<table>
<thead>
<tr>
<th><strong>Title</strong></th>
<th>An outbreak of hepatitis A among injecting drug users</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Author(s)</strong></td>
<td>O'Donovan, Diarmuid</td>
</tr>
<tr>
<td><strong>Publication Date</strong></td>
<td>2001-11</td>
</tr>
<tr>
<td><strong>Link to publisher's version</strong></td>
<td><a href="http://dx.doi.org/10.1017/S0950268801006185">http://dx.doi.org/10.1017/S0950268801006185</a></td>
</tr>
<tr>
<td><strong>Item record</strong></td>
<td><a href="http://hdl.handle.net/10379/2604">http://hdl.handle.net/10379/2604</a></td>
</tr>
</tbody>
</table>
An outbreak of hepatitis A amongst injecting drug users

D. O'DONOVAN¹, R. P. D. COOKE²*, R. JOCE¹, A. EASTBURY³, J. WAITE¹
AND K. STENE-JOHANSEN⁵

¹ Department of Public Health Medicine, East Sussex, Brighton Hove Health Authority, Friars Walk, Lewes, East Sussex, BN7 2PB
² Department of Medical Microbiology, Eastbourne Hospitals NHS Trust, Eastbourne, East Sussex, BN21 2UD
³ Health & Housing Department, Eastbourne Borough Council, 68 Grove Road, Eastbourne, East Sussex, BN21 4UH
⁴ Community Drugs Team, 25 Bedfordwell Road, Eastbourne, East Sussex, BN21 2BQ
⁵ Department of Virology, National Institute of Public Health N-0403 Oslo, Norway

(Accepted 8 July 2001)

SUMMARY

This descriptive study investigated an outbreak of hepatitis A virus (HAV) infection among injecting drug users (IDUs) and their contacts. Twenty-seven cases of acute HAV infection were identified in a 5-month period. Connections with the local injecting drug using (IDU) population were established for 25 of the cases of whom 14 admitted to injecting drug use. HAV RNA genotyping revealed two HAV variants, closely related to variants found in Scandinavian IDUs and in South East Asia. The study demonstrates that once HAV enters the IDU population extensive outbreaks are possible. We recommend that all IDUs should be tested for HAV and hepatitis B virus (HBV) infections and offered combined hepatitis A and B vaccines if non-immune.

INTRODUCTION

Hepatitis A virus (HAV) infection is usually transmitted by the faecal–oral route. Outbreaks usually result from common source exposure to contaminated food and water, and from person-to-person transmission in households, schools and settings where sanitation is poor [1, 2].

Hepatitis B virus (HBV) and hepatitis C virus (HCV) infections are associated with parenteral transmission through injecting drug use [3–5]. Injecting drug users (IDUs) also have an increased risk of HAV infection [5–14]. This may be due to person contact where there is poor personal hygiene, transmission by injecting practices [11, 12] and oral ingestion of faecally-contaminated drugs [14]. Parenteral transmission of HAV has also been associated with haemophiliacs receiving clotting factor concentrates [15–17]. HAV vaccination is now recommended for this group [18].

We report an outbreak of HAV infection among IDUs and their contacts in a town on the south-eastern English coast, which occurred between October 1998 and March 1999. The location is a well known holiday resort. Many of the resident population are retired with over 26% of the population aged more than 64 years, compared to 16% in England and Wales [19].

HAV infection is not endemic in south-east England. In the 3 years preceding this outbreak an average of three cases were identified annually by the local microbiology laboratory; most of these were isolated cases in which the infection was acquired...
abroad. Whenever a case of HAV infection is identified it is routine practice for an environmental health officer (EHO) to visit the case to investigate the origin of the infection and to provide information on infection prevention and control.

**METHODS**

**Epidemiological investigation**

In a 3-week period in November 1998, the local microbiology laboratory identified five cases of acute-HAV infection: all were known to be IDUs. An outbreak control team (OCT) was formed, which included an EHO, a consultant in communicable disease control (CCDC), a medical microbiologist, and the nurse health adviser from the local Community Drugs Team (CDT). Further cases were identified over the following months. A case of HAV infection was defined as an acute illness with symptoms suggestive of the disease, abnormal serum bilirubin and amino-aspartate transaminase levels, and the presence of specific anti-HAV IgM antibody (VIDAS, bioMérieux). Cases were identified through reports by the local microbiology laboratory and general practitioners (GPs).

The EHO and CCDC contacted and interviewed each case. A standardized questionnaire was designed which included demographic details, questions on living conditions, travel, shellfish consumption, contacts with jaundiced people, previous immunoglobulin administration, previous HAV and HBV vaccination, drug use and sexual behaviour. Data were double entered and analysed using Epi-Info [21].

