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An outbreak of hepatitis A virus infection in a secondary school in England with no undetected asymptomatic transmission among students

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Abstract

In June 2019 the Health Protection Team in Yorkshire and Humber, England, was notified of cases of hepatitis A virus (HAV) infection in staff at a secondary school. Investigation revealed that an earlier case worked as a food handler in the school kitchen. Indirect transmission through food from the canteen was considered the most likely route of transmission. Cases were described according to setting of exposure. Oral fluid was obtained from students for serological testing. Environmental investigations were undertaken at settings where food handling was considered a potential transmission risk. Thirty-three confirmed cases were linked to the outbreak. All of those tested ($n = 31$) shared the same sequence with a HAV IB genotype. The first three cases were a household cluster and included the index case for the school. A further 19 cases (16 students, 3 staff) were associated with the school and consistent with indirect exposure to the food handler. One late onset case could not be ruled out as a secondary case within the school and resulted in vaccination of the school population. Five cases were linked to a bakery where a case from the initial household cluster worked as a food server. No concerns about hygiene standards were noted at either the school or the bakery. Oral fluid samples taken at the time of vaccination from asymptomatic students ($n = 219$, 11–16 years-old) showed no evidence of recent or current infection. This outbreak included household and foodborne transmission but limited (and possibly zero) person-to-person transmission among secondary school students. Where adequate hygiene exists, secondary transmission within older students may not occur.

Introduction

Hepatitis A virus (HAV) is a non-enveloped positive-strand RNA picornavirus transmitted via faecal contamination of food and water, or by close contact with an infected person [1]. The mean incubation period is 28 days (range 15–50 days) and individuals are known to be infectious (shedding of virus in faeces) from approximately two weeks prior to the onset of symptoms to one week after the onset of jaundice [1]. Clinical illness is characterised by jaundice, but presentation is extremely variable and more severe in older individuals [1]. In children ⩽5 years of age, <10% of cases develop jaundice, while in adults ~75% of cases develop jaundice [1].

Hand hygiene is critical for preventing spread [2, 3]. HAV may remain infectious on hands for >4 h and easily transferred to food items during handling [4]. Transmission within households is very common, with secondary attack rates in susceptible household contacts between 12 and 34% [5]. Transmission between young children is common, with secondary attack rates of 3–28% in nurseries or day care centres and 3–50% in primary schools in Europe and the US [5]. Vaccination for post-exposure prophylaxis is routinely offered to close contacts and a range of vaccination strategies are available for outbreaks in specific settings, such as schools. Where hygiene practices are sufficient, secondary attack rates are lower in secondary schools compared to primary schools, and immunisation is not routinely recommended in these settings in England as a control measure following single cases [5].

Foodborne outbreaks of HAV infection are frequently reported due to contamination of food at the point of service or during growing, harvesting, processing or distribution [5]. Food handlers who handle uncooked food, or food after it has been cooked, during their infectious period, have been found to be the most common source of published foodborne

outbreaks [6]. There are limited published studies of hepatitis A outbreaks in secondary schools. The extent of asymptomatic transmission within these settings in areas of low endemicity remains an evidence gap [7]. In high endemicity regions asymptomatic transmission in secondary schools may be >50% [8, 9], but no data is available for low endemicity regions, such as the UK. This data is required to inform assessment of the effectiveness of mass vaccination strategies in specific settings [10].

On the evening of 18 June 2019, the Public Health England (now part of the United Kingdom Health Security Agency (UKHSA)) Yorkshire and Humber Health Protection Team (HPT) was contacted by School A, with concerns over the illness of three members of staff. School A is a mixed gender secondary school in City B (a small city with a population of ~17 000 persons) with approximately 650 students aged 11–18 years. Prior to the illness of staff members, a member of the catering staff at the school had been ill for 3 weeks and had reported abnormal liver function tests. Investigation revealed that two of the ill staff members were positive for immunoglobulin M (IgM) antibodies to HAV (anti-HAV IgM). The following day there were eight anti-HAV IgM-positive cases linked to the school. An outbreak control team (OCT) was convened on 19 June 2019.

Methods

Case definitions

A confirmed case was defined as a resident of City B (or who had visited City B) on or after 13 May 2019 and who was HAV IgM-positive. A probable case was defined as a resident of City B (or who had visited City B) on or after 13 May 2019 with jaundice, a history of jaundice or symptomatology indicative of hepatitis A infection. Probable cases were excluded if they had a negative HAV IgM result (test performed at local National Health Service (NHS) laboratory or at the national Virus Reference Department (VRD)). Case ascertainment was through local laboratory testing following clinical presentation with symptoms of HAV infection. Confirmed cases were excluded if HAV of a different genotype or of the same genotype but unrelated to the outbreak strain was detected from a clinical specimen.

