Investigation of an outbreak of hepatitis A simplified by salivary antibody testing

A. R. BULL1, K. J. KIMMANCE1, J. V. PARRY2 AND K. R. PERRY2

1Department of Community Medicine, Odstock Hospital, Salisbury, Wiltshire SP2 8BJ
2Virus Reference Laboratory, Central Public Health Laboratory, 61 Colindale Avenue, London NWP 5EQ

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SUMMARY

In March 1988 a general practitioner notified two cases of hepatitis A in a private boarding school. Epidemiological investigation, including testing for salivary antibodies revealed a further five cases and established immunity to, and recent infection with, hepatitis A virus (HAV). The pattern of the outbreak was described. A number of practices which would encourage cross-infection were corrected. Normal human immunoglobulin was given to contacts.

Repeat salivary testing 10 weeks later revealed that two more boys had become reactive for anti-HAV, though at a low titre. These may have been serological responses to HAV infection modified by the passive immunization.

INTRODUCTION

Hepatitis A is a viral illness with an incubation period estimated at 14–49 days (1). Infection may be sub-clinical but a debilitating illness with frank jaundice occurs in 10% of infected children and 75% of infected adults (2, 3). Virus spread is usually faecal-oral.

The period of maximum infectivity is during the late incubation period but it has been suggested that individuals may be infectious from 2 weeks before to 19 days or more after the onset of jaundice (2). The virus may survive in the environment for up to a month (4). Contamination of food or water may result in large common-source outbreaks.

On 15 and 16 March 1988, two cases of hepatitis in boys attending a private preparatory school were notified to the Medical Officer for Environmental Health for Salisbury. Both cases were serologically confirmed at that time as acute hepatitis A.

Following an inspection of the school an epidemiological investigation was started in which case finding included testing saliva samples from the whole community for IgM and IgG antibodies to HAV twice at an interval of 10 weeks. This recently introduced test enabled additional anicteric cases, and immune and susceptible individuals, to be identified more accurately than is possible from clinical histories, and more acceptably than by widespread phlebotomy. Consent for such testing was given by the headmaster in loco parentis.
MATERIAL AND METHODS

On receipt of the two notifications an inspection of the school was carried out to identify conditions or practices conducive to the spread of the infection. Human normal immunoglobulin (HNIG) was given on 17 March to all pupils and to those staff involved in nursing the affected children.

Immediately before administration of HNIG, saliva was collected from all the boys, the teaching staff and all except two of the kitchen staff, using a disposable ‘salivette’ (Sarstedt, Numbrecht, FRG). The saliva was tested for anti-HAV IgG and IgM at the PHLS Virus Reference Laboratory by a method previously described and validated against tested sera (5-7). Ten weeks later the exercise was repeated for all the boys, the two previously untested kitchen staff, and other staff.

The results of the salivary antibody tests were expressed as a ratio \(T:N\) of the reactivity obtained with the test sample \(T\) to the average of that of five negative controls \(N\). A ratio of > 3 indicates immunological response to the virus. An elevated IgM reaction associated with negative IgG was taken to indicate an early, acute infection; elevated IgM and IgG to indicate recent acute infection (ie. in the previous 3 months); elevated IgG with negative IgM indicated more remote infection.

A questionnaire was compiled for those boys and staff found to be anti-HAV positive. Information was requested on symptoms compatible with the disease, and the data of onset. The symptoms sought were weakness, generalised ache, mild fever, anorexia (both general and food-type specific), cachexia, vomiting, ache in the right hypochondrium, and jaundice. The questionnaire also enquired about travel overseas and contact with known cases of hepatitis.

RESULTS

The school is an isolated institution with approximately 130 resident (male) pupils ages 8–13 years. Most teaching staff live in on-site accommodation. Kitchen and domestic staff live in local villages.

The boys had been home on two occasions (5–7 February and 27–29 February) since term began in early January 1988. Term was due to end for the Easter holidays on 18 March.

Inspection identified several unhygienic practices:

1. The school sanitorium shared toilet facilities with dormitories on the first floor. Excrement from the sanitorium was disposed of in these general purpose toilets.
2. Soiled linen from the sanitorium was sometimes left overnight in the small scullery where eating utensils for the sick are cleaned, and where small meals were sometimes prepared.
3. There was no hot water to the handbasins in the one daytime toilet block. Two single looped towels served this main toilet block; these were changed twice weekly.
4. Before each meal all the boys queued to wash their hands in four handbasins which were served by four single loop towels, changed daily.
Table 1. Positive results of salivary antibody tests

<table>
<thead>
<tr>
<th>Subject No.</th>
<th>Date of specimen</th>
<th>17 March</th>
<th>25 May</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Boys</td>
<td>IgG</td>
<td>IgM</td>
</tr>
<tr>
<td>1*</td>
<td>Positive†</td>
<td>0-8†</td>
<td>1-3</td>
</tr>
<tr>
<td>2*</td>
<td>Positive†</td>
<td>38-6†</td>
<td>1-3</td>
</tr>
<tr>
<td>3*</td>
<td>0-8</td>
<td>7-2</td>
<td>37-1</td>
</tr>
<tr>
<td>4</td>
<td>1-1</td>
<td>18-7</td>
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<td>1-7</td>
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<tr>
<td>11</td>
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<td></td>
<td>Staff</td>
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<tr>
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<td>9-3</td>
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<td>—</td>
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<tr>
<td>16</td>
<td>47-9</td>
<td>1-1</td>
<td>27-6</td>
</tr>
</tbody>
</table>

* Icteric illness.
† Serological test.
‡ This value from a contaminated sample. Later sampling showed IgG T:N = 31-5.

Note: The T:N values on 17.3 and 25.5.88 are not very consistent because they were not tested simultaneously. This would be expected.

