseases, Epidemiology and Surveillance, Centre for Infectious Disease Control, National Institute for Public Health and the Environment (RIVM), Bilthoven, the Netherlands
2. European Programme for Intervention Epidemiology Training (EPIET), European Centre for Disease Prevention and Control (ECDC), Stockholm, Sweden
3. Department of Infectious Disease Control, Public Health Service Amsterdam (GGD), Amsterdam, the Netherlands
4. National Coordination Centre for Communicable Disease Control, Centre for Infectious Disease Control, National Institute for Public Health and the Environment (RIVM), Bilthoven, the Netherlands
5. Centers for Infectious Disease Control, Taipei, Taiwan
6. Centre for Infectious Diseases Research, Diagnostics and Screening, Centre for Infectious Disease Control, National Institute for Public Health and the Environment (RIVM), Bilthoven, the Netherlands

Correspondence: Gudrun S Freidl (gudrun.freidl@rivm.nl)

Citation style for this article:

Article submitted on 09 February 2017 / accepted on 22 February 2017 / published on 23 February 2017

Between July 2016 and February 2017, 48 male cases of hepatitis A were notified in the Netherlands. Of these, 17 identified as men who have sex with men (MSM). Ten of the 13 cases for whom sequencing information was available, were infected with a strain linked with the EuroPride that took place in Amsterdam in 2016. This strain is identical to a strain that has been causing a large outbreak among MSM in Taiwan.

In December 2016, the European Centre for Disease Prevention and Control (ECDC) issued a Rapid Risk Assessment reporting of two distinct hepatitis A virus (HAV) genotype IA strains circulating among men who have sex with men (MSM) in the United Kingdom (UK) and the Netherlands in 2016. Germany, Italy and Spain had also reported a recent increase in male HAV cases [1].

The outbreak is ongoing with 37 cases reported in the UK between July 2016 and January 2017 [2] and 30 cases in Berlin between mid-November 2016 and end of January 2017 [3]. Here we describe the current situation in the Netherlands including potential links to this international hepatitis A outbreak.

Case definition
A case was defined as a person who (i) met the surveillance definition of a case of hepatitis A, (ii) self-identified as MSM or had MSM contact i.e. sexual contact with another man two months before the onset of symptoms, (iii) developed symptoms after mid-2016 (3 July 2016) and (iv) was a resident in the Netherlands.

The surveillance case definition comprises (i) non-specific symptoms (e.g. fatigue, abdominal pain, loss of appetite, intermittent nausea and vomiting), (ii) fever or jaundice and (iii) laboratory confirmation or an epidemiological link with a laboratory-confirmed case i.e. either hepatitis A-specific IgM antibodies in serum or detection of HAV in serum or stool by means of PCR [4].

Surveillance of hepatitis A in the Netherlands
In the Netherlands, hepatitis A is a notifiable disease. Laboratories and physicians report HAV infections within one working day to the regional Public Health Services (PHS). The PHS then collect epidemiological information on demographics, occupation, symptoms, suspected source / country of infection, MSM contact (for males only) and consumption of specific food items. The PHS reports all information in the national surveillance system for notifiable diseases. In addition, serum and / or stool samples of HAV cases are routinely sent to the National Institute of Public Health and the Environment (RIVM) for molecular analysis. In case men did not explicitly report having had MSM contact two months before disease onset, MSM status was assessed by asking whether they identified themselves as MSM.

Molecular analyses
HAV IgM-positive serum samples were analysed by sequence analysis of a 460 nt PCR fragment in the VP1/P2A region according to a shared protocol available through Hepatitis A Lab-Network HAVNET [5].
Outbreak description

In the first half of 2016 (including week 26), 22 sporadic hepatitis A cases were notified through the Dutch national surveillance system. Half of these were men and none reported MSM contact.

On 19 September 2016 (week 38), the outbreak investigation was triggered by the notification of two male cases of hepatitis A, in their 30s and 40s, who fell ill in mid-September. Both cases reported having had MSM contact during the EuroPride. The EuroPride, which took place in Amsterdam between 29 July and 6 August, is an international event to celebrate equality rights of the lesbian, gay, bisexual and transgender community. In 2016, this event attracted over half a million visitors [6]. Sequencing showed that strains from both cases were identical (RIVM-HAV16–090). Given the international character of the EuroPride, alerts were placed on the Early Warning and Response System (EWRS) and on ECDC’s Epidemic Intelligence Information System for Food- and Waterborne diseases (EPIS-FWD) to inform other European countries.

From mid-2016 (week 27) to 7 February 2017, 48 male cases of hepatitis A were reported nationally. Of these, 17 were born outside the Netherlands (Argentina, Brazil, Canada, France, Italy, Lebanon, Peru, Spain (n = 3), Surinam). The median age of the 17 cases was 33 years (range: 26–52). None of the cases were vaccinated and about a third was hospitalised (Table). Sequence information was available for 13 of the 17 cases, which showed co-circulation of three different hepatitis A strains (Table, Figure 2).

Ten of the 13 cases with available typing information were infected with the EuroPride strain. The majority of cases (n = 11), irrespective of sequence type, clustered in the Public Health Service region of Amsterdam, whereas other Public Health Service regions only reported incidental cases (Table, Figure 3).

In comparison, among the 29 male cases who became ill after mid-2016 and were not MSM (median age: 20.5 years, range: 0–82) we found strains that were unrelated to the current outbreak. We detected genotype IA and IB strains from Morocco, IB strains from Egypt, Turkey, West Africa and East Africa, a IIA strain from Cameroon, a IIIA strain from Romania or no hepatitis A virus, respectively. As none of these cases was infected with a strain involved in the current outbreak, we are confident that these cases reported their MSM status truthfully.

