# Multiple Factors Contribute to Positive Results for Hepatitis A Virus Immunoglobulin M Antibody

*Adnan Alatoom, MD, PhD; M. Qasim Ansari, MD; Jennifer Cuthbert, MD*

● ***Context.***—**In the United States, a successful vaccination program for hepatitis A virus (HAV) infection has decreased both its incidence and the true positive rate for diagnostic immunoglobulin M (IgM) antibody to HAV in acute hepatitis.**

***Objective.***—**To survey positive results of HAV IgM tests and determine the effect of changing ordering options.**

***Design.***—**We reviewed all positive results for IgM antibody to HAV between January 2007 and December 2010. Patient demographics, clinical history, and laboratory data were recorded and the encounter, order, and reason for test reviewed. Each result was categorized as indicating acute, recent, resolved, or indeterminate HAV infection.**

***Results.***—**A total of 10 735 tests were performed; 35 patients had 49 positive results. Most positive test results were associated with outpatient visits and were ordered in the assessment of patients with liver disease, but not clinical acute hepatitis. In the final analysis, 4 patients had acute hepatitis A and 20 individual patients had recent and/or resolved hepatitis. All but 1 of the remaining 11 patients had another established cause of liver disease with a positive IgM HAV antibody test result; data to determine causality were insufficient. The total number of tests requested annually decreased more than 35% with the introduction of computerized physician order entry.**

***Conclusions.***—**Current assays for IgM HAV antibodies are overused in the absence of clinical acute hepatitis; future clinical decision support may improve patterns of order entry. Most patients have findings consistent with HAV exposure but not acute hepatitis; dormant viral infection may be a continuing source of antigen.**

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Hepatitis A virus (HAV) infection contributes approximately half of the clinically apparent cases of acute viral hepatitis in the United States.[1] Since the introduction of a safe and effective vaccine and its widespread adoption, the actual number of cases has decreased to approximately 10% of the peak level.[2] Of paramount importance, any bona fide new diagnosis of acute hepatitis A has public health implications. Cases are reported to the local health departments to identify a possible common source of infection and provide postexposure prophylaxis to contacts of the index patient.

Testing for immunoglobulin (Ig) M antibodies against HAV (IgM anti-HAV) is the mainstay of the serologic diagnosis for acute hepatitis A infection and has been highly sensitive and specific.[3–5] The presence of any detectable antibody (total anti-HAV) plus the absence of high-titer IgM-specific antibodies is used to differentiate between past and current infection. In the past few years, isolated reports have documented an increase in the number of positive results for IgM anti-HAV in patients whose illnesses were not consistent with the case definition of hepatitis A in conjunction with the decrease in true incidence.[6–8]

We conducted a retrospective study to determine how commonly we may be encountering potential false-positive results after noticing the occurrence of positive IgM anti-HAV test results in the absence of clinical findings suggesting acute viral hepatitis. We explored possible underlying reasons and the effect of changing ordering options.

## MATERIALS AND METHODS

An institutional review board approved a retrospective medical record analysis for all patients with positive results for IgM anti-HAV antibodies between January 2007 and December 2010. Patients were identified by querying the laboratory information system (Cerner Millennium, Cerner Corporation, Kansas City, Missouri) to generate the list of samples and order type (individual test or group) associated with positive results. Results from internal and external quality control assessments were excluded.

### Data Collection

Patient demographics, clinical history, and laboratory data were obtained through review of electronic and paper medical records. Patient age, sex, and race/ethnicity were recorded for each patient. Laboratory data included test results for bilirubin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), all viral hepatitis serologic assays, rheumatoid factor, and human immunodeficiency virus antibody at the time of diagnosis.

### Test Ordering

Test order information was obtained from the electronic medical record and from review of paper medical records. The ordering

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From the Department of Pathology, University of Texas Southwestern Medical Center, Dallas.

