

VIRAL HEPATITIS TESTING

2009 APHL SURVEY REPORT

In order to characterize the role that the nation's public health laboratories play in the prevention, control and surveillance of viral hepatitis, the Association of Public Health Laboratories (APHL) conducted the 2009 APHL Hepatitis Testing Survey in the summer of 2009. This issue brief summarizes the results of that survey.

Viral hepatitis is inflammation of the liver caused by one of five viruses — hepatitis A virus (HAV), hepatitis B virus (HBV), hepatitis C virus (HCV), hepatitis D virus (HDV) and hepatitis E virus (HEV). In the United States, hepatitis A, B and C are the most common types of viral hepatitis, while hepatitis D and E are less prevalent. Generally speaking, viral hepatitis can cause acute onset of nausea, jaundice and abdominal pain. More specifically, HBV and HCV infection can result in a chronic infection attributed to increased risk of developing chronic liver disease and liver cancer. Currently, safe and effective vaccines exist only for the prevention of HAV and HBV.

Although case rates have declined during the last decade, viral hepatitis continues to be a disease of major public health concern, specifically in terms of morbidity and mortality. A recent report released by the Institute of Medicine (IOM) estimates that approximately 5.3 million people, or 2% of the US population, are living with

chronic hepatitis B or hepatitis C, and attributes approximately 150,000 deaths per year to viral hepatitis-related liver disease. However, the IOM report also concluded that hepatitis B and C are not widely recognized as a serious public health problem and that the resources allocated to viral hepatitis prevention, control and surveillance programs are consistently inadequate.¹

Early identification of the virus is crucial to effective case management and the prevention of further disease transmission. Laboratories that perform diagnostic hepatitis testing play a vital role in identifying cases of the disease. In order to characterize the role that the nation's public health laboratories play in the prevention, control and surveillance of viral hepatitis, the Association of Public Health Laboratories (APHL) conducted the 2009 APHL Hepatitis Testing Survey in the summer of 2009. This issue brief summarizes the results of that survey.

The survey data reveal that the majority of public health laboratories in the United States continue to play a major role in the provision of HAV, HBV and/or HCV testing and that HDV, HEV and liver enzyme testing are not currently offered by US public health laboratories. While the majority of laboratories report being compliant with current testing recommendations, the data did reveal an opportunity to increase

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awareness of the recommendations provided in the 2003 document *Guidelines for Laboratory Testing and Result Reporting of Antibody to Hepatitis C Virus*. This highlights the importance

of periodically reminding public health laboratories of current hepatitis testing recommendations.² APHL will continue to explore areas where member participation in hepatitis activities, including training and guidelines development, can be expanded to improve quality laboratory practice.

METHOD

The 2009 APHL Hepatitis Testing Survey was launched in June and closed in July 2009 to assess the hepatitis testing practices,

capacities and capabilities of the nation's state public health laboratories (SPHLs). The 21-question survey was developed by members of the APHL Infectious Disease Committee along with the Centers for Disease Control and Prevention's (CDC) Division of Viral Hepatitis, and was administered through MRInterview, a web-based survey instrument.

State public health laboratories in each of the 50 states and Washington, DC were invited to participate in the survey. Laboratories were asked to report on their viral hepatitis testing activities from January 1, 2008 – December 31, 2008. APHL received responses from 41 (80%) of the SPHLs invited to participate in the survey.

VIRAL HEPATITIS TESTING IN SPHLs

Thirty-six (88%) of the respondents provide (i.e., perform or refer) some type of viral hepatitis testing to identify hepatitis A, B and/or C infection. Five (12%) of the respondents do not provide any hepatitis testing. Only 15 (42%) public health laboratories report offering hepatitis panels, the most common being panels for acute hepatitis and prenatal screening.

Of the 36 laboratories that offer viral hepatitis testing, 27 (75%) provide testing for hepatitis A, 34 (94%) for hepatitis B and 31 (86%) for hepatitis C. None of the respondents reported providing hepatitis D, hepatitis E or liver enzyme testing. Figure 1 provides an illustration of these results.

Twenty-three (64%) of the 36 responding laboratories offering viral hepatitis testing provide testing for hepatitis A, B and C. Six responding laboratories offer testing for hepatitis B and C solely, while four respondent laboratories offer testing for only hepatitis A and B. Two respondents test only for hepatitis C and one respondent only offers hepatitis B testing.