EuroPride strain RIVM-HAV16–090

When comparing sequence information of the EuroPride strain with available sequences in the databases HAVNET [5] and GenBank, we found that the EuroPride strain was 99.57% identical to a sequence submitted by Japan (accession number: AB020565, release date: 14 August 2001). In addition, in response to a post on ProMED-mail from May 2016 that reported

Of the 17 cases, 11 were born outside the Netherlands (Argentina, Brazil, Canada, France, Italy, Lebanon, Peru, Spain (n = 3), Surinam). The median age of the 17 cases was 33 years (range: 26–52). None of the cases were vaccinated and about a third was hospitalised (Table). Sequence information was available for 13 of the 17 cases, which showed co-circulation of three different hepatitis A strains (Table, Figure 2).

Ten of the 13 cases with available typing information were infected with the EuroPride strain. The majority of cases (n = 11), irrespective of sequence type, clustered in the Public Health Service region of Amsterdam, whereas other Public Health Service regions only reported incidental cases (Table, Figure 3).

In comparison, among the 29 male cases who became ill after mid-2016 and were not MSM (median age: 20.5 years, range: 0–82) we found strains that were unrelated to the current outbreak. We detected genotype IA and IB strains from Morocco, IB strains from Egypt, Turkey, West Africa and East Africa, a IIA strain from Cameroon, a IIIA strain from Romania or no hepatitis A virus, respectively. As none of these cases was infected with a strain involved in the current outbreak, we are confident that these cases reported their MSM status truthfully.
on a hepatitis A outbreak among MSM in Taiwan with 275 notified cases [7], we investigated whether the EuroPride strain might be related to the Taiwanese outbreak strain. Direct comparison and phylogenetic analyses showed that the Taiwanese outbreak strain was identical to the EuroPride strain (Figure 2). Eight of the ten cases reported to have likely been infected in the Netherlands, and a further two cases were likely infected in Barcelona, Spain (n = 2; onset of illness for both cases: week 2, Figure 1).

**Strains VRD_521_2016 and RIVM-HAV16-069**

Two cases were infected with strain VRD_521_2016, first reported by the UK in December 2016 and likely imported from Spain several times [1,2]. One of the Dutch cases reported having travelled to Spain (onset of illness in week 45), whereas the other case stated to have likely been infected in the Netherlands (onset of illness week 52, Figure 1). One case infected with strain RIVM-HAV16–069 reported having travelled to Argentina and became ill shortly before the EuroPride (week 27). The UK also reported one MSM case with the same sequence [2].

**Discussion**

Here we report on an ongoing hepatitis A outbreak among MSM in the Netherlands that started in 2016. Hepatitis A is an acute, self-limiting liver disease which is transmitted via the faecal-oral route. Infection occurs via contaminated food or water, or through person-to-person contact, including sexual contact. The average incubation period is 28 days (range: 15–50 days) [8]. In western Europe hepatitis A endemicity is low [9] and is primarily associated with travelling to endemic countries [10] or consumption of contaminated, imported food [11]. Outbreaks among MSM have also been described [12]. In Europe, the last outbreak of hepatitis A among MSM occurred between 2008 and 2011 [13].

![Figure 2](image-url)

*Phylogenetic analysis of virus strains from hepatitis A cases who self-identified as men who have sex with men, the Netherlands, 2000–2017*

The tree was constructed in PHYLIP (DNADIST) (Joe Felsenstein, Department of Genome Sciences, University of Washington, Seattle, USA). Strains are identified by sample number and cluster. Event 1 and Event 2 refer to terminology used in the Rapid Risk Assessment published by the European Centre for Disease Prevention and Control (ECDC) [1]. Event 1 refers to strains detected in the United Kingdom and Spain [2], Event 2 refers to the EuroPride strain detected in the Netherlands and the strain circulating in Taiwan in 2016, respectively. One asymptomatic case is identical to a sequence that caused a cluster in Germany (Ber/Muc/Fra) [3]. For comparison, we also included older hepatitis A virus strains detected in men who have sex with men (MSM) in 2000, 2001 and 2008, respectively.

![Figure 3](image-url)

*Geographic distribution of hepatitis A cases who self-identified as men who have sex with men, by available sequence information, the Netherlands, July 2016–February 2017 (n = 19)*

**Sequence**

- RIVM-HAV16-090
- RIVM-HAV16-069
- VRD_521_2016
- Results pending

**Exposure**

- MSM contact
- MSM contact unknown
- PHSR: Public Health Service region.

Two cases for whom MSM status was unknown at the time of the investigation, are also shown. Notified cases are centred in the respective Public Health Service region. The majority of cases (n = 11) occurred in the PHSR Amsterdam.
Between 2012 and mid-2016, hepatitis A infection in MSM was only notified twice in the Netherlands. In the currently ongoing outbreak in the Netherlands, the majority of cases for whom sequence information was available, were infected with strain RIVM-HAV16–090. This strain had only been detected once in 2010 and was absent in the Netherlands until it was detected in two MSM cases who attended the EuroPride in 2016. The strain is identical with a strain causing an ongoing outbreak among MSM in Taiwan. At 29 September 2016, Taiwan reported 845 hepatitis A cases among MSM, of which 56% were HIV-positive or had another sexually transmitted diseases [14].

In the Netherlands, information on HIV status is not routinely collected for hepatitis A surveillance purposes. In the course of this outbreak investigation, in week 43, we detected one HAV infection in a HIV-positive MSM who was asymptomatic and therefore did not meet the case definition. Sequencing showed infection with a strain identical to the Berlin/Munich/Frankfurt HAV cluster in Germany (V16–25801) [3]. Asymptomatic individuals, even if they do not fulfil the case definition, can still be epidemiologically relevant and should therefore be included in epidemiological analyses.