Descriptive epidemiology

Cases were described according to setting. The expected distribution of onset dates for cases within settings associated with food handling was calculated using the known distribution of the incubation period for HAV infection (mean 28 days, range 15–50 days) [1] applied to the first and last days when a food handler was known to have worked during the likely infectious period (two weeks prior and one week after onset of symptoms) [1].

Environmental investigation

A joint site visit to School A was made by Community Infection Control, Environmental Health and Public Health England on 20 June to review general hygiene and infection control and any issues arising from management in the canteen and kitchen areas. Environmental health also visited the other named premises linked to the investigation.

Virological investigation

Blood samples were tested at local NHS microbiology laboratories for HAV infection. Those which tested positive for anti-HAV IgM were forwarded to the VRD for HAV RNA detection and sequencing. A 505 base pair fragment bridging the VP1/2PA junction of the HAV genome was amplified and genotype assignment undertaken in MegAlign (DNASTAR, USA).

Serological investigation

Oral fluid swabs were taken from students at School A. Consent was verbally obtained on the day of sampling from each participating child with telephone confirmation from a parent. Those providing consent were informed that although there would be no direct benefit to the individual being tested from this process (and that results would not be returned quickly enough to influence any public health management or decision making for individuals or families) the investigation would inform the outbreak investigation and contingency planning for wider vaccination strategies. Oral fluid kits were transported directly to the VRD laboratory for testing for IgM and immunoglobulin G (IgG) antibodies to HAV [11].

Results

Outbreak management and initial risk assessment

The OCT included membership from Public Health England (HPT, screening and immunisation, field epidemiology, national reference laboratory, national immunisation team), local authority public health, local hospital trust and community infection control. Although there was considerable uncertainty at the time of the initial risk assessment (19 June 2019), the OCT agreed that evidence was suggestive of a point or continuous source (albeit with known, limited duration) outbreak associated with an infected food handler. Person-to-person transmission within the school was considered to be less likely.

Descriptive epidemiology

There were 33 confirmed cases of HAV linked to the outbreak (Fig. 1a). The earliest three cases were all part of the same household: the two earliest cases were household contacts (cases 1 & 2) of the food handler who was the first case associated with the school (case 3). Case 2 reported working part-time at Bakery C in City B.

Including case 3, 20 cases were directly linked to School A (16 students, 4 staff) and a further 2 cases were household contacts of cases linked to School A. Both of these secondary household cases were younger siblings of cases who attended School A and attended separate primary schools.

Nine cases occurred among people who lived in or had visited City B during their expected incubation period but had no direct links to School A. Of these nine cases, five were linked to Bakery C in City B, and four occurred between 19 and 22 June in the community with no likely source of infection known (including no reported exposures to the school or bakery) (Fig. 1a). One of the bakery-associated cases attended a primary school in City B (different to the primary schools attended by the two children who were household contacts of pupils at School A) where there were no known cases or symptomatic students, but the school was known to be attended by siblings of children from School A.

All four cases in the community with no indicated source were residents of City B or had visited City B during their incubation period with onset dates consistent with the primary cases

