



## RAPID RISK ASSESSMENT

# Hepatitis A outbreaks in the EU/EEA mostly affecting men who have sex with men

19 December 2016

### Conclusions and options for response

Since February 2016, 24 hepatitis A cases infected with two distinct strains of sub-genotype IA have been reported by five EU countries. Most cases are reported among adult men who have sex with men (MSM), with only a few women affected, including one suspected person who injects drugs (PWID). Eight cases reported having travelled to Spain within the duration of the incubation period.

ECDC encourages Member States to raise awareness among healthcare providers, in particular those caring for MSM for sexually transmitted infections (STIs), about the possibility of infection with hepatitis A virus. Sharing of microbiological and epidemiological details of new cases through Epidemic Intelligence Information System for Food- and Waterborne Diseases and Zoonoses (EPIS-FWD) is encouraged for the benefit of progressing with multi-country outbreak investigation.

The UK, Spain, Italy and Germany have reported increased numbers of hepatitis A infections in MSM or in the male population during the second half of this year, indicating an increased risk of transmission in these groups.

The options to consider for prevention of sexual transmission among MSM are:

- Raise awareness among healthcare providers about increased detection of hepatitis A virus (HAV) among MSM;
- Encourage healthcare providers to refer MSM hepatitis A cases to sexual health services for further STI/HIV testing;
- Work with civil society to raise awareness among MSM through social media, the gay press and leaflets in health clinics, on the risk of contracting hepatitis A through risky behaviour;
- Encourage healthcare providers to refer sexual contacts, family members or other type of close contacts of MSM cases to healthcare facilities which can offer the hepatitis A vaccine and human normal immune globulin as appropriate, for prevention of secondary cases. Primary prevention advice (i.e. hand washing after toilet use and before food preparation) should be provided. Consider vaccination against hepatitis A and B for MSM contacts in accordance with the national guidelines;
- Target educational efforts toward changing behaviours that would place MSM at increased risk.

For those MSM most at risk, the educational efforts should emphasise the importance of personal hygiene (i.e. washing anal area), of washing hands before and after sex, especially if practicing oral-anal sex, or oral stimulation of the anus (anilingus or 'rimming'), or fingering and fisting, and repeating the message to always wear condoms for anal sex. Latex gloves offer some protection if fingering or fisting.

Outside of outbreak situations, ECDC guidance for HIV and STI prevention among men who have sex with men encourages Member States to promote and deliver vaccination against hepatitis A and B, and consider vaccination for human papilloma virus (HPV) to MSM, in line with the national vaccination recommendations [1]. Information on vaccine availability should be included in health promotion programmes targeting MSM [2].

To prevent hepatitis A outbreaks among PWID, ECDC guidance on prevention and control of infectious diseases among PWID, recommends offering hepatitis A vaccination in combination with hepatitis B [3]. Priority should be considered for those with HIV and/or HCV co-infections due to observed higher hepatitis A fatality rate [4].

Travellers to countries of high and intermediate endemicity should be advised to avoid exposure to hepatitis A through contaminated food and water. Hepatitis A vaccination should be offered to individuals travelling to countries where the disease is endemic in line with the national recommendations.

## Source and date of request

ECDC internal decision, 13 December 2016, following EPIS FWD urgent enquiry from the United Kingdom on occurrence of clusters of hepatitis A virus (HAV), with identical viral RNA sequence belonging to sub-genotype IA, and EWRS message from the Netherlands on hepatitis A cases in MSM associated with Europride, Amsterdam 2016.

## Public health issue

Ongoing transmission of hepatitis A virus (HAV) infection mainly affecting men who have sex with men (MSM) in EU/EEA countries.

## Consulted experts

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## Disease background information

Hepatitis A is an acute, usually self-limiting infection caused by the hepatitis A virus (HAV). Transmission is predominately by the faecal-oral route, through contaminated water or food-products and/or by person-to-person contact. Transmission through sexual exposure has been associated with outbreaks in men who have sex with men (MSM) and transmission through sharing of needles and syringes with outbreaks in injecting drugs users. Parenteral transmission through infected instruments or, rarely, blood components has been documented as well [5].

The infection is asymptomatic or mild in children but often symptomatic in adults who may develop jaundice and present with more severe clinical symptoms. The mean incubation period is 28 days, ranging from 15 to 50 days. The maximum infectivity is in the second half of the incubation period (i.e. while asymptomatic) and most cases are considered non-infectious after the first week of jaundice. The diagnosis is made by serology or molecular tests. Anti-HAV IgM serology and detection of HAV-RNA indicate acute infection. Almost all human hepatitis A viruses belong to genotypes I and III, with genotype I being divided into sub-genotypes IA and IB. Genotype I is the most prevalent, comprising at least 80% of circulating human strains [6,7].