In the Netherlands, besides risk groups, i.e. persons with chronic liver disease or occupational exposure to HAV, hepatitis A vaccination is recommended to individuals who travel to HAV endemic countries. Hepatitis A vaccine uptake is unknown. Because of several outbreaks among European and Dutch MSM [15,16], hepatitis A vaccination is also recommended to MSM in the Netherlands. For MSM, vaccination against HAV is available at reduced costs and is administered in combination with hepatitis B vaccine that is free of charge for this risk group. The uptake of hepatitis B vaccination among MSM in Amsterdam is high and hepatitis B incidence has dropped markedly since 2005 [17]. In contrast, financial aspects might hamper wide uptake of hepatitis A vaccination. Vaccination coverage among MSM is unknown.

In the Netherlands, hepatitis A control is based on vaccination of household- and other close contacts [4]. Tracing and vaccination of sexual contacts of MSM can be challenging due to anonymous sexual contacts. To better understand transmission chains and the epidemiology of this outbreak, we recently introduced an additional, more detailed questionnaire for hepatitis A-positive MSM to complement routinely collected epidemiological data. Given the high outbreak potential of hepatitis A in the MSM community and the high interconnectedness through global travel of this risk group [18], increasing awareness of hepatitis A among MSM as well as health professionals at sexually transmitted disease clinics and public health services should be emphasised. To increase hepatitis A vaccination uptake, the Regional Public Health Services and ‘STI AIDS the Netherlands’ (centre of expertise for HIV and

### Table

<table>
<thead>
<tr>
<th>Characteristics of hepatitis A cases by MSM status and strain, the Netherlands, July 2016–February 2017 (n = 19)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Men who have sex with men (MSM)</strong></td>
</tr>
<tr>
<td><strong>Hepatitis A strain</strong></td>
</tr>
<tr>
<td><strong>Number of cases</strong></td>
</tr>
<tr>
<td><strong>Number per 10-year age group</strong></td>
</tr>
<tr>
<td><strong>Number of cases hospitalised</strong></td>
</tr>
<tr>
<td><strong>Number of cases vaccinated against hepatitis A</strong></td>
</tr>
<tr>
<td><strong>Suspected place of infection</strong></td>
</tr>
</tbody>
</table>

MSM: men who have sex with men; UK: United Kingdom.

* One case reported Portugal as second suspected country of infection.

* For one case information on suspected place of infection was not available.

Ages were estimated because only year of birth was known.

Characteristics of two male cases of hepatitis A for whom MSM status was unknown at the time of the investigation, are shown separately.
other sexually transmitted infections) have been engaging in activities to remind professionals and the Dutch MSM community of the availability of hepatitis A vaccination within the hepatitis B vaccination programme.

Acknowledgements

We would like to thank staff from the Public Health Service regions (GGD) involved in the investigation and management of the outbreak. We would also like to thank Ben Bom from SSC Campus / RIVM for creating the map and Christopher Williams for critical review of the manuscript.

No external funding was required to carry out this work.

Conflict of interest

None declared.

Authors’ contributions


References


License and copyright

This is an open-access article distributed under the terms of the Creative Commons Attribution (CC BY 4.0) Licence. You may share and adapt the material, but must give appropriate credit to the source, provide a link to the licence, and indicate if changes were made.

This article is copyright of the authors, 2017.
Rapid communications

Ongoing outbreaks of hepatitis A among men who have sex with men (MSM), Berlin, November 2016 to January 2017 – linked to other German cities and European countries

D Werber ¹, K Michaelis ², M Hausner ³, D Sissolak ³, J Wenzel ⁴, J Bitzegeio ¹, A Belting ⁵, D Sagebiel ¹, M Faber ²

1. State Office for Health and Social Affairs (LAGeSo), Berlin, Germany
2. Robert Koch Institute, Berlin, Germany
3. Local Public Health Authority, Berlin Mitte, Germany
4. National Consultant Laboratory for Hepatitis A and Hepatitis E, Institute of Clinical Microbiology and Hygiene, University Medical Center Regensburg, Regensburg, Germany
5. Bavarian Health and Food Safety Authority (LGL), Oberschleißheim, Germany

Correspondence: Dirk Werber (dirk.werber@lageso.berlin.de)

Since 14 November 2016, 38 cases of hepatitis A have been notified in Berlin; of these, 37 were male and 30 reported to have sex with men (MSM). Median age of MSM cases is 31 years (range: 24–52 years). Phylogenetic analysis revealed three distinct sequences, linking cases in Berlin to those in other German cities and to clusters recognised in other European countries in 2016.

On 14 December 2016, the local public health authority (LPHA) of the Berlin district Mitte informed the State Office for Health and Social Affairs (SOHSA) in Berlin, of two male cases of hepatitis A, notified in calendar week 50, who identified themselves as men who have sex with men (MSM). At that time, no increase in hepatitis A cases was apparent in the notification data.

Immediately following this information, we enhanced epidemiological and virological surveillance of hepatitis A in Berlin and report here preliminary findings.

Enhanced surveillance and molecular analyses

In the absence of an increase of hepatitis A in the notification data of Berlin in calendar week 50/2016, we (arbitrarily) considered a possible outbreak beginning as of calendar week 46/2016 (starting 14 November), i.e. four weeks (mean incubation period of hepatitis A) before the hepatitis A cases in MSM were first recognised. This coincided with when notified hepatitis A cases started to be predominantly male adults. We applied the case definition that is also used for surveillance purposes in Germany, i.e. symptomatic disease defined as fever or one of the following: abdominal discomfort, increase in serum transaminases, jaundice, plus laboratory confirmation, i.e. detection of hepatitis A virus (HAV) nucleic acid or HAV-specific IgM or a distinct increase in IgG [1]. We requested all 12 LPHAS in Berlin to systematically collect additional information on hepatitis A cases, notified as of calendar week 46/2016, in a specifically designed spreadsheet, including information on sexual contacts, sex in non-household venues and drug use, during their assumed period of infection. SOHSA collated case information submitted electronically by LPHAS.