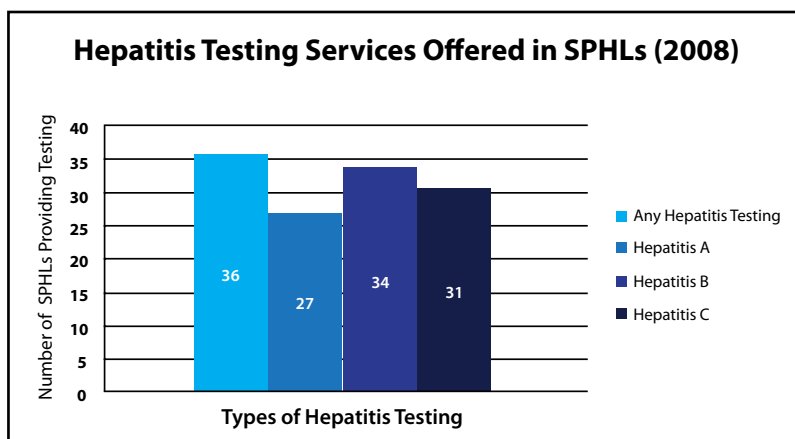


Figure 1. Number of state public health laboratories providing testing for each type of viral hepatitis (n=41).

58% of the 36 laboratories that provide viral hepatitis testing report that the funding received is insufficient for laboratory testing needs.

FUNDING SOURCES

Public health laboratories receive funding for viral hepatitis testing from a variety of sources. However, 58% of the 36 laboratories that provide viral hepatitis testing report that the funding received is insufficient for laboratory testing needs. The majority of responding laboratories (28, or 78%) use state general budget funds to support at least part of their hepatitis testing program. Thirteen (36%) hepatitis testing laboratories charge fees to at least a portion of their specimen submitters for hepatitis testing services. None of the laboratories that responded to the survey report having a budget-line item dedicated for hepatitis testing. A complete summary of funding data is located in Figure 2.

HEPATITIS A TESTING PRACTICES

Testing for hepatitis A virus (HAV) was the least frequently reported type of viral hepatitis testing offered among survey-participating laboratories, with 27 state public health laboratories providing this service. Currently, there are two serological tests used for the detection of hepatitis A: IgM anti-HAV and total HAV.³ Both assays detect the presence of antibodies against HAV and confirm a diagnosis of the virus. While all 27 laboratories that offer hepatitis A testing provide anti-HAV IgM testing, only 19 (70%) of those laboratories also provide anti-HAV total testing. Figure 3 summarizes the number of laboratories performing both types of HAV testing in-house versus those that contract the testing to a referral laboratory.

HAV TESTING VOLUME

Quantitative comparison of HAV testing volumes (as well as hepatitis B and C) across states is challenging, as regions have varying population sizes and incidence rates as well as varying levels of testing conducted in the private sector. For example, testing volume for anti-HAV total varied from a low of 2

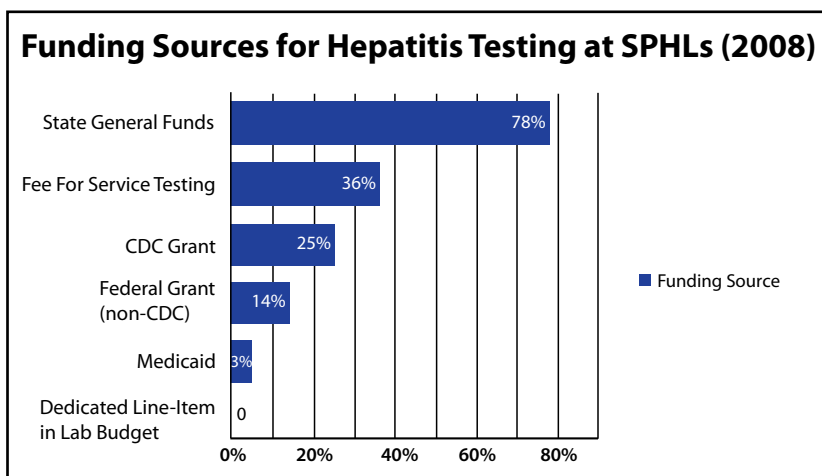


Figure 2. Percentage of state public health laboratories that receive various types of funding sources for viral hepatitis testing, out of responding laboratories that offer hepatitis testing services (n=36).

specimens to a high of 58,790 samples, with the median number of anti-HAV total tests equal to 292. Because several responding states reported considerably larger testing volumes than others, there is a disparity between the maximum and the median volume. Comparatively, tests for anti-HAV IgM were reported in fewer numbers than the anti-HAV total test – with a range of 1 to 1,250 (median 42.5) specimens received – among SPHLs that responded to this survey.

