


Eurosurveillance publishes a special issue on hepatitis B and C

To tie in with World Hepatitis Day on 19 May, the scientific journal Eurosurveillance is today publishing a special issue on viral hepatitis, highlighting issues and challenges related to hepatitis B and C.

Immunisation Week

On 17 April 2008, Eurosurveillance is publishing a special issue with articles on the measles situation in Europe. The publication is linked to European Immunisation Week which runs from 21-27 April.

Eurosurveillance publishes special issue on tuberculosis

World Tuberculosis Day on 24 March commemorates the date in 1882 when Robert Koch presented his findings of the causing agent of tuberculosis (TB) – Mycobacterium tuberculosis. In the run up of this day Eurosurveillance publishes a special issue on the situation of TB in Europe.

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Special issue on meningococcal disease

Today (6 March, 2008), Eurosurveillance, the European peer-reviewed journal of infectious diseases, publishes a special issue on meningococcal disease. It includes two in-depth articles and an editorial by the European Centre for Disease Prevention and Control (ECDC).

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All press releases

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**In this issue**



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## Surveillance and outbreak reports

# A food-borne outbreak of hepatitis A virus (HAV) infection in a secondary school in Upper Normandy, France, in November 2006

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**In November 2006, six symptomatic cases of hepatitis A in pupils of a secondary school in Upper Normandy, France, were reported to the district health service. This paper describes the outbreak investigation undertaken with the aim to identify the vehicle and source of infection, implement control measures and estimate the size of the outbreak.**
**A primary case at the secondary school was defined as a pupil or a member of the staff with IgM anti-HAV detected in the serum and with onset of symptoms between 12 and 21 November 2006; a secondary case was defined as a contact to a primary case and who developed symptoms and had IgM anti-HAV two to seven weeks later. We performed a case control study of primary cases, controls being pupils visiting the same school (cases/controls 1:4) and inspected the canteen facilities. All 13 canteen employees were examined for anti-HAV IgM antibodies. A phylogenetic analysis of HAV of cases was performed.**
**We identified 10 primary and 5 secondary cases. Among primary cases 90% reported eating liver pate at the canteen compared to 62% among controls (OR 5.5, 95% CI 0.62-256.9). One liver pate sample contained markers of faecal contamination. HAV genotypes were of one identical type. All 13 canteen employees were negative for IgM anti-HAV while four had anti-HAV total antibodies. We found deficiencies regarding food preparing procedures and insufficient hand washing facilities.**
**The vehicle of the outbreak was believed to be the liver pate but the source of HAV could not be identified. Insufficient facilities in the canteen hindered staff from maintaining a high hygiene standard and were subsequently improved.**

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## Introduction

The hepatitis A virus (HAV) is transmitted faeco-orally by direct contact with an infectious person or through contaminated food. The incubation period ranges from 15 to 50 days with a mean of 30 days [1]. Acute hepatitis A is usually diagnosed by detection of immunoglobulin M antibodies to hepatitis A virus (IgM anti-HAV) in the serum. In the past 10 years, surveillance was based on a sentinel physician network, however due to a decline in the number of cases reliable incidence estimates could not be provided anymore [2]. Mandatory notification of hepatitis A was introduced in November 2005. The notification rate in 2006 was 2.2/100,000 [3]. With the decreasing incidence the risk of infection during early childhood declined and teenagers and young adults who lack immunity against HAV are at risk of developing symptomatic hepatitis A if exposed [4]. In France prevention of transmission of hepatitis A person to person relies mainly on hygienic measures like hand washing. Recommendations on vaccinating close contacts of cases are currently under debate [5,6].

Between 17 and 20 November 2006, the district health service in Rouen received reports on six symptomatic cases of hepatitis A in pupils of a secondary school in a town in Upper Normandy. The school is frequented by close to seven hundred pupils aged 10 to 15 years most of whom regularly eat at the school canteen.

On 20 November 2006, the Interregional Epidemiological Unit of Upper Normandy in collaboration with the Institut de Veille Sanitaire launched an investigation to identify the vehicle and source of infection and contributing factors, to devise and implement control measures, and to estimate the size of the outbreak.

## Methods

*Case definition and case finding*
A primary case at the secondary school was defined as a pupil or a member of the staff with IgM anti-HAV detected in the serum and with onset of symptoms between 12 and 21 November 2006.