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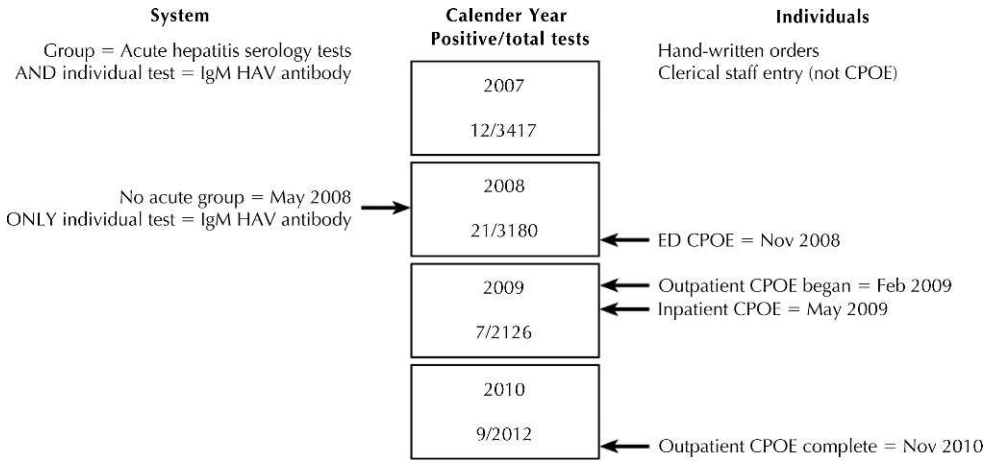
Reprints: M. Qasim Ansari, MD, Department of Pathology, University of Texas Southwestern Medical School, 5323 Harry Hines Blvd, Dallas, TX 75390-9073 (e-mail: qasim.ansari@utsouthwestern.edu).




*Number of positive test results for hepatitis A virus (HAV) immunoglobulin M (IgM) for each year in the 2007–2010 period, and method of test ordering. Abbreviations: CPOE, computerized physician order entry; ED, emergency department.*

user, ordering provider, reason for test, and any associated code from the International Classification of Diseases-Ninth Revision were recorded for each positive test result. Until 2009, all orders were hand-written by providers or conveyed as a telephone order to authorized staff and then entered into the electronic medical record by clerks (Figure). For outpatients, the serologic tests for viral hepatitis were together in 1 section on a paper order form. In 2007, there were 2 groups of hepatitis tests, as well as individual tests. The groups consisted of acute hepatitis serology tests (IgM anti-HAV, hepatitis B surface antigen, total anti–hepatitis B core with reflex IgM if positive, anti–hepatitis C virus) and chronic hepatitis serology tests (hepatitis B surface antigen, total anti–hepatitis B core, and anti–hepatitis C virus). Paper forms contained an individual check box for IgM HAV testing but did not contain a check box for total HAV antibody.

Starting in May 2008, all IgM anti-HAV tests were ordered individually. There was only 1 group available: hepatitis panel (hepatitis B surface antigen and anti–hepatitis C virus), which did not include HAV testing. Providers also hand-wrote nonstandard orders. These included "hepatitis labs" and "hepatitis serologies." They were interpreted by order entry staff choosing from the available tests for clerk order entry. Starting in November 2008 and continuing throughout 2009 and 2010, computerized physician order entry was introduced to the hospital system. Its implementation in the Emergency Services Department (November 2008) and inpatient areas (late April 2009) was completed en bloc, whereas in outpatient clinics, the process was slow. Some outreach programs are still using paper forms.

### IgM Anti-HAV Measurements

All assays were performed with the VITROS anti-HAV IgM assay on the VITROS ECI System (Ortho-Clinical Diagnostics, Rochester, New York) that uses the antibody class capture technique and chemiluminescence. Results were calculated as a normalized signal relative to the signal/cutoff (S/CO) value, with S/CO below 0.8 interpreted as negative; S/CO of at least 0.8 but below 1.2, as borderline; and S/CO of 1.2 or above, as positive.

### Data Analysis Definitions

After review of all available information, each positive test result was associated with a specific diagnostic category. (1) Acute hepatitis A: elevated aminotransferase levels with peak value above 500 U/L and negative serology test results for hepatitis B and hepatitis C infections; (2) Recent acute hepatitis A: elevated aminotransferase levels with peak value below 500 U/L and either evolving S/CO (positive to borderline or negative) or resolving aminotransferase values (normal AST level); (3) Resolved acute hepatitis A: aminotransferase levels normal; (4) Indeterminate: elevated aminotransferase levels below 500 U/L; neither evolving S/CO nor resolution of abnormal aminotransferase values.