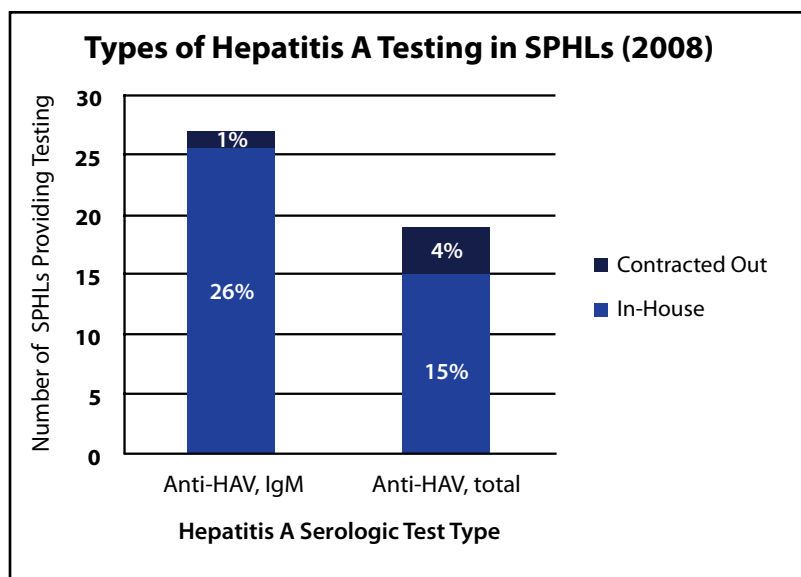


Figure 3. Types of Hepatitis A testing offered by state public health laboratories in 2008 (n=27).

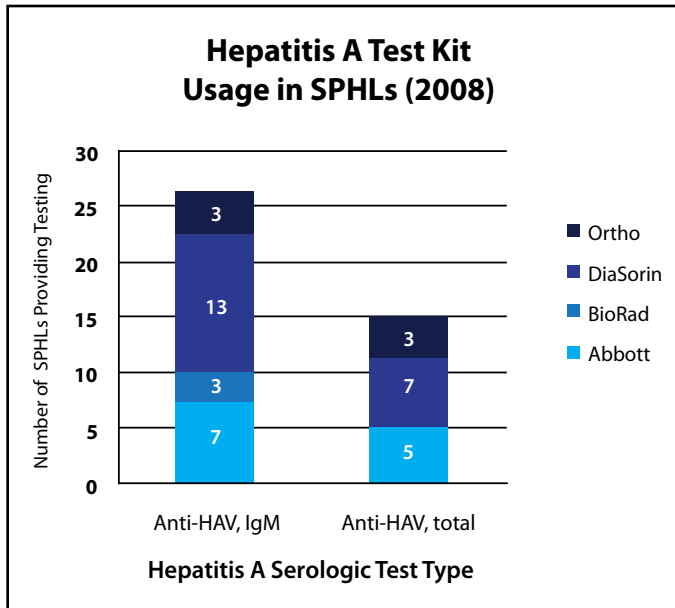


Figure 4. Hepatitis A diagnostic kit usage of state public health laboratories offering HAV testing in 2008 (n=27).

HAV TEST KITS

Among participating laboratories, Diasorin® kits are most frequently used for hepatitis A testing, followed by Abbott® diagnostic kits. Figure 4 provides details on the use of various hepatitis A test kits in SPHLs.

HEPATITIS B TESTING PRACTICES

Detection of HBV infection is the most common type of viral hepatitis testing offered among participating SPHLs, with