LPHAs were also asked to organise sequencing of hepatitis A virus (HAV) from IgM positive serum samples or stool samples of cases notified as of calendar week 50 at the National Consultant Laboratory for Hepatitis A and Hepatitis E in Regensburg. Nucleic acid isolation, quantitative reverse transcription PCR (RT-qPCR) and sequencing were conducted as described elsewhere [2]. Sequencing primers were chosen according to the HAVNET unified typing protocol [3]. We queried GenBank for sequences with high similarity using the BLAST algorithms. A rooted maximum likelihood phylogenetic consensus tree for sequences of a 437 nucleotide (nt) long fragment in the VP1/P2A junction region was inferred using MEGA version 7.0.18 software.

In order to obtain information about possibly linked cases in other European Union countries, we communicated the information about the increase of hepatitis A in Berlin together with sequence information via the European Centre for Disease Prevention and Control.
(ECDC)’s Epidemic Intelligence Information System (EPIS) for food- and waterborne diseases and zoonoses (FWD) and the EPIS for sexually transmitted infections.

**Description of the outbreak**

As at 20 January 2017, 38 cases of hepatitis A have been notified in Berlin since 14 November 2016 (calendar week 46). Of these, 37 are male, and one is female (Table).

Sexual orientation is known for 32 cases (31 men, one woman); 30 identified themselves as MSM, one as heterosexual and the woman as having sex with women (WSW). Median age of the 30 MSM cases is 31 years (range: 24–52 years); they live in seven of the 12 districts in Berlin, and most of them in Mitte (n = 10). Disease onset of MSM cases ranges over an 11-week period (calendar weeks 43/2016–2/2017, Figure 1), which is incompatible with a common exposure to a point source. Three cases are epidemiologically linked to three other notified cases, supporting the assumption of transmission by interpersonal spread. Six cases have a travel history outside Germany (Spain (n = 2), Austria, Greece, Malta, Taiwan (n = 1 each) during the assumed period of infection, but the majority was apparently infected in Germany (likely in Berlin).

None of the MSM cases reported intravenous drug use. One MSM case was vaccinated with one dose of a monovalent hepatitis A vaccine 11 months before disease onset (a second dose within 6 to 12 months after the first dose is usually recommended by manufacturers to provide long-term protection); all others for which information on vaccination is available (n = 27) were unvaccinated (n = 23) or their vaccination was incomplete (n = 3, single doses of HAV/HBV combination vaccine or unknown vaccine more than one year before disease onset) or outdated (n = 1, last dose in 2001).

Sequencing results and phylogenetic analysis show three distinct clusters of MSM-related HAV strains currently circulating in Berlin (Figure 2).

The five sequences in the cluster Ber/Muc/Fra (including the WSW) are identical (100% match in the investigated 437 nt long fragment) to the HAV strain first observed in a MSM patient in August 2016 in Munich and later in a MSM patient in Frankfurt (prototype sequence V6–25801). The HAV sequences of three cases in the cluster Ber/NL are identical to the previously reported MSM-related HAV sequence RIVM-HAV16–090, which was isolated from two patients in September 2016, who had visited the EuroPride in Amsterdam in August 2016 [4]. Two of the identified cases fit in the third cluster Ber/UK with also identical sequences as compared with the MSM HAV outbreak strain UK VRD 521 circulating in the United Kingdom (UK) and reported in 2016 [4]. The closest match in the National Center for Biotechnology Information (NCBI) sequence database for the Ber/Muc/Fra cluster was isolated in 2013 in Italy during a multi-country European food-borne outbreak (IZSLLR-005, acc. KU570286.1, 99.5% identity) [5], matches for the other clusters are described in [4].

Through EPIS-FWD, colleagues from Austria, Denmark and the Netherlands reported sporadic cases with sequence identity to the Ber/Fra/Muc-Cluster, some of which reported having sex with men in Berlin before disease onset.

**Background**

HAV is predominantly transmitted via the faecal-oral route through person-to-person contact or contaminated food and water. The mean incubation period is 28 days (range: 15 to 50 days). Infected persons are most likely to transmit HAV before the onset of jaundice, when HAV concentration in stool is highest [6]. Transmission through sexual contact, particularly in MSM [7] as well as through sharing of needles and syringes has also been described [8]. Hepatitis A is a vaccine preventable disease and the German Standing Committee on Vaccination recommends vaccination of people with sexual behaviour at high-risk for HAV infection (such as homosexual contacts) [9]. Recommended vaccinations are paid for by health insurances in Germany.

Germany is a low incidence country with 0.9 notified cases per 100,000 population in 2016. Virtually all HAV infections are directly or indirectly imported [10].

**General and specific public health measures in Germany**

In response to the present outbreak, LPHAs educated cases about personal hygiene, traced cases and their contacts and recommended vaccination or post-exposure prophylaxis to contacts according to their risk profile. In addition, LPHA’s, the SOHSA and the Robert Koch Institute (RKI, German national public health institute) formulated prevention recommendations to
Molecular Phylogenetic analysis of the VP1/P2A junction region of selected HAV isolates by Maximum Likelihood method. Genotype VII was used as an outgroup. Sequences are denoted by GenBank ID (reference strains in blue) or isolate ID. Roman numerals indicate genotype; numbers at the nodes indicate bootstrap values.

The evolutionary history was inferred by using the Maximum Likelihood method based on the Tamura-Nei model. All positions containing gaps and missing data were eliminated. There were a total of 437 positions in the final dataset. Sequences from the Netherlands and the United Kingdom are from [4].

HAV: hepatitis A virus.
reinforce offering (i) vaccination to people with sexual behaviour at high-risk for HAV infection [10], and (ii) post-exposure prophylaxis to exposed contacts (active and passive immunisation is effective if administered within two weeks after exposure) [11].