## RESULTS

Between January 2007 and December 2010, a total of 10 735 IgM anti-HAV tests were performed (Table 1). The percentage of positive test results during this time period was 0.5%; 35 individual patients tested positive for IgM anti-HAV. In addition, 3 of the patients had a borderline test result on blood taken 6 months previously (n = 1) and 1 or 13 days later (n = 1 each). The mean age of the patients was 41 years (median, 43 years; range, 9–81 years); 20 of 35 were male; 13 were black, 14 were Hispanic, 6 were non-Hispanic white, and 1 was Asian.

A total of 49 separate tests had positive results. Eight patients had 2 or more positive test results, of which 2 were inadvertent duplicate orders during a single hospital admission. One patient had 5 positive test results, 3 patients had 3 positive test results, whereas the remainder had 2 positive results. Signal/cutoff results for the 2 duplicate orders were essentially identical (S/CO of 2.70 and 7.02, compared with 2.44 and 6.95, respectively). The demographic, laboratory, and assay data are shown in Table 2 for each diagnostic category of HAV.

**Table 1. Results of Hepatitis A Immunoglobulin M Tests Each Year in 2007–2010 Period**

| Year | Total | Positive | Low Level[a] | Borderline | Negative |
|---|---|---|---|---|---|
| 2007 | 3417 | 12 | 10 | 8 | 3397 |
| 2008 | 3180 | 21 | 11 | 2 | 3157 |
| 2009 | 2126 | 7 | 4 | 4 | 2115 |
| 2010 | 2012 | 9 | 4 | 7 | 1996 |
| **Total** | **10 735** | **49** | **29** | **21** | **10 665** |

[a] Signal/cutoff <1.95.

Table 2. Demographic, Laboratory, and Assay Data for 37 Positive Results for Hepatitis A Virus (HAV) Immunoglobulin M

| Parameter | Acute HAV (n = 4) | | | Recent HAV (n = 8[a]) | | |
|---|---|---|---|---|---|---|
| | Mean | Median | Range | Mean | Median | Range |
| Age | 20 | 19 | 13–30 | 47 | 52 | 27–66 |
| AST | 2255 | 2028 | 984–3981 | 111 | 68 | 38–411 |
| ALT | 3275 | 2920 | 1508–5750 | 119 | 108 | 36–243 |
| Bilirubin | 7.4 | 6.3 | 4.2–12.9 | 1.0 | 1.0 | 0.4–1.4 |
| S/CO | 8.1 | 7.5 | 2.0–15.5 | 2.7 | 2.0 | 1.2–7.4 |

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; S/CO, signal/cutoff value.

[a] Two subjects appear twice, in both recent HAV and resolved HAV infection.

In 2008, the highest number of positive tests (n = 21) was obtained. This included 1 patient with classical acute hepatitis, 1 patient with prior symptoms consistent with acute hepatitis, 2 patients (3 tests) with potential false-positive results (Table 3), and 10 low-level positive results. In Dallas County, a few more cases of acute hepatitis A were reported in 2008 (n = 46) than in 2007 (n = 42) or 2009 (n = 40), potentially leading to a greater number of positive results.

The order-associated data for the 49 encounters with the 35 patients are depicted in Table 4. Between 2007 and 2008, orders were initially written on paper by providers and entered into the electronic medical record by clerical staff (Figure). In 3 instances, no order was found in the medical record in association with the encounter information. The commonest encounter site was an outpatient clinic (33 of 49, 67%). More than half of the orders (26 of 49, 53%) were either acute hepatitis serology tests or the individual test. When the individual test was ordered, all providers also ordered hepatitis B and hepatitis C tests (data not shown). In most instances, the test was ordered for either laboratory evidence of liver disease (elevated aminotransferase level) or as a repeat after an earlier positive result; together, these accounted for 39 of 49 orders (80%).

