A possible outbreak of hepatitis A associated with semi-dried tomatoes, England, July–November 2011

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In October 2011, two primary cases of hepatitis A virus (HAV) infection with identical HAV genotype IB strains to those seen in other outbreaks associated with semi-dried tomatoes were reported in England. Both cases had consumed semi-dried tomatoes. Epidemiological investigations revealed two additional cases of genotype IB strains with different sequences who also reported having consumed semi-dried tomatoes. In November, five cases of HAV infection with closely related strains were identified in the Netherlands. A foodborne multiple-strain outbreak is suspected.

In October 2011, two cases of hepatitis A with a genotype IB strain identical to that seen in a previous outbreak associated with consumption of semi-dried tomatoes, Hu/Netherlands/RIVM-006/2010 [1], were reported to the Health Protection Agency (HPA) in England [2]. The strain was identified based on 100% sequence identity over 505 base pairs of the VP1-2PA junction.

Neither of these patients had travelled to an endemic country within 50 days before the onset of symptoms [3] and both reported substantial consumption of semi-dried tomatoes (also known as sun-dried tomatoes). In this preliminary report of the ongoing investigation we highlight the finding of this rare hepatitis strain which may be related to the possible consumption of semi-dried tomatoes in at least two European countries, the United Kingdom (UK) and the Netherlands.

Background

To date, only one serotype of HAV has been identified worldwide [4]. However, sequence variability between HAV isolates from different parts of the world is substantial, which allows for HAV strains to be classified into different genotypes. Based on the sequencing of VP1-P2A protein regions, different HAV strains have been classified into six different genotypes designed I-VI, Genotypes I, II and III have been further divided into subgenotypes A and B.

The Hu/Netherlands/RIVM-006/2010 strain, closely related to the strain detected in Australia in 2009 [5-7], was identified in 2010 in a hepatitis A outbreak in the Netherlands [1,8]. In 2010, three cases with that same strain were reported in England to the HPA, one in January, in a traveller returning from Amsterdam [2], and a further two in October [data not shown].

Epidemiological evidence has linked previous hepatitis A outbreaks to semi-dried tomato products [1,7,9], but the virus has only been isolated from samples of semi-dried tomatoes during an Australian outbreak in 2009 [7].

In 2011 the number of reported hepatitis A cases in England was below that reported for previous years. However, the finding of a rare HAV strain that had been associated with previous outbreaks in non travel-related cases in the Netherlands and in the UK, 2010, triggered an epidemiological investigation. The additional report of substantial semi-dried tomatoes consumption from two further cases with distinct strains (99.6% and 91.7% homology to the Hu/Netherlands/RIVM-006/2010 strain respectively) in the second part of 2011 raises the possibility that a single food source may be contaminated with more than one strain.

Simultaneously, a cluster of initially five cases with similar strains and exposure to semi-dried tomatoes was reported in the Netherlands [10] raising the concern that these events could be related to an internationally distributed food source.

Outbreak investigation

As a part of the ongoing investigation a case definition was developed. A case was described as any individual living in England with laboratory-confirmed

genotype IB hepatitis A infection, genotyped by the Virus Reference Department at the HPA Microbiology Services (MS) Colindale, London, with date of symptom onset from 1 July to 31 December 2011. Travel to a country where hepatitis A is endemic and contact with a laboratory-confirmed hepatitis A case within 50 days before the onset of symptoms, were considered exclusion criteria.

The cases were described in terms of time, place and person. Possible exposure to semi-dried tomato products was ascertained by staff of the local HPA Health Protection Unit (HPU), who used standard questionnaires in interviews with cases as part of their usual investigations of persons with hepatitis A. The HPUs provided the relevant exposure information to colleagues at the HPA national centre in Colindale, London.

Active case finding

All the HPUs in England were requested to report all cases of hepatitis A that had been identified between 1 July and 31 December 2011 to the national centre (HPA Colindale, London) and to provide appropriate information for each case. The United Kingdom (UK) national surveillance centres in Wales, Scotland and Northern Ireland were alerted.

Enhanced laboratory surveillance was instituted. Laboratories were requested to forward all hepatitis A serum samples taken during this period to the HPA Virus Reference Department in order to genotype and sequence samples that had not previously been analysed.

Laboratory surveillance data

In 2011, a total of 237 cases of laboratory confirmed hepatitis A were reported by laboratories from England, corresponding to an annual rate of 0.45 per 100,000 population. This number is well below the laboratory-confirmed rates observed during the five previous years (average 0.71 per 100,000) in England and almost eight times lower than the average rate in the European Union in 2009 [11].