This information was sent to practitioners who focus on treating HIV patients in Berlin, as well as to gay-oriented magazines, newsletters, webpages and specialised healthcare organisations. Furthermore, information was published in the weekly newsletter of the SOHSA and the Epidemiological Bulletin of the RKI [12].

Discussion

We report on a recent increase of notified hepatitis A cases in Berlin, attributable to cases in MSM. The age distribution of MSM is comparable to that of MSM in previously described hepatitis A outbreaks [7,13]. The vast majority of cases was not vaccinated against hepatitis A indicating a need for targeted risk communication and vaccination campaigns. Of note, condom use is not a safeguard against HAV infection because it does not block the faecal-oral transmission route.

Interestingly, two different HAV sequences detected in cases from Berlin were recently identified in clusters of MSM in the Netherlands and in the UK [7]. The third sequence was identified in a cluster of six MSM cases in Munich and Frankfurt from August through October (data not shown). It is unclear why three different HAV strains concurrently circulate in Berlin among MSM. Apparently, Berlin’s MSM scene is nationally and internationally well connected allowing for ‘importation’ and ‘exportation’ of HAV strains from or to various places in Europe.

For hepatitis A, the German electronic notification system does not capture sexual orientation. Thus, the magnitude of sexually transmitted hepatitis A is likely underestimated. The outbreak described here highlights the interconnectedness of MSM in Europe and the need to increase coverage of hepatitis A vaccination in this group.

Acknowledgements

We would like to thank colleagues from the local public health authorities for collecting case data and organising to forward blood and stool specimens for strain typing. We also would like to acknowledge the following colleagues who reported to EPIS on possibly linked cases in other countries: Luise Müller (Denmark), Solveig Jore (Norway), Franz Allerberger (Austria), Leila Thornton (Ireland), Harry Vennema (The Netherlands) and Lena Sundqvist (Sweden).

This work was supported by the Robert Koch-Institute and the German Federal Ministry of Health [grant number 1369-386 to J. Wenzel].

Conflict of interest

None declared.

Authors’ contributions

DW JB and DSa have conducted enhanced surveillance of hepatitis A in Berlin, DW has written the manuscript MH and DSi have discovered the link of recent hepatitis A cases and MSM in Berlin Mitte and provided detailed case information. KM has monitored the situation at the federal level and communicated with European colleagues via EPIS. AB has investigated the cluster in Munich with links to Frankfurt, JW conducted the sequencing of hepatitis A viruses in this outbreak. MF has conducted the phylogenetic analysis and co-written the manuscript. All authors have revised the manuscript.

References


6. Mao JS, Yu PH, Ding ZS, Chen NL, Huang BZ, Xie RY, et al. Patterns of shedding of hepatitis A virus antigen in feces and...


License and copyright

This is an open-access article distributed under the terms of the Creative Commons Attribution (CC BY 4.0) Licence. You may share and adapt the material, but must give appropriate credit to the source, provide a link to the licence, and indicate if changes were made.

This article is copyright of the authors, 2017.
Rapid communications

Outbreak of hepatitis A associated with men who have sex with men (MSM), England, July 2016 to January 2017

K Beebeejaun ¹, S Degala ², K Balogun ¹, I Simms ³, SC Woodhall ³, E Heinsbroek ⁴, PD Crook ⁴, I Kar-Purkayastha ⁵, J Treacy ⁵, K Wedgwood ⁶, K Jordan ⁷, S Mandal ¹, SL Ngui ⁸, M Edelstein ¹

2. Field Epidemiology Services East Midlands, Public Health England, United Kingdom
4. Field Epidemiology Services London, Public Health England, United Kingdom
5. Hampshire & Isle of Wight Health Protection Team (South East), Public Health England, United Kingdom
6. East Midlands Health Protection Team, Public Health England, United Kingdom
7. South West Health Protection Team, Public Health England, United Kingdom
8. Virus Reference Department, Public Health England, Colindale, London, United Kingdom

Correspondence: Kazim Beebeejaun (kazim.beebeejaun@phe.gov.uk)

Citation style for this article:
DOI: http://dx.doi.org/10.2807/1560-7917.ES.2017.22.5.30454

Between July 2016 and January 2017, 37 confirmed cases of hepatitis A with two unique IA genotype strains primarily among men who have sex with men, were reported across eight areas in England and Northern Ireland. Epidemiological and laboratory investigations indicate that these strains may have been imported several times from Spain, with secondary sexual transmission in the United Kingdom. Local and national public health services are collaborating to control this ongoing outbreak.

Infection with the hepatitis A virus (HAV) is most commonly acquired through ingestion of contaminated food and water, and through faeco-oral contact. In the United Kingdom (UK) hepatitis A is a rare and mainly travel-associated disease, preventable by vaccination [1,2]. Sexually transmitted hepatitis A outbreaks among men who have sex with men (MSM) are well documented [3-6]. We describe an ongoing outbreak in the UK, primarily affecting MSM, caused by two concurrently circulating HAV strains previously not seen in the UK, as well as the intervention strategies that have been instigated to control the outbreak. Cases with the identical strains have been reported in other European countries, prompting the European Centre for Disease Prevention and Control (ECDC) to issue a rapid risk assessment in December 2016 [7]. A probable case was defined as a laboratory-confirmed HAV infection (not yet sequenced) with symptom onset after 31 June 2016, with contact with a confirmed case and/or who identifies as MSM.

Outbreak description
Between July 2016 and January 2017, 37 confirmed cases with either strain 1 or 2 were detected across England as well as Northern Ireland (Figure 1), of which 28 identified as MSM. Of the 37 cases, 24 were Strain 1 and 13 were Strain 2. In addition, 15 probable cases (all MSM), primarily in London, were identified, and typing results are awaited.

Strain 1 was first identified by the Virus Reference Department, Public Health England, London, in July 2016. The sequence had not been seen previously in the UK and phylogenetic analysis (Figure 2) showed a clear relation to sequences derived from travellers returning from Central and South America.