### Liver Disease

The results of liver tests that are frequently abnormal in patients with acute viral hepatitis (aminotransferases and bilirubin) are shown in Table 5 in association with the reason for ordering the IgM anti-HAV test. The peak values around the time of the initial test order are depicted. Four patients had aminotransferase levels greater than 500 U/L; they presented with jaundice (n = 3) or abdominal pain (n = 1). Three of these patients were hospitalized. For 11 patients, all test results were normal. The patient who was tested because of household exposure to an index case had normal AST and bilirubin levels.

### Other Serologic and Immunologic Markers

Other immunologic test results are shown in Table 3. All patients were tested for hepatitis B surface antigen and hepatitis C antibody. One patient was confirmed positive for hepatitis B surface antigen, whereas 2 had false-positive results. Three patients had a false-positive hepatitis C virus antibody result by enzyme-linked immunosorbent assay. There were 8 other patients with a positive antibody test result for hepatitis C virus infection. Hepatitis C viremia was confirmed in 5 patients, one of whom had a positive rheumatoid factor. The other patients with chronic hepatitis C were not tested for rheumatoid factor.

### Diagnostic Analysis

Patients were classified as having acute hepatitis A, recent hepatitis A, or resolved hepatitis A by the combination of peak aminotransferase levels and the change in aminotransferase levels and S/CO over time. We also divided the cohort into 2 groups, by the absolute S/CO value (Table 6). The value of 1.90 was used to divide the group into higher (n = 26) and lower (n = 31) S/CO because this value was below that observed for all patients with symptoms, signs, and laboratory test results consistent with acute hepatitis.

In the final analysis, acute hepatitis A was the diagnosis for 4 patients with 5 positive test results. Another 8 patients (12 results) had findings consistent with recent hepatitis A, while 14 patients (17 results) were classified as having resolved acute hepatitis A. Of the latter group, 2 were also in the recent hepatitis A group at an earlier time point. The final 11 patients (15 results) could not be classified. All had abnormal aminotransferase levels and 10 of 11 had reasons for hepatic enzyme elevation other than hepatitis A. The remaining patient, a 38-year-old homeless man (S/CO, 1.36), had no follow-up data and no alternative diagnosis. The findings in the 4 patients with acute hepatitis A were the same as those reported previously from our institution.[5] The only difference between the past period and the present period was the incidence. Between 1997 and 1998, 13 patients were hospitalized with acute hepatitis A, as compared with 3 patients during the past 4 years.

## COMMENT

We found that a positive result for IgM antibody to HAV is now relatively rare (0.5% of all performed tests). Furthermore, only a minority of patients with a positive result have a concomitant clinical diagnosis of acute hepatitis A (4 of 35, 11%). The number of assays decreased with the abandonment of paper forms and introduction of physician order entry. However, even in 2010, more than 2000 tests were ordered. With operationalization of clinical decision support systems, decreasing inappropriate test orders may be possible. One intriguing unanswered question is whether the persistence of IgM antibody correlates with persistence of antigen in a clinically dormant state. While acute symptomatic hepatitis A is now a much rarer disease than in the past, it remains important to make this diagnosis, which has significant public health implications.

Acute hepatitis A infection is diagnosed by the combination of an appropriate clinical presentation and laboratory testing with IgM anti-HAV.[1,4,5,8,9] Possible explanations for positive results without clinical acute hepatitis include asymptomatic infection, previous infection with persistent IgM antibodies, cross-reacting antibodies, or commercial

**Table 2. Extended**

| Resolved HAV (n = 14[a]) | | | Indeterminate (n = 11) | | |
|---|---|---|---|---|---|
| Mean | Median | Range | Mean | Median | Range |
| 39 | 36 | 9–81 | 47 | 46 | 36–67 |
| 21 | 22 | 10–29 | 101 | 82 | 29–185 |
| 18 | 16 | 7–43 | 90 | 88 | 26–161 |
| 0.6 | 0.4 | 0.2–2.0 | 3.4 | 1.5 | 0.3–16.9 |
| 2.1 | 1.6 | 1.3–5.2 | 3.1 | 1.4 | 1.2–8.7 |

kits with a falsely low cutoff value. We found evidence supporting these scenarios.