Genotyping of hepatitis A viruses is not routinely performed in the UK. Local laboratories are not required to send samples to the Reference Laboratory at HPA MS Colindale, London, and tend to do so only when an outbreak is suspected. For cases from July to December 2011, 32 serum samples were received and genotyped by the Reference Laboratory at the HPA. Five of the 32 cases were genotyped as IA, 14 as IB (including the cases from October) and 13 as IIIA.

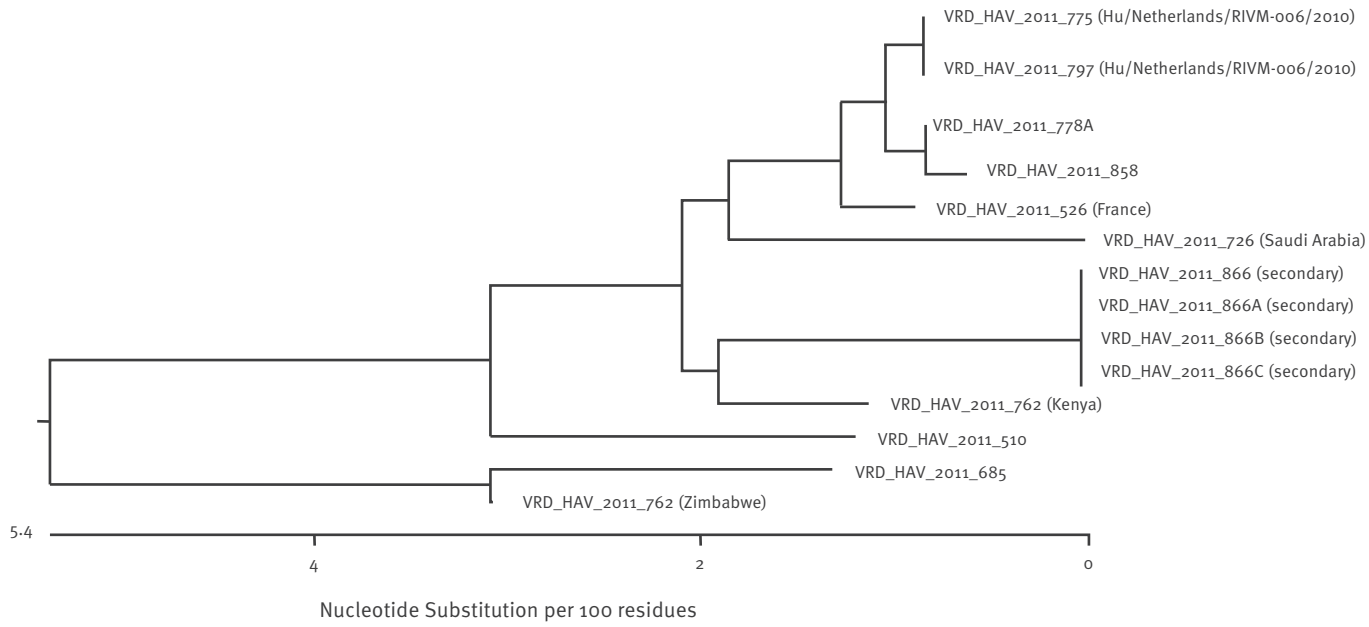
The two HAV genotype IB cases that triggered this investigation were identified as the Hu/Netherlands/RIVM-006/2010 strain based on 100% sequence identity over 505 base pairs of the VP1-2PA junction. A third case was identified based on a 99.6% sequence identity over the same region. The remaining HAV genotype IB strains included three primary non-travel related cases, one primary case with travel history to France, three cases with travel history to hepatitis A endemic countries and four secondary cases (Figure 1).

Epidemiological investigation

By the end of 2011, seven patients met the case definition. The onset of symptoms ranged from 6 July to 1 November 2011 (Figure 2).

Figure 1

Phylogenetic tree of hepatitis A virus sequences derived from genotype IB cases identified in England, July–December 2011



The cases resided in distinct areas of England, four in the East (around 5.5 million inhabitants), two in London (around 8 million inhabitants) and one in the Southwest (around 5 million inhabitants).