Strain 1 cases were reported in eight geographically distinct areas in England and Northern Ireland (Figure 3).

Of 24 Strain 1 cases, 22 were male, median age 35 years (19–63 years), 19 identified as MSM and eight reported travel within the incubation period, seven of which to Spain (Table).
Strain 2 was first notified through the European Union Early Warning and Response System (EWRS) message from the Netherlands in October 2016 related to two MSM cases at EuroPride 2016, which took place in Amsterdam in July/August 2016. This genotype sequence was detected in 13 cases across six regions in England between November 2016 and January 2017 (Figure 3). Of the 13 cases, 12 were male, median age 39 years (range: 29–78), nine identified as MSM and 11 travelled during the incubation period, of which seven to Spain and two to Germany (Table). Of note, Strain 2 has mainly been reported in MSM in London to date. Characteristics of concern among cases were noted, including infection in a sex worker with multiple partners, co-infection with sexually transmitted infections (STIs) and use of sex-on-site premises and apps (Grindr, Recon) (Table).

Control measures
Public Health England (PHE) declared a national incident in December 2016. Local and national laboratory, epidemiology and health protection teams contributed to the response, which comprised: (i) enhanced surveillance for MSM-associated cases through an adapted questionnaire [8], (ii) a joint letter with the British Association for Sexual Health and HIV (BASHH) to all members alerting them to the outbreak and recommending vaccination of at-risk MSM in outbreak areas, according to national guidelines [9,10], testing cases for other STIs and partner notification, (iii) disease information and targeted hygiene advice to the public through the National Health Service web portal [11], (iv) liaising with lesbian, gay, bisexual, and transgender (LGBT) and sexual health charities, gay-dating apps and gay venues to raise awareness through social media and health promotion visuals, and (v) giving post-exposure prophylaxis to household and sexual contacts.

Discussion
As at 24 January 2017, 37 HAV infections with two sequences have been identified in eight UK areas, mostly among MSM (median age: 35 years; range: 19-56). HAV infection is most commonly acquired through contaminated food or water. In this outbreak however, epidemiological and laboratory investigations suggest multiple importations from several regions of Spain with secondary sexual transmission within the MSM population in the UK, as nine of the confirmed MSM cases reported travelling to Spain during the incubation period. Ireland, Sweden, Luxembourg and Germany have reported hepatitis A cases with identical viral sequences, some with history of travel to Spain during the incubation period. Spain has reported an increase in male HAV infections, but no further details were available [7]. This outbreak highlights the key role sequencing can play in outbreak detection, as well as the added value of a common European platform to share epidemiological and virological information.

While the two concurrently circulating strains are virologically distinct, the public health response is intended to address both. Although it has not been possible to establish epidemiological links between all cases within geographical clusters, it is likely that cases are related either through undisclosed sexual contacts or other routes since neither strain is commonly circulating in England. These missing epidemiological links are not unexpected when trying to capture sexual history via short questionnaires, particularly since some cases reported anonymous sex with multiple partners. However, the questionnaires revealed sex-on-premises venues (saunas, clubs) and social networking (dating apps) as potential drivers of the outbreak. While these findings can help focus interventions, they are of particular concern in areas with
**Figure 2**
Phylogenetic analysis of virus strains from hepatitis A cases in England and Northern Ireland, July 2016–December 2016

HAV: hepatitis A virus; MSM: men who have sex with men.

The tree was constructed in MegAlign (DNAstar) using Clustal Key.
Figure 3
Geographical distribution of hepatitis A cases among men who have sex with men, England and Northern Ireland, July 2016–January 2017 (n=52)