## Clinical Acute Hepatitis

The classic IgM-specific assay acquires diagnostic sensitivity for acute hepatitis A with substantial dilution of the original serum or plasma sample.[3] Thus, the HAVAB-M (Abbott Laboratories, Abbott Park, Illinois) radioimmunoassay introduced in 1981 diluted the sample 1:4000.[3] The current assays use a similar IgM antibody capture system, but detection of the antibody is made by enzyme-linked chemiluminescence or another nonradioactive method. Regardless, sample dilution is critical for diagnosis of patients with the symptoms and signs of acute hepatitis.[3] Occasionally, dilution may result in an initially negative test result that becomes positive days or weeks later.[10–12]

The balance between sensitivity (correctly identifying all patients with acute hepatitis A) and specificity (correctly excluding all those without acute hepatitis A) is chosen to allow optimum assay performance in a defined clinical setting, acute hepatitis. Owing to the low levels of IgM antibodies after vaccination, commercially available tests rarely detect these antibodies[1,9] unless the sample dilution is decreased.[13]

IgG antibodies to HAV appear soon after IgM, persist for years after infection, confer lifelong immunity,[1,5,9] and are not measured in the IgM-capture technique.[3] In the United States, IgG-specific HAV antibody is not measured separately; rather, all classes (IgM, IgG, and IgA) are measured in the total HAV antibody assays. The sample is not similarly diluted, thereby greatly increasing the sensitivity of the assay. Over time, the IgM component decreases but current clinical assays do not indicate the proportion of IgM in the total. Research studies[14,15] have shown the potential for differentiating prior infection by assessing IgG avidity, but such assays are not commercially available.

**Table 3. Other Serologic and Immunologic Test Results for Patients With Positive Hepatitis A Virus Immunoglobulin M**

| Test | Abnormal Result | Abnormal, No. |
|---|---|---|
| Hepatitis A total antibody | Positive | 9/11[a] |
| Hepatitis B surface antigen | Positive | 1/35 |
| | False positive[b] | 2/35 |
| Hepatitis C virus antibody | Positive | 8/35 |
| | False positive[c] | 3/35 |
| Human immunodeficiency virus antibody | Positive | 2/16 |
| Rheumatoid factor | Positive | 1/4 |

[a] One patient tested negatively for total hepatitis A virus (HAV) antibody 6 months before the positive immunoglobulin M (IgM) result; 1 patient tested negatively for total HAV antibody simultaneously with a positive IgM result.
[b] Not confirmed on neutralization.
[c] Negative recombinant immunoblot assay result; patient also had a false-positive result for hepatitis B surface antigen.

## Other Hepatitis A

Our finding of positive results for IgM-specific HAV antibody in asymptomatic infection and recent infection is expected. IgM antibodies will be produced regardless of the disease severity. The apparent persistence of IgM-specific HAV antibody in a small number of patients after the resolution of all clinical evidence of hepatitis is well documented.[16,17] The antibody levels in such patients are generally low, similar to some of the findings reported herein.

In 2005, the Centers for Disease Control and Prevention (CDC) reported an increase in the number of persons "with positive serologic tests for acute hepatitis A virus infection whose illness was not consistent with the clinical criteria of the hepatitis A case definition."[8] Data from state public health officials in Connecticut (19 not consistent of 127 = 15%) and Alaska (10 not consistent of 37 = 27%), as well as

**Table 4. Encounter and Order Information for Patients With 49 Positive Results for Hepatitis A Virus (HAV) Immunoglobulin M (IgM)**

| Parameter | Options | Positive IgM anti-HAV, No. (%) |
|---|---|---|
| Encounter | Emergency department | 1 (2) |
| | Inpatient | 15 (31) |
| | Outpatient | 33 (67) |
| Provider order[a] (n = 49) | Acute hepatitis serology tests (= group) | 7 (14) |
| | HAV IgM | 19 (39) |
| | HAV IgM and total | 7 (14) |
| | Other standard tests | 5 (10) |
| | Nonstandard test | 10 (20) |
| Reason for test | Symptoms and signs[b] | 7 (14) |
| | Exposure to HAV | 1 (2) |
| | Liver disease[c] | 17 (36) |
| | Other[d] | 14 (29) |
| | Unknown[e] | 10 (20) |