A secondary case was defined as a family contact of a primary case or a pupil of the school in whose serum sample IgM anti-HAV were found during the period of two to seven weeks after week 46 and 47 (weeks 49 of 2006 to 2 of 2007). We actively looked for cases through two private laboratories in the town where the outbreak took place and the University hospital of Rouen.

*Case investigation*
On 22 November, we interviewed all primary cases by telephone, using a standardised questionnaire. The questions included a list of symptoms experienced after 1 November and exposures that had taken place between 2 October (50 days before the first cases developed symptoms) and 24 October 2006 (start of school holidays). Pupils of the school use electronic cards to pay at the canteen, which allowed us to determine for each child the exact dates and times of having a meal at the canteen. To generate the epidemic curve we plotted the week of onset of jaundice for each primary case and, as the date of jaundice was unknown for the secondary cases, the week of blood testing for each secondary case.

*Environmental investigation*
The veterinary and environmental health service of the district inspected the canteen on 21 November 2006. Water samples were taken for microbiological analyses. Two microbiological analyses of food items are being done routinely each month. Their results were reviewed for the last 10 months.

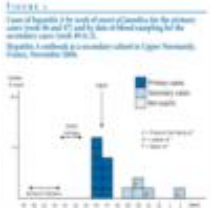
*Microbiological examinations*
Blood samples were taken from persons working in the canteen during the exposure period to look for anti-HAV total antibodies and IgM antibodies. Sera of the ten primary cases and one secondary case (mother of a primary case) were sent to the National Reference Centre for virus genotyping and phylogenetic analysis (sera of the remaining four secondary cases were not available for genotyping after the serological examinations had been completed). Viral RNA was extracted using the QIAmp Viral RNA kit (QIAgen, Les Ulis, France) and subjected to reverse transcription and polymerase chain reaction (RT-PCR) by using the One-Step RT-PCR kit (QIAgen). A 508 base-pair fragment encompassing the VP1/2A junction was amplified with the following primers: +2870 5'- GACAGATTCTACATTTGGATTGG-3' and -3381 5'- CCATTTCAAGAGTCCACACACT-3'. The nucleotide sequences were aligned with Clustal X software. Phylogenetic trees were constructed with the MEGA software by the Neighbor-Joining method from a Kimura two-parameter distance matrix, and bootstrap values were determined from 1,000 bootstrap resamplings of the original data. The HAV genotype was determined by comparing the phylogenetic analysis with the reference sequences of different HAV genotypes. GenBank accession numbers were X75215, AB020567, AB020564 and AF357222 for IA; M14707 and M20273 for IB; AY644676 for IIA; AY644670 for IIB; AY644337 and AJ299464 for IIIA and D00924 for V.

*Case control study*
We conducted a case control study including the ten primary cases. To select controls we asked parents of all children who had eaten at the canteen between 2 and 24 November (n=570) for a written consent authorising us to interview their child. Among children with parental written consent, we randomly selected four controls per case. We interviewed the controls face to face on 8 December. For each food item we calculated the percentage of cases and controls who reported having eaten it during the exposure period and the corresponding odds ratios (OR) with 95% confidence intervals (95% CI). The Fisher exact test was used for statistical inference ($p<0.05$).

**Results**

*Description of cases*
In total, 15 cases of hepatitis A were associated with the outbreak, having occurred during nine weeks from week 46 of 2006 to week 2 of 2007 (Figure 1). The epidemic curve suggested a common source of contamination with secondary transmission. Hepatitis A has been a notifiable disease in France only since November 2005 therefore the number of cases reported in the area during the same period of 2005 was not available. For comparison, in August, September and October 2006 (weeks 31-44) no cases had been declared.
We identified 10 primary cases among the pupils of the secondary school, aged 10 to 14 years, six of them girls. Six cases were in the sixth grade (11-12 years old) but only two of them attended the same class, three were in the fourth grade (13-14 years old) but all three in different classes, and one was in the third grade (14-15 years old). None of the affected students had travelled during the 50 days preceding the onset of disease and none remembered having been in contact with a jaundiced person. All had febrile jaundice with abdominal discomfort. Three were hospitalised for two days because of a low prothrombin blood level.