As no new cases had been identified for 2 months by 1 April 1999, the outbreak was considered to have ended.

**Prevention and control measures**

Expert advice was sought from Communicable Disease Surveillance Centre at Colindale, London, UK. All cases were visited and informed about transmission of HAV infection. Advice was given on enteric precautions, hand washing and injecting practices. Known household and sexual contacts were offered HAV vaccine as soon as possible after case identification. All cases were asked to identify everyone who had shared facilities with them for one night or more during the previous 3 months. These people were advised to contact their GP, or to attend the local CDT clinic. HAV vaccination was advised if this contact was within the 2 weeks before the case’s diagnosis was made.

Letters were sent to all local drug agencies, pharmacies, needle exchange co-ordinators and GPs to inform them about the outbreak and to ask them to offer HAV vaccine to contacts. Letters with information on HAV and details of vaccination were sent to all registered clients of the drug agencies, and to other residents in hotels and hostels where cases had lived. HAV infection was discussed with, and vaccination offered to, all clients attending the local drug agencies. Clients were encouraged to talk to their peers about the issue.

**Hepatitis virus assays**

Salivary specimens were tested on a voluntary basis from IDUs attending the CDT low threshold programme to determine the prevalence of recent and past exposure to HAV infection. We obtained salivary kits from the Public Health Laboratory Service Hepatitis and Retrovirus Laboratory, Colindale where saliva was tested for both IgG and IgM specific anti-HAV antibody [20]. All serum samples were tested for HBV surface antigen (VIDAS, bioMérieux). We did not test for HCV as we did not have informed consent for this.

Five IgM anti-HAV positive serum specimens (taken from cases with no obvious links identified at the beginning, middle and end of the outbreak) were sent to the National Institute of Public Health, Oslo, for RNA genotyping by reverse transcriptase–polymerase chain reaction (RT–PCR) and subsequent sequencing as previously described [12].

**RESULTS**

Between October 1998 and March 1999, 27 cases of HAV (13 male, 14 female) were identified in the area. The age range was 5–41 years (mean 24–8). Two were children (boys aged 5 and 6 years attending the same school) who were both considered to be secondary cases: one was the son of a case, both presented in January 1999. The range of AST levels at presentation was 52–2284 mmol/l (normal range 0–45).

Fourteen of the 25 adult cases admitted to ever having injected heroin, 10 of whom had injected heroin in the 2 months before their illness. Two admitted to smoking heroin, one in the 2 months before their illness. Six cases had been on methadone
programmes, 5 in the 2 months before their illness. Of the other drugs asked about, 6 individuals had used ecstasy, 2 people had used amphetamines, but only 3 admitted to smoking cannabis. Four people knew their drugs had been carried by mouth, none admitted to knowing that their drugs had been carried rectally. Twenty-three of the cases had known contact with a person who subsequently became jaundiced. Five had shared injecting drugs: 4 of the 5 had shared water for injection and spoons, and three had shared needles, syringes and filters with such a person. Fourteen of the cases had shared drinks, 9 had shared food and 12 had shared bathrooms with people who became jaundiced.

None of the cases had eaten shellfish in the 2 months preceding their illness. Six of the cases lived in housing of multiple occupation with shared bathroom and kitchen facilities. There were anecdotal reports that a number of people in one of the properties had been jaundiced, but we were unable to confirm this. One male case was the sexual partner of two of the female cases. None of the cases said they were homosexual. Twenty-two of the adults were unemployed. Thirteen were admitted to hospital, some for social reasons such as living alone.

All cases were HBsAg negative. Of the 27 salivary samples submitted from the CDT, 20 were anti-HAV IgG and IgM negative: two of these people presented as cases later. Five were anti-HAV IgG positive, of whom 2 had been vaccinated in the past, and 2 were anti-HAV IgM and IgG positive (indicative of HAV infection in the previous 1–2 months), one of whom presented as a case within days.

HAV RNA was detected by RT–PCR in 3 of 5 serum samples. Two samples were identical in the whole region of 348 base pairs analysed by sequencing. The third sample differed in a single base pair within this region. These two HAV-variants clustered in genotype 111A and are closely related to variants identified in Norwegian IDU communities in 1997–8 [22] and among Swedish IDUs in the 1980s [23]. Related variants have been detected in people infected in South East Asia [12].

**DISCUSSION**

An outbreak of HAV infection among IDUs has not previously been reported in the United Kingdom. Such outbreaks have been reported in North America [6–8] and from Scandinavia [11–14]. These outbreaks pose a significant threat to the general population.