<table>
<thead>
<tr>
<th>Region</th>
<th>Case status (strain)</th>
<th>Cases (n)</th>
<th>Median age (years)</th>
<th>MSM (n)</th>
<th>Spain (n)</th>
<th>Notable characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>East Midlands</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Confirmed (Strain 1)</td>
<td>9</td>
<td>28</td>
<td>6</td>
<td>2</td>
<td></td>
<td>One cluster of three cases of Strain 1 transmitted in a factory through environmental exposure.</td>
</tr>
<tr>
<td>Confirmed (Strain 2)</td>
<td>3</td>
<td>55</td>
<td>2</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Probable</td>
<td>0</td>
<td>NA</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>12</td>
<td>36</td>
<td>8</td>
<td>4</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>South West</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Confirmed (Strain 1)</td>
<td>4</td>
<td>45</td>
<td>3</td>
<td>1</td>
<td></td>
<td>One case operated a private meeting place, used by contacts and multiple anonymous men.</td>
</tr>
<tr>
<td>Confirmed (Strain 2)</td>
<td>1</td>
<td>NA</td>
<td>0</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Probable</td>
<td>0</td>
<td>NA</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>5</td>
<td>46</td>
<td>3</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Hampshire</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Confirmed (Strain 1)</td>
<td>3</td>
<td>35</td>
<td>3</td>
<td>1</td>
<td></td>
<td>Probable case is index case in this area. This case was diagnosed in Spain but never sequenced. Further spread through household and sexual contacts.</td>
</tr>
<tr>
<td>Confirmed (Strain 2)</td>
<td>0</td>
<td>NA</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Probable</td>
<td>1</td>
<td>NA</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>4</td>
<td>32</td>
<td>4</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>North East</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Confirmed (Strain 1)</td>
<td>3</td>
<td>41</td>
<td>3</td>
<td>1</td>
<td></td>
<td>First identified case with likely importation from Spain. Further spread to two cases through household and sexual transmission.</td>
</tr>
<tr>
<td>Confirmed (Strain 2)</td>
<td>0</td>
<td>NA</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Probable</td>
<td>0</td>
<td>NA</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>3</td>
<td>41</td>
<td>3</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>London</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Confirmed (Strain 1)</td>
<td>2</td>
<td>31</td>
<td>2</td>
<td>0</td>
<td></td>
<td>One Strain 1 case was a sex worker with multiple sexually-transmitted co-infections who reported sex in several gay saunas in London. Three cases reported using apps and websites to meet partners. One Strain 2 case reported 20 sexual contacts within the eight weeks prior to disease onset.</td>
</tr>
<tr>
<td>Confirmed (Strain 2)</td>
<td>6</td>
<td>35</td>
<td>4</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Probable</td>
<td>12</td>
<td>34</td>
<td>12</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>20</td>
<td>32</td>
<td>18</td>
<td>4</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Yorkshire and Humber</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Confirmed (Strain 1)</td>
<td>1</td>
<td>NA</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Confirmed (Strain 2)</td>
<td>1</td>
<td>NA</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Probable</td>
<td>1</td>
<td>NA</td>
<td>1</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>3</td>
<td>NA</td>
<td>2</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>North West</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Confirmed (Strain 1)</td>
<td>0</td>
<td>NA</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Confirmed (Strain 2)</td>
<td>1</td>
<td>NA</td>
<td>1</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Probable</td>
<td>1</td>
<td>NA</td>
<td>1</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>2</td>
<td>43</td>
<td>2</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>East of England</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Confirmed (Strain 1)</td>
<td>0</td>
<td>NA</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Confirmed (Strain 2)</td>
<td>1</td>
<td>NA</td>
<td>1</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Probable</td>
<td>0</td>
<td>NA</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>1</td>
<td>NA</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>South Midlands</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Confirmed (Strain 1)</td>
<td>1</td>
<td>NA</td>
<td>1</td>
<td>1</td>
<td></td>
<td>All but one case reported travel; three to Spain and to Germany. One Strain 2 case reported sexual contact with multiple partners at a gay sauna in London.</td>
</tr>
<tr>
<td>Confirmed (Strain 2)</td>
<td>0</td>
<td>NA</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Probable</td>
<td>0</td>
<td>NA</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>1</td>
<td>NA</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Belfast</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Confirmed (Strain 1)</td>
<td>1</td>
<td>NA</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Confirmed (Strain 2)</td>
<td>0</td>
<td>NA</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Probable</td>
<td>0</td>
<td>NA</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>1</td>
<td>NA</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Grand total</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>52</td>
<td>36</td>
<td>43</td>
<td>16</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

MSM: men who have sex with men; NA: not applicable.
large, active MSM populations, such as London, where several of the recent cases have been reported.

This outbreak also highlights the need for HAV awareness among MSM and sexual health professionals and the need for health promotion materials that focus on both infection and vaccination. Innovative and evaluated communication strategies with targeted messaging through social media, apps and venues also need to be readily available to public health agencies.

Hepatitis A vaccination for MSM in England is currently a risk-based recommendation [9,10]. For the purpose of this investigation, the vaccination status of the cases was not included in the analysis. While some may advocate for a universal MSM vaccination policy, it may not be cost-effective or affordable for local governments who commission sexual health services. Vaccine availability also needs to be taken into account as it may impact the ability to vaccinate a large number of individuals in a short timeframe. Enhanced surveillance for HAV in MSM will allow monitoring of the evolving outbreak as well as evaluating intervention impact, and gain a better understanding of HAV transmission in this population.

Acknowledgements

We would like to thank all the regional PHE health protection staff involved in the outbreak investigation and management to date.

Conflict of interest

None declared.

Authors’ contributions

All the authors contributed to the outbreak investigations described here, the presentation of information and the final drafting of the manuscript.

References


License and copyright

This is an open-access article distributed under the terms of the Creative Commons Attribution (CC BY 4.0) Licence. You may share and adapt the material, but must give appropriate credit to the source, provide a link to the licence, and indicate if changes were made.

This article is copyright of the authors, 2017.
National Bulletins

AUSTRIA
Mitteilungen der Sanitätsverwaltung
Bundesministerium für Gesundheit Familie und Jugend, Vienna
Monthly, print only. In German.
http://www.bmgfj.gv.at/cms/site/thema.html?channel=CH0951

BELGIUM
Vlaams Infectieziektebulletin
Department of Infectious Diseases Control, Flanders
Quarterly, print and online. In Dutch, summaries in English.
http://www.infectieziektebulletin.be

Belgium bulletin d’information de la section d’Épidémio logie
Institut Scientifique de la Santé Publique, Brussels
Monthly, online. In French.

BULGARIA
Bulletin of the National Centre of Infectious and Parasitic Diseases, Sofia
Print version. In Bulgarian.
http://www.ncipd.org/

CYPRUS
Newsletter of the Network for Surveillance and Control of Communicable Diseases in Cyprus
Medical and Public Health Services, Ministry of Health, Nicosia
Biannual, print and online. In Greek.
http://www.moh.gov.cy

CZECH REPUBLIC
Zpravy CEM (Bulletin of the Centre of Epidemiology and Microbiology)
Centrum Epidemiologie a Mikrobiologie Státního Zdravotního Ústavu, Prague
Monthly, print and online. In Czech, titles in English.
http://www.szu.cz/cema/adefaultt.htm

EPIDAT (Notifications of infectious diseases in the Czech Republic)

DENMARK
EPI-NEWS
Department of Epidemiology, Statens Serum Institut, Copenhagen
Weekly, print and online. In Danish and English.
http://www.ssi.dk

FINLAND
Kansanterveyslaitos
Department of Infectious Disease Epidemiology, National Public Health Institute, Helsinki
Monthly, print and online. In Finnish.
http://www.ktl.fi/portal/suomi/osasto/infekte/tutkimus/tartuntatautien_seuranta/tartuntatautilaakarin_komentit/