[a] Other standard tests: chronic hepatitis serology tests in 4 instances and hepatitis B core IgM test in 1 instance. Nonstandard tests cannot be selected and were interpreted by the entering user from the handwritten order ("Hepatitis A core IgM," "Hepatitis labs"). For 1 patient, there was no provider order in the record; the clerk ordered HAV IgM and total.
[b] Jaundice (n = 4), abdominal pain (n = 2), other gastrointestinal symptoms (n = 1). All 7 patients had a final clinical diagnosis of either acute hepatitis (aspartate aminotransferase [AST] >500 U/L) or recent hepatitis A (AST <500 U/L).
[c] Cirrhosis (n = 2), hepatitis C (n = 2), hepatitis B (n = 1), elevated hepatic enzymes (n = 12).
[d] Repeat after previous positive test (n = 13), duplicate order (n = 1).
[e] Provider or clerical error (n = 5), no note retrieved (n = 2), homeless outreach (n = 3).

| Table 5. Levels of Liver Enzymes and Bilirubin and the Reason for Ordering Hepatitis A Virus Immunoglobulin M Test | | | | | | |
|---|---|---|---|---|---|---|
| | Bilirubin, mg/dL | | | AST, U/L | | |
| Reason | Mean ± SD | Median | Range | Mean ± SD | Median | Range |
| Symptoms and signs (n = 6) | 5.4 ± 4.5 | 4.5 | 1.0–12.9 | 1527 ± 1541 | 1190 | 38–3981 |
| Abnormal enzymes (n = 8) | 1.0 ± 0.6 | 0.9 | 0.4–2.1 | 122 ± 119 | 82 | 45–411 |
| Chronic liver disease (n = 7) | 4.1 ± 6.4 | 1.5 | 0.3–16.9 | 84 ± 63 | | |
| Unknown (n = 10) | 0.4 ± 0.1 | 0.3 | 0.2–0.6 | 29 ± 22 | 22 | 15–82 |
| Reference range | | | 0.2–1.3 | | | 13–40[a] |

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase.

[a] Females: 10–35 U/L and males: 10–50 U/L for both AST and ALT since mid 2009.

the Sentinel Counties Study (87 not consistent of 140 = 62%), were quoted. The positive results came from different licensed IgM anti-HAV tests (Connecticut, n = 3 tests; Alaska, n = 3 tests from 2 manufacturers). An editorial[8] concluded that IgM anti-HAV testing should be restricted to "persons with clinical hepatitis," not those with abnormal liver enzyme levels. The Kentucky Department for Public Health also had similar findings during a 3-year period.[7] There were 156 diagnostic false-positive results reported (156 of 269 = 58%) in the absence of acute hepatitis, compared with 113 confirmed cases.

Our data provide not only a numerator for IgM anti-HAV positive results but also a unique denominator, all ordered tests. In addition, the reason for ordering the test was retrievable from the electronic health record, data not previously obtainable in the public health studies. Only when IgM anti-HAV tests were ordered for patients with symptoms or signs suggesting acute hepatitis was the final analysis acute hepatitis A. The percentage of patients with acute disease (15%) is lower than that in the published literature. The likely explanation is that the previous data were pulled from public health notifications, not only from clinical laboratories.

Whether the persistence of IgM-specific antibody is associated with persistent antigen stimulation is unclear. In the report from the CDC,[8] the testing of IgM HAV antibody–positive specimens for HAV RNA yielded only 1 positive result from 25 persons with no symptoms of acute hepatitis, compared with 34 positive results for HAV RNA in 51 symptomatic cases.[8] The single positive result was associated with a follow-up IgM anti-HAV result that was negative, implying recent asymptomatic HAV. In hepatitis B, IgM antibody and hepatitis B virus DNA "reappear" with activation of dormant virus associated with immune suppression. As with HAV, the diagnostic accuracy of IgM testing for acute hepatitis B infection is dependent on sample dilution. IgM-class antibodies continue to be produced in chronic hepatitis B infection albeit usually at lower levels undetectable in the diluted samples.[18]