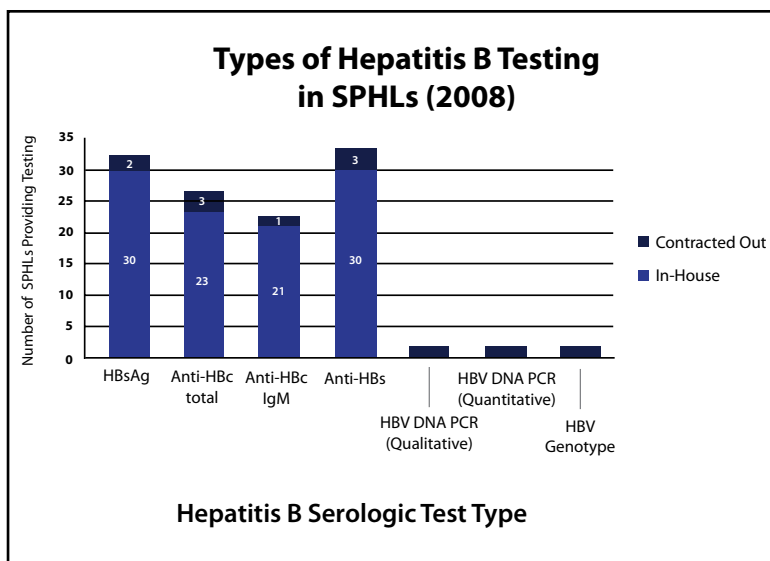


Figure 5. Types of hepatitis B testing offered by state public health laboratories in 2008 (n=34).

34 laboratories that provide testing. HBV is diagnosed using one or more serological assays that identify the presence of hepatitis B antigen or antibody in an individual. The stage of infection is determined by interpreting the results of these assays in combination. The assays used include those for detecting hepatitis B surface antigen (HBsAg), hepatitis B surface antibody (anti-HBs), total hepatitis B core antibody (anti-HBc) and IgM antibody to hepatitis B core antigen (anti-HBc, IgM).⁴ The anti-HBs test is also used to determine whether or not an individual has been successfully vaccinated against HBV.

Anti-HBs testing is the most commonly offered hepatitis B assay in public health laboratories with 33 respondents providing the test, followed by the HBsAg assay offered by 32 of the participating laboratories. While 30 public health laboratories offer the HBsAg assay in-house, only 22 (73%) routinely offer a confirmatory neutralization assay on all specimens that test positive for HBsAg.

Additional types of hepatitis B tests include both qualitative and quantitative hepatitis B DNA PCR testing and hepatitis B virus genotyping; however, while a few laboratories offer these tests through a reference lab, none of the responding laboratories reported performing these tests in-house. Figure 5 illustrates the various types of hepatitis B testing offered in US state public health laboratories.

HBV TESTING VOLUME

As seen with testing volumes reported for HAV, there were significant differences noted in the testing volumes among the respondents. During 2008, state public health laboratories that offer hepatitis B surface antigen (HBsAg) testing reported a minimum of 77 specimens, and a maximum of 66,728 specimens. The median was 14,780. For the total hepatitis B core antibody (anti-HBc) specimen volume, labs reported a range of 3 to 59,174 specimens, with a

median of 1,032. The hepatitis B surface antibody (anti-HBs) test included reported volumes of as few as 11 specimens, as many as 59,456 and a median value of 707. Of the four hepatitis B detection assays commonly used in SPHLs, the anti-HBc IgM assay was used least frequently, with the smallest volume of tests reported equal to 8, the largest number of tests equal to 984 and a median value of 108.

HBV TEST KITS

Public health laboratories reported using a wide variety of hepatitis B test kits. While no particular kit manufacturer was consistently more popular across all the HBV markers, public health laboratories report using DiaSorin® and Abbott® test kits most frequently. Figure 6 illustrates kit usage by hepatitis B analysis.

HEPATITIS C TESTING PRACTICES

HCV was the second most commonly tested hepatitis virus among survey respondents, with 31 (86%) public health laboratories offering hepatitis C testing. Serologic and molecular assays are currently available for the diagnosis of HCV infection. Serological testing assesses the presence of antibodies to the virus to indicate exposure to HCV.⁵ Anti-HCV testing includes initial screening with an immunoassay. CDC recommendations indicate that specimens yielding positive anti-HCV screening test results should supplement testing with the anti-HCV strip immunoblot assay (RIBA). A positive supplemental test result is interpreted as anti-HCV positive, while a negative RIBA result is interpreted as negative and indicates a false positive screening test result. All 31 of the respondents that offer hepatitis C testing provide anti-HCV screening, while 16 responding laboratories report providing the supplemental anti-HCV assay.