This outbreak may have been larger than described since sub-clinical cases are difficult to identify. We were aware of anecdotal reports of jaundiced IDUs who did not seek medical advice. The difficulties of studying this patient population are well recognized, as may IDUs live in a subculture where illicit drug taking and other illegal activities are the norm, so they may be reticent about giving information that may be perceived as incriminating, and unwilling to name other IDUs. Some estimates suggest that only 20% of IDUs are know to health services [24]. It is possible that several of those who said they were not IDUs were in fact users.

We were unable to confirm the route of transmission in this outbreak, as in previous reports. It is likely to be multi-factorial, possibly a combination of person-to-person spread and some parenteral spread. HAV may be associated with poor living conditions and personal hygiene among addicts. Injecting drugs is often a group activity and HAV infected individuals may faecally contaminate ‘works’ such as spoons, filters, water used for injection or the drug itself while preparing the drugs for injection by a group. Faecal contamination of drugs associated with the transportation of illegal drugs by rectum has been suggested as a mode of transmission of HAV [14]. None of the cases in this outbreak knew of drugs being carried in this way, but two knew that drugs they had used had been carried by mouth.

While HBV and HCV infections are common among IDUs, there is less data on parenteral transmission of HAV [15–17]. Parenteral transmission is only possible during the relatively short viraemic period. Needle sharing has been linked to transmission [11–13]. Persons who have shared illegal drugs with a person who has serologically confirmed HAV infection should receive prompt HAV vaccine and immunoglobulin [25]. However HAV vaccine alone has been used successfully in the containment of outbreaks [26, 27] and in the prevention of secondary cases among household contacts.

Serological testing for anti-HAV IgM is the best method for detection of acute/recent HAV infections among symptomatic cases [29] but we found salivary HAV antibody testing a useful and more acceptable alternative to serum assays for determining the prevalence and incidence of HAV infection in IDUs. However, detection of HAV RNA by RT–PCR is possible before onset of symptoms and before immunological markers appear. It is therefore a useful tool in early detection of cases and in identifying outbreaks.
RNA genotyping can be useful to identify whether cases are sporadic or connected to a larger outbreak. This outbreak suggests the possibility that HAV genotype IIIA variants may have disseminated in IDU communities across Europe [22, 23]. Relative HAV variants have been detected among travellers to the Far East indicating the possibility of drug contamination either in the Far East or somewhere along the route to the users [12].

The incidence of infection in children in developed countries has reduced dramatically due to improvements in living conditions; thus more young adults are susceptible [2, 29]. Although the infection is usually a mild disease in childhood, serious morbidity and mortality may result in older people, leading to recent calls for universal early childhood immunization [30]. HAV infection in HCV infected individuals can cause fulminant fatal hepatitis [31]. In Europe the prevalence of HCV is highest in the IDU population [3]. Co-infection with HBV may accelerate HCV related liver damage [32]. Hence, immunization of IDUs against HBV has been described a priority, [33] although HBV coverage in IDUs in England is low: over half of all unvaccinated IDUs tested in 1995–6 were susceptible to infection [33]. The Unlinked Anonymous Prevalence Monitoring Programme United Kingdom found that 21% of IDUs in England and Wales and 12% of IDUs in the South East of England in 1997–8 were hepatitis B anti-HBc positive, indicating past or current HBV infection [35]. Testing for immunity to HAV, HBV and HCV has been recommended [35]. In the USA vaccination against HAV is recommended for all users of illegal drugs [25]. We support the call for more creative strategies to ensure delivery of hepatitis B vaccine to IDUs, including more opportunistic vaccination at the time of testing [36]. Hepatitis A vaccination could also be offered to this population. Because of the risk of spread to the wider population and the risk of HAV in older individuals, in particular those who have HCV infection, we recommend that all IDUs should be offered testing for evidence of previous infection to both HAV and HBV. Non-immune IDUs should be offered HAV and HBV vaccines, which are now available in a combined formulation [37]. The first dose of combined vaccine could be given at the time of testing, along with risk reduction messages, as delay may represent a missed opportunity in this potentially difficult population, some of whom may become infected between visits. A decision could be made on the remainder of the schedule when the test results are available. Single antigen vaccine for hepatitis A contains a larger antigen dose and may be needed in the outbreak situation where protection is required quickly.

ACKNOWLEDGEMENTS

We thank the patients who participated in the study; the staff of the Lodge; Eastbourne and County Healthcare NHS Trust; laboratory staff at Eastbourne Hospitals NHS Trust; Dr J. V. Parry and staff at the Hepatitis and Retrovirus Laboratory, PHLS Central Public Health Laboratory who processed the salivary specimens; and general practitioners in Eastbourne. We thank Dr J. V. Parry for comments on an earlier draft of this paper.

REFERENCES