### False-Positive and Low-Positive Results

Rheumatoid factor can interfere with IgM anti-HAV testing.[19] One patient with chronic hepatitis C had a high titer for rheumatoid factor, which possibly interfered with the IgM anti-HAV testing by bridging the capture antibody and the signal antibody, leading to false-positive results. Chronic hepatitis C in 7 other patients, at least 4 of whom were viremic, may also be associated with rheumatoid factor; they were not tested. The presence of false-positive results from cross-reactivity with other antigenic epitopes in the assay is another potential explanation, particularly since false-positive tests for hepatitis B surface antigen and hepatitis C were encountered for 2 and 3 patients, respectively. Cross-reactions among viral hepatitis antibodies have been reported previously.[20] Finally, 1 patient had a result that was either a false positive or the consequence of a

| Table 6. Final Analysis for 49 Positive Results With Hepatitis A Virus (HAV) Immunoglobulin M Divided by Signal/Cutoff (S/CO) Value and Liver Enzymes | | | | | |
|---|---|---|---|---|---|
| | | AST and/or ALT, U/L | | | |
| Analysis | No. | > 500 | Elevated (< 500) | Normal | % |
| Higher S/CO (≥1.90)[a] | 21 | 5 | 10 | 6 | |
| Acute hepatitis A | | 5 | | | 31 |
| Recent HAV | | | 6 | | 23 |
| Resolved HAV | | | | 6 | 27 |
| Indeterminate[b] | | | 4 | | 19 |
| Interference?[c] | | | 4 | 1 | |
| Lower S/CO (<1.90)[a] | 28 | 0 | 18 | 10 | |
| Recent HAV | | | 6 | | 16 |
| Resolved HAV | | | 1 | 10 | 45 |
| Indeterminate[d] | | | 11 | | 39 |
| Interference?[c] | | | 2 | 5 | |

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase.

[a] The lowest S/CO value for a patient with aminotransferase levels >500 U/L was 1.95. The value 1.90 was chosen to separate the positive results into 2 nonoverlapping groups.

[b] Other potential causes of elevated aminotransferase levels: hepatitis C (n = 3), cirrhosis (n = 1). One patient had a total Hepatitis C Virus antibody test performed simultaneously; the result was negative, indicating a probable false-positive immunoglobulin M (IgM) result.

[c] Rheumatoid factor (n = 1 patient, 2 Hepatitis C Virus IgM tests), false-positive Hepatitis B surface antigen test result (n = 3 patients, 4 Hepatitis C Virus IgM tests), false-positive Hepatitis C Virus antibody test result (n = 2 patients, 6 Hepatitis C Virus IgM tests).

[d] Other potential causes of elevated aminotransferase levels: hepatitis C (n = 1), cirrhosis (n = 5), other chronic liver disease (n = 4), insufficient data (n = 1).

| Table 5. Extended | | |
|---|---|---|
| ALT, U/L | | |
| Mean ± SD | Median | Range |
| 2216 ± 2142 | 2189 | 46–5750 |
| 119 ± 75 | 115 | 26–243 |
| 72 ± 48 | 66 | 23–136 |
| 36 ± 52 | 14 | 8–161 |
| | | 10–40[a] |

technical error; this conclusion is based on the simultaneous negative total HAV antibody and positive IgM antibody results in a more dilute sample. Simultaneous measurement of total antibody and IgM can be performed and may prove to be beneficial in helping physicians correctly interpret HAV serology.

In conclusion, positive results for IgM anti-HAV testing have multiple etiologies. Previous reports have recommended that clinicians limit laboratory testing for acute hepatitis A infection to persons with clinical findings typical of hepatitis A or to persons who have been exposed to settings where HAV transmission is suspected.[6,8] However, an approach targeting individual providers may not result in a decrease in the number of positive results for IgM anti-HAV in the absence of acute hepatitis. In contrast, system approaches, whereby clinical decision support guides appropriate testing, may engineer change. Restricting orders to a subset with acute hepatitis (liver aminotransferase levels >500 U/L) can also decrease the number of positive results for HAV IgM. New tests that allow simultaneous measurement of total antibody and the proportion of IgM may be the most useful addition to the laboratory testing menu.

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