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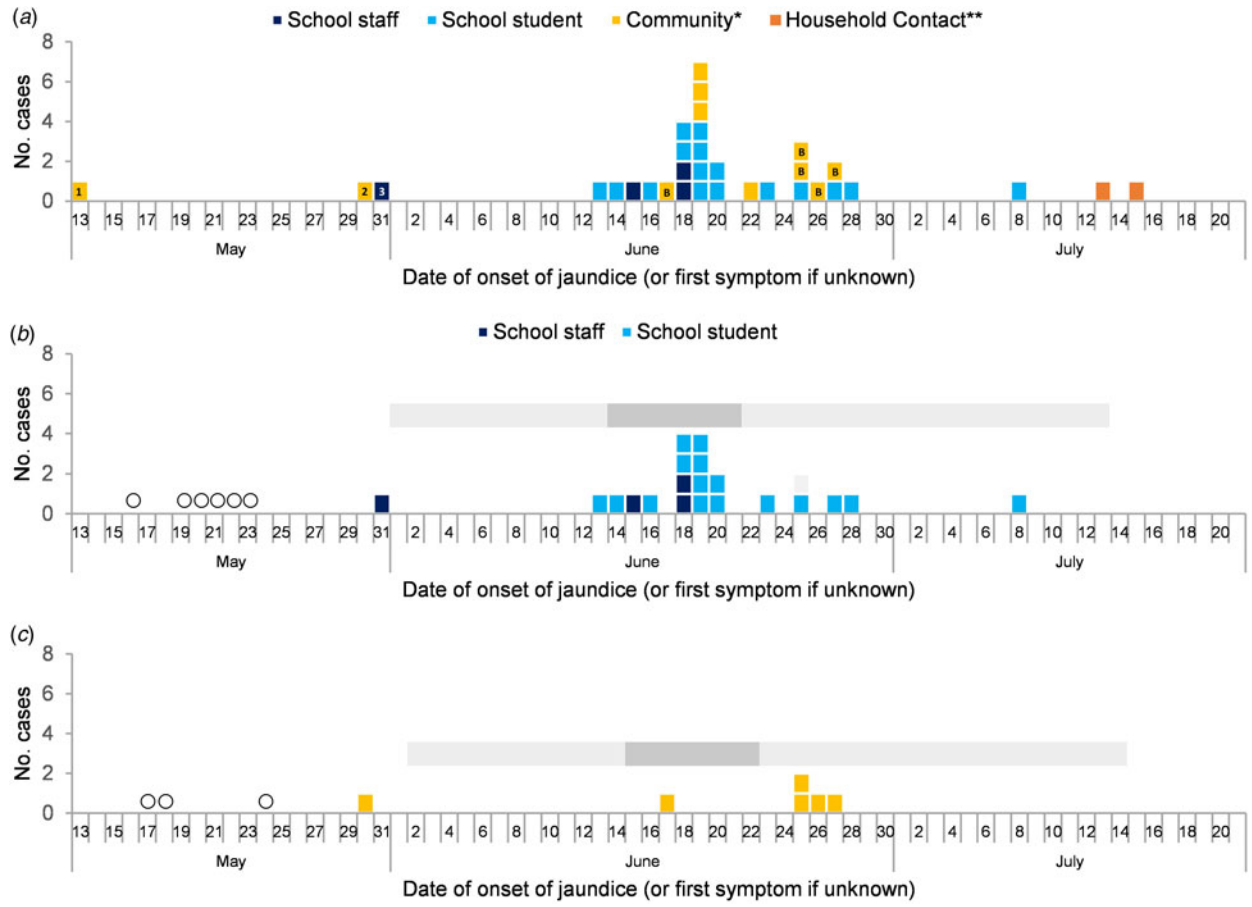

Fig. 1. Distribution of cases of confirmed hepatitis A virus infection by likely setting of exposure (all cases) (a) and for school-associated cases only (b) and bakery-associated cases only (c). The expected interval of symptom onset dates for school- and bakery-associated cases is based on mean (dark grey bar) and range (light grey bar) of the incubation period for HAV infection. The interval assumes exposure of individuals during the working days when a food handler was likely infectious at the setting (indicted by open circles). 1–3 = indicate first three cases, as described in the main text * Community cases include the household contacts (cases 1 & 2) of the first case among school staff (case 3). ** Household contacts are contacts of a school case. B = cases linked to Bakery C.

associated with the school and bakery (Fig. 1a). One of these cases was a food handler at Restaurant D in City B and was reported to have been ill at work on the same day as onset of jaundice.

Setting-based investigations

Family cluster

Only limited information was provided by the three initial cases in the household cluster at the time of diagnosis. Links to School A (case 3) and Bakery C (case 2) were only identified after the outbreak had been detected. Neither of these cases were aware of their diagnoses or potential risk to others while working in these settings.

School A

The distribution of school-associated cases which occurred subsequent to the onset of illness for case 2 was generally consistent with exposure (probably indirect) to case 2, with a peak of primary cases occurring on 18–19 June, among staff and students (aged 11–16 years) (Fig. 1b). Case 2 was known to have worked in the school canteen (preparing cold, ready-to-eat food items) for 6 days during the likely infectious period. The interval of expected mean onset dates included 68% (13/19) of school-associated cases (Fig. 1b). All 19 cases reported regular consumption of food from the school canteen. Although onset dates of all school-associated cases are included in the expected range of onset dates of primary cases, the last case (onset on 8 July) was considered as a potential secondary case (due to person-to-person transmission) within the school setting as this individual had no history of eating food from the school canteen.

During an environmental health visit on 20 June, several areas for improvement in the use of appropriate cleaning products and management and care for these products were noted, but no major issues were identified that were considered to have contributed to within-school transmission.