Four of the cases reported substantial consumption of semi-dried tomato products. In one additional case a history of food consumption could not be collected, as the patient was a non-UK resident who had left the country prior to the notification being received, and in the two other cases the consumption of semi-dried tomatoes could not be clearly ascertained as they had not eaten semi-dried tomatoes as such, but had eaten products which could contain semi-dried tomatoes as an ingredient). The infecting HAV strains were related but differed between 0.4% and 8.3% of the base pairs compared with to the Hu/Netherlands/RIVM-006/2010 strain (Table).

Of the seven patients (two males and five females), four were admitted to hospital with symptomatic hepatitis A infection and were discharged some days later.

Figure 2

Cases of hepatitis A meeting the case definition, by month of onset of symptoms, and respective homology percentage to the Hu/Netherlands/RIVM-006/2010 strain, England July– December 2011 (n=7)

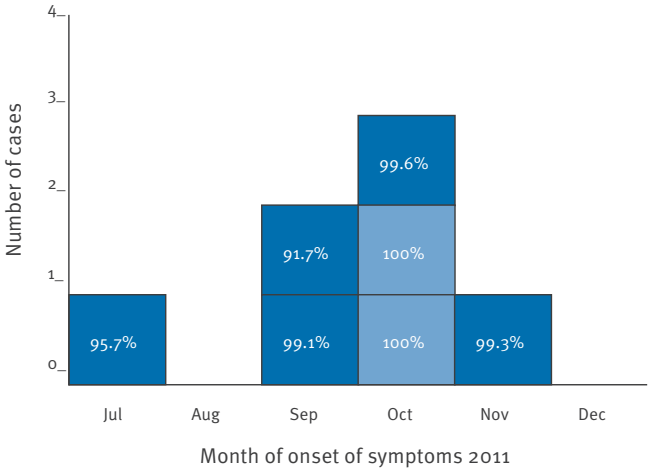


Figure 3

Geographical distribution of cases of hepatitis A meeting the case definition, England July–December 2011 (n=7)

Potentially related outbreaks

From July to November 2011 the Hu/Netherlands/RIVM-006/2010 strain was identified in four patients of a cluster of seven reported in the Netherlands by the Dutch National Institute for Public Health and the Environment (RIVM) [10]. The HPA and RIVM are collaborating to identify the source of these clusters in both countries.

Discussion

Given the fact that the mutation rate of HAV is usually very low [12], the reported consumption of semi-dried tomatoes in patients with different strains suggests the possibility that semi-dried tomatoes could have been contaminated with multiple strains of the virus.

The UK sent a message via the Epidemic Intelligence Information System (EPIS) on 15 November 2011 and a joint message from the HPA and the RIVM was sent via the European Early Warning and Response System (EWRS) on the 21 November 2011, alerting countries to the cluster of cases.

In England an analytical case-control study will be initiated as soon as active case-finding is completed. Based on interviews with the first cases, the main

Table

Description of cases of hepatitis A meeting the case definition, England July–December 2011 (n=7)

Week of onset of symptoms	Age	Region	Lab reference	Strain homology[a]
27	24	East of England	2011_510	95.7%
35[b]	10	South West	2011_526	99.1%
35[c]	22	East of England	2011_685	91.7%
40[c]	57	London	2011_775	100%
40[c]	51	East of England	2011_797	100%
40[c]	64	East of England	2011_778A	99.6%
44	18	London	2011_858	99.3%

[a] Homology related to Hu/Netherlands/RIVM-006/2010 strain
[b] Travel to France reported within the incubation period
[c] Substantial exposure to semi-dried tomato products

hypothesis to be formally tested is that semi-dried tomato products are associated with primary sporadic (non-travel related) cases of hepatitis A diagnosed in England between July and December 2011. Exposure to other foods such as shellfish, berries, salads and raw vegetables, will be considered and explored. To compare consumption of specific food items in cases with consumption in a group of controls, four age- and residence area-matched controls will be assigned to each case: two patients with *Campylobacter* infection in the same month and two case-assigned controls. In order to reduce recall bias, food preferences and probable food consumption history will be collected.

The enhanced laboratory surveillance, in place since November 2011, should identify new cases more rapidly. Because no specific brands have been implicated to date, and given the fact that there are currently no validated HAV detection methods for environmental samples in the UK, no food samples have as yet been tested. The HPA is liaising with the UK Food Standards Agency.

A foodborne outbreak with multiple strains in at least two European countries is suspected and all those charged with investigation and control of hepatitis A may want to consider semi-dried tomatoes as a possible source in sporadic cases of hepatitis A in order to identify a possible common source.

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