**Figure 1.** Cases of hepatitis A by week of onset of jaundice for the primary cases (week 46 and 47) and by date of blood sampling for the secondary cases (week 49 to 2).
Hepatitis A outbreak at a secondary school in Upper Normandy, France, November 2006.



The only common exposure identified was having regularly eaten at the canteen. No primary cases outside the school were found. No other cases were identified by the laboratories.
Five secondary cases have been identified, with the onset of symptoms (jaundice) between 9 December 2006 (week 49) and 14 January 2007 (week 2), two of them pupils of the same school who had been in contact with a primary case in their class, and three cases (two parents and a friend) who had been exposed to a single primary case at home.

*Environmental investigations*
The inspection of the school canteen revealed malfunctioning of equipment (dysfunction of the cold chamber, insufficient food storage capacities, no protection against insects) and deficiencies regarding food preparation procedures (insufficient separation of food items allowing cross contamination, uncovered chocolate dessert bowl, defrosting procedures not following the guidelines). There was no hand washing facility in the cold food preparation area, so food handlers had to cross the hot food preparation area and exit the clean area to access the hand washbasin next to the cloakroom. A liver pate sampled on 23 October had revealed a contamination with faecal coliform bacteria.

*Microbiological investigations*
Of the 13 persons who worked at the canteen during the exposure period, four were positive for anti-HAV total antibodies, but none of them had IgM antibodies. Serum samples of 11 cases (10 primary and one secondary case) were sent to the National Reference Centre for HAV genotyping. The eleven sequences were identical over an analysable fragment of 457 bp, and clustered with genotype IB strains (Figure 2).

**Figure 2.** Phylogenetic tree of hepatitis A sequences obtained during an outbreak at a secondary school in Upper Normandy, France, November 2006

*Case control study*
Completed questionnaires were available for 10 cases and 39 eligible controls (n=49). Information on 76 food items were collected and the questionnaires were completed in more than 80% (four or less missing values) by 93% (n=44) of all children. No child left more than nine food item questions empty. Nine of the 10 cases (90%) reported eating liver pate compared to 23 controls (62%, OR 5.5, 95% CI: 0.6-256.9, Table). Liver pate was served on 13 and 23 October. All 10 cases were present at school on these two days and nine (90%) had reported having eaten the liver pate. Of the 37 controls who answered the corresponding question, 21 (57%) were present on 13 October and reported eating liver pate for an OR = 6.9; 95% CI: 0.78-319; and 19 (51%) were present on 23 October and reported eating liver pate for an OR = 8.5; 95% CI 0.97-394.

**Table.** Exposure of cases and controls to different food items served at the canteen during the exposure period (2-24 October 2006). Hepatitis A outbreak at a secondary school in Upper Normandy, France, November 2006.

**Control measures**
Two information letters were sent to the parents of all pupils attending the school, one on 20 November, shortly after the first cases had been notified, and one on 14 December. The letters described the common manifestations of hepatitis A and the ways to limit the transmission of infection by following basic hygiene rules. Deficiencies regarding the equipment and the food preparation process were reported to the canteen operator in order to prevent future food contamination. A renovation of the canteen and its kitchen in particular was scheduled for the first half of 2007. In line with the French vaccination guidelines it was recommended to check the vaccination status and if necessary to vaccinate individuals with a higher risk of an adverse outcome of hepatitis A, namely patients with a chronic hepatitis B infection or individuals with chronic liver diseases (notably due to hepatitis C virus infection or excessive alcohol consumption). The French guidelines include no recommendations to vaccinate the contacts of cases.

**Discussion**
We described a typical example of what we believe to be a food-borne hepatitis A outbreak with 10 primary and five secondary cases. Person-to-person transmission as an alternative route of infection can not be excluded, but seems improbable as only two of the 10 cases belonged to the same class and shared the same classrooms. Although most cases of hepatitis A are a result of person-to-person transmission, food-borne outbreaks from a common source still occur in western countries [7-12]. About 5% of all hepatitis A cases between 1997 and 1999 in France were estimated to be due to contaminated food [13]. Contamination of a food item can occur at any point during cultivation, harvesting, processing, distribution or preparation (e.g. through infected food handlers) [8].