Bakery C

A total of five cases were linked to Bakery C (Fig. 1c) and were likely infected through indirect contact with case 2. The bakery reported that case 2's duties were to serve food while wearing gloves and using tongs. Three of the bakery-associated cases were residents of City B and reported eating food from Bakery C on a regular basis. One of these cases attended a primary school in City B (a different school to that attended by one of the community cases). Both non-resident cases reported visiting City B and consuming food purchased from Bakery C on a single day, a day that case 2 was known to have worked when infectious. Although onset dates for only one of the five bakery-associated

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cases were within the expected range of mean onset dates based on exposure to case 2's infectious-working days, the other four are just 3–5 days outside this period (Fig. 1c). An environmental health visit on 1 July noted that hygiene standards at Bakery C were good and the premises clean.

Virological investigation

Samples from 31 of 33 cases were genotyped; 29 were found to have the same HAV IB sequence (VRD19_HAV060) and two were found to have highly related sequences differing by 1 base pair (VRD19_HAV089, VRD19_HAV090). Two cases were diagnosed through oral fluid testing and sequencing was not possible. Analysis of all HAV samples from 2019 that had been sequenced at VRD revealed that the initial household cluster (cases 1–3) shared an identical sequence with four other cases (two pairs of household contacts) in England. These four cases were residents of other regions (South East and West Midlands) and known to be linked to consumption of date fruits. Contamination of date fruits is known to be associated with outbreaks of HAV [12, 13].

Food chain investigation

Following the establishment of a link between the four cases in other regions and consumption of date fruits, case 1 was re-interviewed. During this interview case 1 reported heavy consumption of date fruits of the same brand as the cases from other regions. Food chain investigation of the date fruits, imported from Iran, determined that regular testing for HAV of the imported product was not standard practice. The suppliers in Iran reported that workers' hands were tested monthly for HAV but did not report any positive results. Two samples of date fruits from the identified brand were tested under the authority of the Food Standards Agency in the UK and were found to be negative for HAV.

Control measures including vaccination

The primary control measures for this outbreak were: prompt identification of cases and vaccination of household contacts; emphasising the need for hand hygiene in the school setting and for cases and their contacts; exclusion of identified cases from school or work; identifying and advising any contacts or cases in at risk professions (specifically food handlers). Production of cold, ready-to-eat foods in the school canteen was temporarily stopped for the period 20–28 June.

Of 146 household contacts assessed, 97 were recommended for vaccination and seven for human normal immunoglobulin. Eleven workplace contacts from Restaurant D were offered vaccination. The decision to undertake vaccination in School A (vaccination carried out on 16 July) was taken following notification of a (then) probable case on 9 July that was considered to potentially be a secondary case within School A. An additional mop-up session for school staff and students took place on 25 July. Vaccination was carried out on 8 July (two schools) and 19 July (one school) at three of the four primary schools where a case was known to have attended. Vaccination was not carried out at the remaining primary school due to the older age of the case (10 years-old). Parents were informed of the rationale and decision to undertake vaccination by letter and consent obtained from them verbally or by signed letter.

Almost 75% of students (505/677, 74.5%) and over 50% of staff (74/132, 56.0%) at School A were vaccinated in response to the outbreak. Vaccine uptake was higher at the three primary schools, for students (302/321, 94.0%) and staff (60/99, 60.6%).

Serological investigation

Oral fluid samples were obtained from 224 students at School A aged 11–16 years-old and three students aged 18–19 years-old on 16 July (at the same time as vaccination was undertaken on site). Seventeen students gave histories of previous vaccination against HAV. Five HAV IgM-reactive results were obtained, all for confirmed cases identified during the outbreak investigation. Of 219 asymptomatic students who were tested, none showed serological evidence of recent or current asymptomatic infection through oral fluid testing. One sample from an asymptomatic student showed low-level IgM reactivity (IgG-negative) but the significance of the result was unclear. Two samples for asymptomatic students were IgG-reactive (IgM-negative) indicating past infection or immunisation (although neither student had given a history of previous immunisation). Serological investigation did not indicate that any unidentified person-to-person transmission had occurred at School A.