No specific treatment is available for hepatitis A infection. Strict control measures such as enforcing personal hygiene, contact tracing and administration of the vaccine to exposed persons have shown to be effective. Active and passive immunisation is effective if administered within two weeks after exposure. Several inactivated vaccines are available for prevention. [8]

In 2015, 12 527 confirmed hepatitis A cases were reported to the European Surveillance System (TESSy) by 30 EU/EEA countries. Romania accounted for 41% of the cases and Bulgaria for 9%. Cases were reported in all age groups with most cases among 5–14 years-olds (39%) and 25–44 years-olds (19%). Male cases were more frequent than female ones, particularly in age groups 15–24 and 25–44 years (male to female ratio 1.3 and 1.2, respectively). The majority (91 %) of infections were domestically acquired. Among travel-associated cases, Syria, Morocco and Turkey were the most common travel destinations.

Hepatitis A seroprevalence presents a high degree of temporal and spatial variability across the EU/EEA. There is an overall decreasing trend over time in most countries and an important geographical increasing pattern of seroprevalence from northern to central, southern and eastern EU/EEA. Conversely, the susceptibility to infection among adults ranged between low (three countries) to very high (five countries) with a marked south to north geographical susceptibility increase pattern [5].

Outbreaks of hepatitis A among MSM have been recognised since the 1970s [9-12]. Several multinational outbreaks have been described, one of which involved at least eight cities across three countries and two continents, North America and Australia, and occurred from January through June 1991[13]. Several European countries reported national outbreaks in MSM, with the main risk factor related to direct faecal-oral contact during sex [14-17].

## Event background information

### Descriptive epidemiology

#### Event 1, EPIS FWD UI-389

On 6 December 2016, through an EPIS FWD urgent inquiry, the United Kingdom (UK) reported 15 hepatitis A cases infected with an identical viral RNA sequence of genotype IA, geographically grouped in three clusters in England and one case in Northern Ireland. All cases are males, aged between 23 and 63 years, most (12/15) identifying themselves as MSM. Five cases reported travel history to Spain and had symptoms onset between July and November 2016. Since the EPIS enquiry, an additional case with the same sequence has been reported in the UK in an individual returning from Spain who self-identified as MSM.

As of 16 December, three additional countries reported cases with identical HAV RNA sequence:

- Ireland reported one female case with onset in early October 2016 and a history of travelling to Madrid, Spain.
- Sweden reported one female case that travelled to Tenerife, Spain within the duration of the incubation period in February 2016.
- Luxembourg reported one female case, an injecting drugs user with HIV and HCV co-infections. No travel information is available.

Three countries reported increases of HAV infection among MSM or among the male population in 2016:

- Italy observed an increase of cases in one region in November 2016, affecting mainly MSM. To date, only two genetic sequences were obtained from adult males with symptoms onset in November. One patient did not report the MSM risk factor; no data are available for the other. The sequences were very similar (one case showed 1 nt difference) or identical to VRD\_521\_2016 (complete overlapping in 460 nt).
- Spain observed an increase in hepatitis A with a similar sequence in one region mainly in adult men and increases in other regions that are being investigated. Further epidemiological and microbiological investigations are ongoing.
- Germany reported a recent cluster of hepatitis A in MSM but no cases had the similar RNA sequence.

Austria, Denmark, Finland, Georgia and the Netherlands have not identified recent cases with this sequence.

#### Event 2, EPIS-FWD news item - 18 October 2016

On 14 October, the Netherlands, through the Early Warning and Response System (EWRS), notified two cases of hepatitis A in MSM that participated in the Europride, Amsterdam, 23 July–7 August 2016. The cases were infected with an indistinguishable IA genotype sequence, but different from the Event 1. The two individuals visited the same location on the 2 and 3 August 2016 during Europride where they engaged in anonymous sexual activities. They developed symptoms on 11 and 15 September 2016, respectively. The clustering in time and place of the cases, along with an identical viral sequence suggest a person-to-person transmission through the sexual route, but cannot exclude food or water borne transmission. Since the Europride is an international event, the description of the event was shared through EPIS FWD and EPIS STI.

On 12 December, the UK reported two MSM cases and one female case with identical sequence in individuals with a travel history to Gran Canaria, Spain within the duration of the incubation period.