Although the results are not statistically significant, our case control study suggests that the vehicle of infection was the liver pate. Faecal contamination found in a pate sample reinforces this hypothesis. The food questionnaires were relatively complete and only two children did not answer the question whether they had eaten liver pate or not. However, due to the long incubation period of hepatitis A the children had to provide information on food items they had eaten six to nine weeks before. Their answers may therefore reflect not only the actual food intake but also the food preferences, and should be treated with caution.

The specific source of HAV could not be identified. None of the 13 food handlers working in the canteen had IgM antibodies when serum samples were taken but elevated anti-HAV total antibodies were found in four. HAV RNA has been detected in serum for as long as six to 12 months after infection (mean three months) [14]. In the majority of patients IgM anti-HAV declines to undetectable levels less than 6 months after infection [15]. In a study from 1986, IgM persisted even less than 30 days [16]. In the outbreak investigation described here, one of the four canteen employees who had elevated anti-HAV total antibodies may still have been infectious when the pate was served but the IgM anti-HAV level may have declined under a detectable level when the serum sample was taken six to eight weeks later.

HAV can remain infectious up to one month on environmental surfaces at ambient temperature [17]. Survival is inversely correlated to temperature and humidity favouring survival in refrigerators [18]. HAV can remain infectious on hands for more than four hours and be easily transferred from contaminated surfaces to food items by a food handler, regardless of whether the food handler excretes HAV or not [19]. Hand washing seems to be efficient in reducing the virus transfer to food [20]. The hand washing facilities in the canteen were insufficient. A contamination of the pate at an earlier stage (production process) seems improbable as we did not identify any cases outside the affected school and all primary cases were pupils who ate regularly at the canteen.

Since we chose a case control study design we could not directly estimate the attack rate among those exposed. About 570 children regularly eat at the canteen and 62% of the controls stated having eaten liver pate. The number of those exposed to the HAV contaminated pate can therefore be estimated at 353 which indicates a food specific attack rate of about 3 per 1000. Such a low estimated attack rate is in line with relatively low attack rates found in food-borne hepatitis A outbreaks [8] but could also indicate that not all portions served had been contaminated.

Guidelines for prevention of hepatitis A in close contacts of a case vary across western countries and depend on whether or not human normal immunoglobulin (HNIG) is licensed for this use in a given country. On the basis of the results of a randomized trial performed in Italy in which contacts received either the vaccine or no intervention within one week after the onset of symptoms in the index case [21] some countries introduced the use of vaccine for post-exposure prophylaxis. The British guidelines recommend vaccination of close contacts within seven days from the onset of illness in the primary case to prevent secondary cases [22] and the application of HNIG to close contacts identified too late to be protected by vaccine. In Germany vaccination of persons in contact with hepatitis A cases in collective facilities and schools is recommended. The use of HNIG is recommended in individuals with a higher risk of an adverse outcome due to a chronic liver disease [23;24].

In the United States, until recently guidelines recommended the administration of HNIG within 15 days to all unvaccinated household and sexual contacts of persons with serologically confirmed hepatitis A [25]. Since 2007, single-antigen hepatitis A vaccine is preferred for healthy persons aged 12 months to 40 years. For persons aged >40 years IgG is preferred [26]. This policy change was brought about by a clinical trial suggesting that vaccine performance approaches that of HNIG in healthy children and adults under 40 [27]. The Canadian guidelines prefer the use of active vaccination of close contacts within seven days after exposure and the use of HNIG only in individuals who may not respond to the vaccine such as infants under one year and immunocompromised individuals [28].

In France, HNIG are not licensed for post-exposure prophylaxis of hepatitis A. The French advisory committee for vaccination has recently launched a working group whose task is to make a proposal on the use of vaccine for contacts in household or school settings. In this outbreak, apart from the reinforcement of hygiene, it was recommended that household contacts at higher risk of severe hepatitis A, as defined by the advisory committee for vaccination, should be vaccinated [5]. Considering the age group concerned, the risk of secondary transmission in the school setting was considered to be low.

**Conclusion**

We concluded that the vehicle of the outbreak was the liver pate but could not identify the specific source of HAV. Insufficient facilities in the canteen hindered staff from maintaining a high hygiene standard and these were subsequently improved.

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