Discussion

Outbreaks of HAV are often difficult to control – the long infectious period and relatively long (and variable) incubation period combine to create an epidemiological picture where control requires proactive steps, anticipating future waves of (and settings for) spread, often based on limited information at the time decisions for public health action need to be made. This outbreak involved both household transmission and foodborne but, importantly, likely no person-to-person transmission within a secondary school setting. While it is well known that younger children often develop asymptomatic HAV infection and may spread HAV due to poor hygiene, this outbreak suggests that, where there is appropriate hand hygiene, older children may not spread HAV easily. Despite a considerable number of cases in school children aged 11–16 years, the serological evidence showed that there was no evidence of asymptomatic transmission. As this evidence was not available at the time, the decision to undertake mass vaccination within the school had to be taken based on the information available at that time and after careful risk assessment. In retrospect, the impact of vaccination on the control of this outbreak at the secondary school was likely negligible and, if this finding is generalisable to other similar situations, it provides important evidence that outbreaks in these settings may be readily controlled without the need for mass vaccination.

The option to undertake mass vaccination at the secondary school was reviewed regularly by the OCT during the course of the investigation. Given the low risk of person-to-person transmission by older children, national guidance does not recommend the routine vaccination of secondary school populations following single cases within that setting [5]. The trigger for mass vaccination in this outbreak was the notification of a case in a school pupil whose onset was outside of the main temporal cluster of primary cases within the school and who did not report eating food from the canteen. Clearly, this case could have been a result of secondary, person-to-person transmission at the school. However, the incubation period for this case is also not incompatible with indirect exposure to the food handler. At the time, there was some local anxiety about the size of the outbreak and the

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potential for further community spread and at primary schools attended by siblings of pupils from the secondary school. As a result, adopting a precautionary approach, it was agreed by the OCT with the local authority's Director of Public Health that mass vaccination at the school was warranted. That no further secondary cases occurred and there were no undetected, asymptomatic cases suggests that vaccination was not required to control transmission of HAV infection within the secondary school.

Transmission that occurred at the secondary school and bakery was probably a result of indirect transmission – direct handling of food (in a school canteen) and serving food (at a bakery). Exposure to HAV at both settings preceded awareness of public health authorities that the index cases worked with food.

Lapses in hygiene and safe food practices at both workplaces probably contributed to transmission. Exposure to an individual food item was considered plausible initially, and a cohort study using canteen records was implemented to test this hypothesis, but the findings were inconclusive due to limited data availability (results not shown). The index case within the secondary school had responsibility for activities known to be a risk for HAV transmission, including the preparation of cold, ready-to-eat foods. However, hygiene measures in place at the school (which upon inspection were found to be in place and suitably monitored) should have prevented indirect transmission via food. Absolute monitoring of individual adherence to safe practices for food preparation cannot be guaranteed, and one or more breaches in protocol on one or more of the six infectious-working days for the food handler likely resulted in nineteen secondary and two tertiary cases. Within the bakery setting, the reported activities of the index case did not include direct contact with food, only serving of food, while wearing gloves and using tongs. Again, some breach in practice most likely occurred (on one or more of three infectious-working days), leading to five secondary cases. This transmission of HAV reinforces the need to promote correct and consistent hygiene practices for all those working with food.

A debrief following conclusion of the outbreak investigation recognised the major lesson learned was that rapid vaccination in school settings requires co-ordination between multiple agencies. For this outbreak, having in place a mass vaccination and treatment plan for the local area prior to the outbreak was invaluable in establishing connections and building trust between agencies – such a plan should be considered for areas where one is not currently in place.

This outbreak of HAV infection involved multiple settings. Transmission within a secondary school was likely self-limiting due to assumed sound hygiene of the population at risk. Consistent with the basis for national guidance [5], limited (perhaps even zero) secondary transmission occurred through student-to-student spread and there were no undetected, asymptomatic cases. The findings of this investigation contribute to an evidence gap in quantifying asymptomatic transmission in secondary schools [7] that can be used to help inform guidance and risk assessments [10]. Almost certainly the route of transmission, both in the secondary school and also from a local bakery, was indirect contamination of food items. HAV remains highly likely to spread through this route and continued communication and adherence to appropriate practices for safe food preparation and handling (including serving) within this sector remains the key control measures for reducing the number of transmission events that occur with food items as the vehicle.

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Conflict of interest. Authors declare no conflicting interests.

Ethical standards. Public Health England had legal permission provided by Regulation 3 of The Health Service (Control of Patient Information) Regulations 2002 to collect confidential patient information under Sections 3(i) (a) to (c), 3(i)(d) (i) and (ii) and 3(3) as part of its outbreak response activities.

Data availability statement. The data that support this outbreak investigation were collected as part of a public health response, are considered sensitive and not made publicly available. Reasonable requests for access to anonymised data will be considered by the authors.

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