Molecular assays determine the presence (qualitative) or amount (quantitative) of HCV RNA in a particular serum specimen.⁵ Only

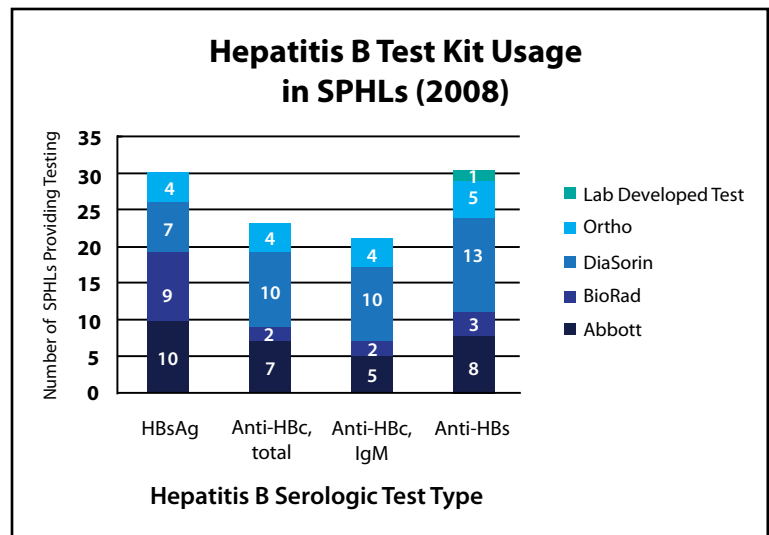


Figure 6. Hepatitis B diagnostic test kit usage of state public health laboratories offering HBV testing in 2008 (n=34).

nine public health laboratories reported providing either qualitative or quantitative molecular assay detection methods.

Genotyping may be done to distinguish which of the six different HCV genotypes is present in the test sample;⁵ only four public health laboratories report providing this type of testing.

USE OF SIGNAL-TO-CUT-OFF (S/CO) RATIOS IN HCV TESTING

In 2003, CDC's Division of Viral Hepatitis published *Guidelines for Laboratory Testing and Result Reporting of Antibody to Hepatitis C Virus*.² The guidelines provide recommendations for anti-HCV screening and supplemental testing, and include an option for reflex supplemental testing that is based on the s/co ratios of anti-HCV positive screening tests. This advice—to perform supplemental anti-HCV testing only on specimens with values below a given s/co ratio—provides laboratories with an opportunity to reduce the cost and burden of supplemental testing necessary to confirm infection.

Although most respondents reported using a s/co ratio of 3.8 as the threshold, there was variation in the way SPHLs use and report

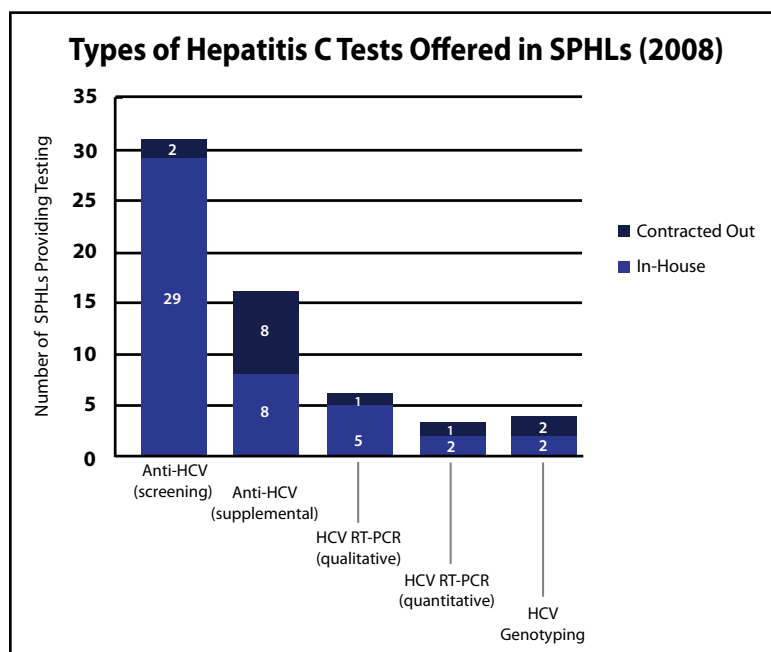


Figure 7. Types of hepatitis C testing offered in state public health laboratories in 2008 (n=31).

the s/co ratio. Thirteen laboratories reported that only specimens below the specified s/co ratio receive supplemental anti-HCV testing. Six laboratories reported that supplemental testing is performed only by physician request, regardless of the s/co value. Seven public health laboratories only perform and report anti-HCV screening results, referring all patients to care for supplemental testing; however, two of those laboratories include language recommending supplemental testing if the s/co ratio is below the predetermined threshold. Three laboratories reported performing supplemental anti-HCV testing on all positive anti-HCV screening specimens regardless of s/co ratio.