FRANCE
Bulletin épidémiologique hebdomadaire
Institut de veille sanitaire, Saint-Maurice Cedex
Weekly, print and online. In French.
http://www.invs.sante.fr/beh/default.htm

GERMANY
Epidemiologisches Bulletin
Robert Koch-Institut, Berlin
Weekly, print and online. In German.
http://www.rki.de/DE/Content/Infekt/EpidBull/epid__bull__node.html

GREECE
HCDCP Newsletter
Hellenic Centre for Disease Control and Prevention (HCDCP/KEELPNO), Athens
Monthly, online. In English and Greek.
http://www.2.keelpno.gr/blog/?lang=en

HUNGARY
Epinfo (az Országos Epidemiológiai Központ epidemiológiai információs hellapja)
National Center For Epidemiology, Budapest
Weekly, online. In Hungarian.
http://www.oek.hu/oeek.web?to=839&nid=41&pid=7&lang=hun

ICELAND
EPI-ICE
Landlaeknisembættið
Directorate Of Health, Seltjarnarnes
Monthly, online. In Icelandic and English.
http://www.landlaeknr.is

IRELAND
EPI-INSIGHT
Health Protection Surveillance Centre, Dublin
Monthly, print and online. In English.
http://www.hpsc.ie/hpsc/EPI-Insight

ITALY
Notiziario dell’Istituto Superiore di Sanità
Istituto Superiore di Sanità, Reparto di Malattie Infettive, Rome
Monthly, online. In Italian.
http://www.iss.it/publ/noti/index.php?lang=1&tipo=4

Bolletino Epidemiologico Nazionale (BEN)
Istituto Superiore di Sanità, Reparto di Malattie Infettive, Rome
Monthly, online. In Italian.
http://www.epicentro.iss.it/ben

LATVIA
Epidemiologijas Bileteni
Sabiedribas veselibas agentura
Public Health Agency, Riga
Online. In Latvian.
http://www.sva.lv/epidemiologija/bileteni

LITHUANIA
Epidemiologijos žinios
Užkreciamuju ligu profilaktikos ir kontroles centras
Center for Communicable Disease Prevention and Control, Vilnius
Online. In Lithuanian.

NETHERLANDS
Infectieziekten Bulletin
Rijksinstituut voor Volksgezondheid en Milieu
National Institute of Public Health and the Environment, Bilthoven
Monthly, print and online. In Dutch.
http://www.rivm.nl/infectieziektenbulletin

NORWAY
MSIS-rapport
Folkehelseinstituttet, Oslo
Weekly, print and online. In Norwegian.
http://www.folkehelse.no/nyhetsbrev/msis
POLAND
Meldunki o zachorowaniach na choroby zakazne i zatruciach w Polsce
Panstwowy Zaklad Higieny,
National Institute of Hygiene, Warsaw
Fortnightly, online. In Polish and English.
http://www.pzh.gov.pl

PORTUGAL
Saúde em Números
Ministério da Saúde,
Direcção-Geral da Saúde, Lisbon
Sporadic, print only. In Portuguese.
http://www.dgs.pt

ROMANIA
Info Epidemiologia
Centrul pentru Prevenirea si Controlul Bolilor Transmisibile, National Centre of Communicable Diseases Prevention and Control, Institute of Public Health, Bucharest
Sporadic, print only. In Romanian.

SLOVENIA
CNB Novice
Inštitut za varovanje zdravja, Center za nalezljive bolezni, Institute of Public Health, Center for Infectious Diseases, Ljubljana
Monthly, online. In Slovene.
http://www.ivz.si

SPAIN
Boletín Epidemiológico Semanal
Centro Nacional de Epidemiología, Instituto de Salud Carlos III, Madrid
Fortnightly, print and online. In Spanish.
http://revista.isciii.es

SWEDEN
Folkhälsomyndighetens nyhetsbrev
Folkhälsomyndigheten, Stockholm
Weekly, online. In Swedish.
http://www.folkhalsomyndigheten.se

UNITED KINGDOM
ENGLAND AND WALES
Health Protection Report
Weekly, online only. In English.

NORTHERN IRELAND
Communicable Diseases Monthly Report
Communicable Disease Surveillance Centre, Northern Ireland, Belfast
Monthly, print and online. In English.
http://www.cdscni.org.uk/publications

SCOTLAND
Health Protection Scotland Weekly Report
Health Protection Scotland, Glasgow
Weekly, print and online. In English.
http://www.hps.scot.nhs.uk/ewr/

EUROPEAN UNION
"Europa" is the official portal of the European Union. It provides up-to-date coverage of main events and information on activities and institutions of the European Union.
http://europa.eu

EUROPEAN COMMISSION - PUBLIC HEALTH
http://ec.europa.eu/health/

HEALTH-EU PORTAL
The Health-EU Portal (the official public health portal of the European Union) includes a wide range of information and data on health-related issues and activities at both European and international level.
http://ec.europa.eu/health-eu/

EUROPEAN CENTRE FOR DISEASE PREVENTION AND CONTROL
The European Centre for Disease Prevention and Control (ECDC) was established in 2005, it is an EU agency with aim to strengthen Europe's defences against infectious diseases. It is seated in Stockholm, Sweden.
http://www.ecdc.europa.eu
Visit our website at www.eurosurveillance.org

The Eurosurveillance print edition is a compilation of short and long articles that have previously been published on our website.

All the articles in this issue are available online: you can print each page separately or download the whole quarterly in pdf format.

The website archives all articles since 1995, and offers a search facility.

To receive Eurosurveillance’s free electronic releases and e-alerts by email, please subscribe on our website.

Papers published in the former monthly release are indexed for MEDLINE since January 2001, and papers published in the weekly release from January 2005 (with the exception of short, non-scientific notices) are also indexed for MEDLINE.

The Index Medicus abbreviation for Eurosurveillance is Euro Surveill.

Follow us on Twitter: #eurosurveillance