Steps were immediately taken to rectify these unsatisfactory practices.

Of the 121 pupils (excluding the two boys (nos. 1 and 2) originally notified and shown to be positive by serum testing) the initial salivary tests (17 March) showed that two boys (nos. 3 and 4) had evidence of early infection, one boy (no. 5) had had a recent infection, and four boys (nos. 8–11) were immune with no indication of recent infection (Table 1).

The two boys whose antibody pattern indicated an early infection (nos. 3 and 4) both developed symptoms in the week following the salivary test and one of them (no. 3) developed frank jaundice.

The questionnaire revealed that boy no. 5, whose test showed recent infection, had had one episode of anicteric illness, compatible with hepatitis A, 10 weeks before the first salivary test. None of the four boys found to be immune had a history of jaundice. The father of one of these boys (no. 10) had had proven hepatitis A in late February 1988. Two immune boys (brothers) had been in contact with a case of hepatitis in 1984. The fourth gave no history of exposure.

Of 31 adults tested on the first occasion, five (nos. 12–16) were found to be immune to hepatitis A (Table 1). There was no laboratory or clinical evidence of recent HAV infection. The second salivary antibody tests (25 May) showed two boys (nos. 6 and 7) to have an altered immune status to hepatitis A, indicative of recent infection (Table 1). One had a weak IgG reaction (T:N = 5-1) but with a
negative IgM response ($T:N = 1.4$); the other had a strong IgG ($T:N = 21.9$) and a weak IgM reaction ($T:N = 3.0$). These results were confirmed by repeat analysis. In both cases the questionnaire elicited a history of non-specific, non-icteric illness with nausea and vomiting in the 2 weeks following the administration of HNIG and the first salivary test.

In case nos. 1, 2 and 3, IgM was no longer detectable ($T:N = 1.3, 1.3, 1.3$), in case no. 4 it had declined to low levels ($T:N = 5.8$), and in case no. 5 it was borderline ($T:N = 2.3$). Apart from case no. 1, all those that had had acute infection diagnosed in March had high levels of IgG at follow up. The sample collected from case number 1 on 25 May was repeatedly unreactive, but it was noted that it was turquoise in colour. Because of doubts about the provenance of this sample a further sample was obtained on 30 August. This sample was found to contain IgG anti-HAV (IgG $T:N = 31.5$; IgM $T:N = 1.6$). The other boys showed no alteration in their HAV immune status. Sixteen of 23 teaching staff were available for retesting, and they, too, showed no change in immune status.

**DISCUSSION**

The results of the IgG anti-HAV testing showed the expected low level of immunity amongst the children and the adults of this type of community. It also demonstrated the potential for the wide spread of HAV infection within the school. Passive immunization with anti-HAV in the form of HNIG to halt the outbreak did not interfere with test interpretation at follow-up; this was expected because of the mechanism of operation of GACRIA type assays, the reactivity of which depends upon the proportion of total IgG that is specific for the virus under examination (5). In the case of administered HNIG this would be an undetectably small proportion of the recipient's total serum IgG.

Follow-up testing at 10 weeks indicated that no new cases of hepatitis A had occurred after the administration of HNIG, except in those boys already well into the incubation period. In four boys with initial high levels, anti-HAV IgM persisted in saliva for only 2-3 months after jaundice and this concurs with other investigations (7). It makes interpretation of saliva results somewhat easier than serum results, where some individuals will continue to produce moderate levels of anti-HAV IgM for over a year. The antibody responses mounted by case no. 7 and to some extent case no. 6, seem to have been suppressed by administration of HNIG, which was probably given in the latter part of the incubation period.

It is possible that this outbreak of hepatitis A occurred in three waves, case no. 5 being the first case, cases nos. 1-2 the second wave, and cases nos. 3, 4, 6, 7, the final wave of infection (Fig. 1.) However, in view of the observation that IgM does not persist in saliva for as long as it does in sera, one or more of the immune boys (case nos. 8-11) might have had a sub-clinical infection before the outbreak was recognized and so been an earlier source.

In particular this might apply to the boy whose father had suffered icteric hepatitis in February (case no. 10). It would, with hindsight, have been helpful to have tested this boy's blood for serum IgM, since his illness may have occurred in late December/early January. He could thus have been both the source of infection for his father, and an earlier link in the chain of this outbreak.
Fig. 1. Pattern of the outbreak. ■, Jaundice onset; □, symptoms onset; ×—×, limits of incubation; ■—■, limits of infectivity.

It is also possible that cases nos. 1–4, 6 and 7 were infected from a common source. The interval during which they could together have been infected with HAV ran from 6 February to 22 February (Fig. 1). All six were in the junior half of the school, but they were not in the same class or dormitory, and did not share a table at meals. Neither had they shared any food or drink outside the school. Had there been a common source involving food or drink consumed by the whole school, it is unlikely that only these few boys would have been affected.

Action taken on notification of two cases of hepatitis A led to a general improvement in standards of hygiene and a reduction in the risk of transmission of gastroenteric infection. Study of the course of an outbreak such as this is simplified by the ability to screen many contacts with the salivary antibody test in a way that would not be practical using blood samples. The worth of the salivary antibody test for this type of investigation was demonstrated by its ability to identify clinically unrecognized cases of acute HAV infection (4 of 7 diagnosed). Rapid identification of immune individuals offers the opportunity to reduce the number of doses of HNTG given. (In this instance the administration of immunoglobulin could not be delayed pending the saliva test results because the school term ended on March 18 and the boys would not return for a month.) Uncertainties about the incubation and infectivity periods of hepatitis A make epidemiological investigation difficult. The prompt administration of immunoglobulin probably arrested the outbreak and may have prevented a more severe illness in at least two children (1, 8).

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REFERENCES