HCV TESTING VOLUME

As previously noted, viral hepatitis testing volume across states shows wide variation, and the data for HCV are no exception. For example, the lowest number of anti-HCV screening tests performed was 8 and the largest was 59,207, with a median of 1,345 tests. As expected, confirmatory anti-HCV

tests were reported in lower volumes than the screening anti-HCV, with a minimum of 4 tests, a maximum of 719 tests, and a median of 90 tests.

The number of quantitative HCV molecular assays performed by SPHLs in 2008 ranged from 141 to 183, with a median of 162. The largest volume of qualitative HCV molecular assays conducted in SPHLs was 896, with a median of 313. As previously reported, only four laboratories receive specimens for genotyping, and the number of specimens was very low, ranging from 40 to 80, with a median of 60.

HCV DIAGNOSTIC KIT USAGE

In most cases, the public health laboratories that responded to this survey are using standard FDA-approved diagnostic kits from a variety of manufacturers. For a detailed categorization of diagnostic kits used for HCV testing, please see Figure 8.

CONCLUSIONS

This survey provides insights into the current viral hepatitis testing practices in state public health laboratories in the United States. The fact that the majority of responding public health laboratories provide HAV, HBV and/or HCV testing suggests APHL should explore areas where member participation in hepatitis activities, including training and guidelines development, can be expanded.

According to CDC's website, both HDV and HEV are thought to be uncommon in the United States. This may point to the reason for the lack of HDV and HEV testing conducted in United States public health laboratories. The lack of a commercially available test for HEV diagnosis may also contribute to the lack of testing laboratories. Testing for HDV and HEV in the United States is mainly performed in commercial laboratories.

The majority of laboratories surveyed were familiar with, and followed the recommendations in, the 2003 *Guidelines for Laboratory Testing and Result reporting of Antibody to Hepatitis C Virus*.² APHL will look for ways to increase awareness about the hepatitis C recommendations among its membership in an attempt to obtain 100% compliance among public health laboratories.

Adequate funding for hepatitis testing remains a significant challenge for many public health laboratories. The wide availability of viral hepatitis testing in the private sector often leads to low testing volumes in public health laboratories, leading to diminished capacity and occasionally elimination of the testing service. Public health laboratories continue to play an important role in supporting public health detection and control measures for hepatitis A, B, and C viruses, providing testing in-house using a variety of test methods and assays and, in some cases, referring testing to another laboratory. In the future, APHL will continue to seek opportunities to work with federal, state, local and nongovernmental partners to address viral hepatitis testing challenges and improve viral hepatitis testing practices in the nation's public health laboratories.

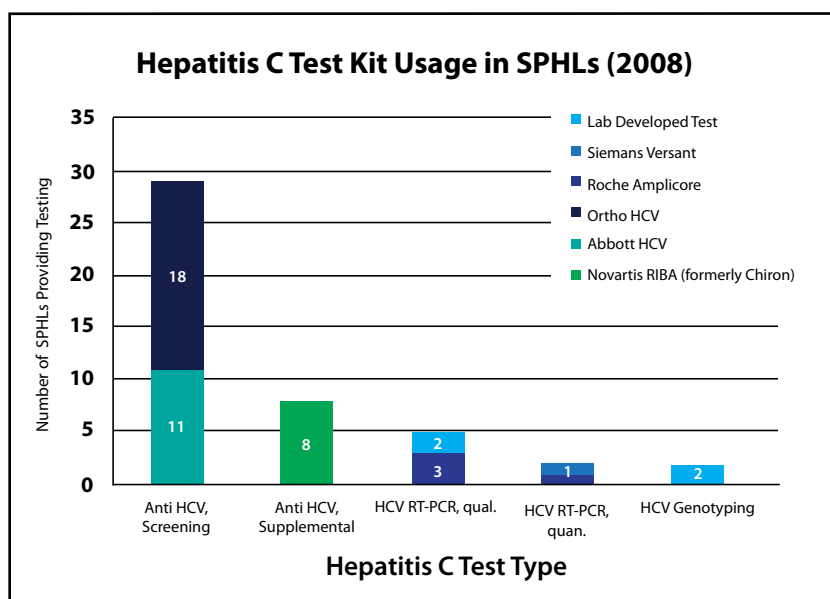


Figure 8. Hepatitis C diagnostic kit usage in public health laboratories offering HCV testing in 2008 (n=31).

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The Association of Public Health Laboratories is a national non-profit located in Silver Spring, MD, that is dedicated to working with members to strengthen governmental laboratories with a public health mandate. By promoting effective programs and public policy, APHL strives to provide public health laboratories with the resources and infrastructure needed to protect the health of US residents and to prevent and control disease globally.

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