## Microbiological investigation

### Event 1

The 16 hepatitis A cases reported by the UK are infected with a HAV strain of sub-genotype IA characterised by an identical viral RNA sequence of 505 nucleotides from the VP1/2A region (see Annex 1). The UK shared this sequence (VRD\_521\_2016) with the European FWD network, and ECDC informed the STI contact points through EPIS STI. The strain is phylogenetically related to isolates derived from Central/South America, based on analysis of European databases.

### Event 2

The five hepatitis A cases reported by the Netherlands and the UK were infected with an indistinguishable IA genotype sequence (*RIVM-HAV16-090*) that was shared in EPIS FWD and EPIS STI with the respective networks.

The sequence is a 460 nucleotides long fragment from the region VP1/2A according to HAV-Net. The sequence is phylogenetically related to isolates from Thailand and Cambodia. In 2015, the UK detected this sequence in a traveller returning from Hong Kong, China.

The sequences between Event 1 and Event 2, over a 505 nucleotide fragment, are 94.9% similar, suggesting separated transmission events.

## ECDC threat assessment for the EU

From February 2016 to December 2016, five EU countries have reported clusters or sporadic cases associated with two different HAV sequences of genotype IA. Three other countries, Spain, Italy and Germany, reported regional increases of hepatitis A in MSM or adult male populations. The difference between the two sequences is 24 nt on an overlapping fragment of 505 nt in the region VP1/2a. The genetic distance indicates that the two sequences have not evolved from a common ancestor in recent months/years.

The two sequences are most likely associated with independent events and mostly associated with MSM population groups at increased risk for HAV infection. No infected foodhandlers have been implicated in these events. Female cases may have been infected by ingesting contaminated food or water or through sexual transmission. One female case is a suspected injecting drugs user, highlighting the risk for PWID.

On the basis of current evidence, the European population groups most at risk of being affected by this outbreak are MSM possibly participating in higher risk sexual practices, and their contacts. Mass gathering events related to this specific population groups may increase transmission opportunities.

Person-to-person sexual transmission is the most likely hypothesis for the spread of this outbreak, as a foodborne transmission would tend to result in more cases affecting the general population.

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## Annex 1. Outbreak sequences

### VRD\_521\_2016

CAATCATTCTGATGAATATTTGTCTTTTAGTTGTTATTTGTCTGTACAGAGCAATCAGAGTTCTATTTTCCTAGAGCTCCATT  
AAATTCAAATGCTATGTTGTCCACTGAGTCCATGATGAGTAGAATTGCAGCTGGAGATTTGGAGTCATCAGTGGATGATCCCA  
GATCAGAAGAGGACAGAAGATTTGAGAGTCACATAGAATGTAGGAAACCATATAAAGAATTGAGACTGGAGGTTGGGAAACA  
AAGACTCAAATATGCTCAGGAAGAGTTATCAAATGAAGTGCTTCCACCTCCTAGGAAAATGAAGGGGCTATTTTCACAAGCTA  
AAATCTCTCTTTTTTATACTGAGGAGCATGAAATAATGAAATTTTCTTGGAGAGGAGTAACTGCTGATACTAGGGCCTTGAGA  
AGATTTGGATTTTCTCTGGCTGCTGGTAGAAGTGTGTGGACCCTTGAAATGGATGCTGGAGTTCTTACTGGAAGATTGATCA  
GATTGAAT

### RIVM-HAV16-090\_Sept-2016

CAATCATTCTGATGAATATTTGTCTTTTAGTTGCTATTTGTCTGTACAGAACAATCAGAGTTCTATTTTCCTAGAGCTCCATT  
AAATTCAAATGCTATGTTGTCCACTGAGTCCATGATGAGTAGAATTGCAGCTGGAGACTTGGAAATCATCAGTGGATGATCCTA  
GATCTGAGGAGGACAGAAGATTTGAGAGTCACATAGAATGTAGGAAACCATACAAAGAATTGAGATTGGAAGTTGGCAAACA  
AAGACTCAAATATGCTCAGGAAGAGTTGTCAAATGAAGTGCTTCCACCTCCTAGGAAAATGAAGGGGGTCTTTTCACAAGCAA  
AAATTTCTCTTTTTTATACTGAGGAGCATGAAATAATGAAATTTTCTTGGAGAGGAGTACTGCTGATACTAGGGCCTTTGAGA  
AGATTTGGATTTTCTATGGCTGCTGGTAGAAGTGTGTGGACTCTT