CME CREDIT

ONE MINUTE CONSULT

BRIEF QUESTIONS AND ANSWERS ON CURRENT CLINICAL CONTROVERSIES

Q: In diagnosing hepatitis C, which patient needs which test?

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A: IN DIAGNOSING chronic hepatitis C virus (HCV) infection, one uses antibody tests in conjunction with tests for HCV RNA.[1–3] The use and interpretation of these tests must be guided by the patient's risk for HCV infection.

ANTIBODY TESTS

Enzyme immunosorbent assay

The enzyme immunosorbent assay (EIA) is currently considered the first-line screening test for chronic hepatitis C. Most widely used is the second-generation EIA, which has a sensitivity of 92% to 95%.[2–7] However, most blood banks have recently adopted a third-generation EIA, which is probably more sensitive and specific.

Because the EIA detects antibodies to HCV and not HCV itself, giving rise to possible false-positive tests, one has to consider the patient's baseline risk for HCV infection in interpreting the EIA result.

In most situations,[1,3] a negative EIA is most likely truly negative (see below). However, a positive EIA may well be falsely positive and should be followed up (FIGURE 1).

In persons with a risk for HCV (eg, history of parenteral drug abuse, transfusion prior to 1992) a positive EIA establishes chronic hepatitis C and a test for HCV RNA will determine the level of viremia.[3–7]

However, in this setting, a negative EIA does not necessarily rule out HCV infection. EIA testing can give false-negative results in two situations:

- Recent exposure to HCV (eg, through transfusion, accidental needle-stick, recent intravenous drug use, etc.). In some of these patients, anti-HCV may take up to 3 to 6 months to become detectable.
- Anti-HCV may never develop in an immunosuppressed person.

In both situations, testing for HCV RNA by polymerase chain reaction (PCR) assay is helpful. If HCV RNA is negative, HCV infection is unlikely. An alternative approach to an immunocompetent patient with recent exposure is to repeat the EIA test in 6 months.

Radioimmunoblot assay (RIBA)

In interpreting the result of a radioimmunoblot assay (RIBA), two or more positive bands is considered positive and only one positive band is considered indeterminate. An indeterminate RIBA can be further evaluated with an HCV RNA test.

The RIBA can be used to follow up a positive EIA result in a person at low risk (eg, blood donors, persons with no known risk factors). However, given the clinical relevance and availability of HCV RNA assays, we would more often obtain an RNA test in this situation.

One situation in which a RIBA is helpful is in a person with a positive EIA but a negative HCV RNA test. In this situation, if the RIBA is definitely positive, the person most likely had an infection but has cleared the virus. If the RIBA is negative, the EIA most likely was falsely positive.

The EIA is the first-line test for HCV screening

TESTS FOR HCV RNA

There are two types of HCV RNA tests: qualitative and quantitative.

Qualitative tests, performed by the PCR method, determine only if the virus is present. These assays are very sensitive but carry significant variability between laboratories.

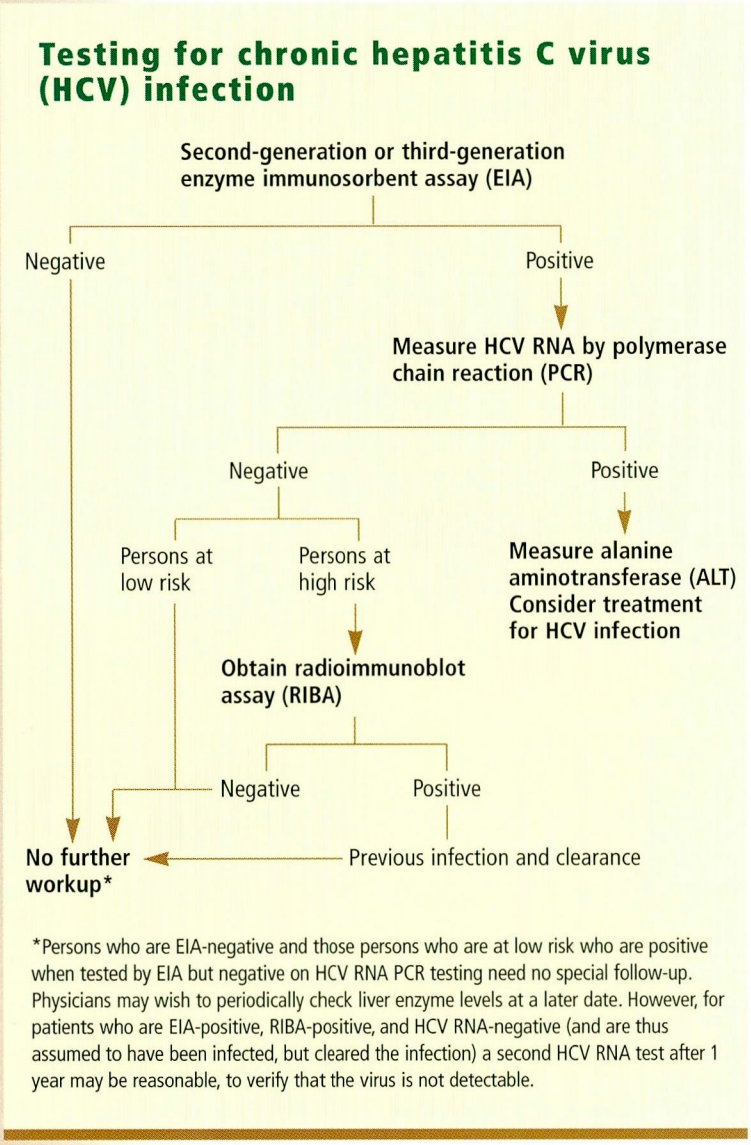

FIGURE 1

Qualitative HCV RNA assays are used less frequently than are quantitative tests.

Quantitative tests can detect the amount of viral RNA—as few as 100 copies of the virus per mL.[6]

Some quantitative RNA tests use the PCR method, while others use the branched DNA method. The most widely used quantitative PCR assays are MONITOR (Roche), which has a threshold for detection of 1,000 copies per mL, and SuperQuant (National Genetics Institute), which has a threshold of detection of 100 copies per mL. The most widely used branched DNA assay is Quantiplex (Chiron), which is well standardized but has a higher threshold of detection (200,000 copies per mL).

Caveats

Because the results of these tests are not interchangeable, it is extremely important to use the same test in following a patient over time.

Of note: The Food and Drug Admini-stration has not yet approved any of the HCV RNA assays, although they are widely available and used clinically. In addition, these techniques are not subject to independent quality controls and are not fully standardized.

During therapy it is important to use a sensitive PCR RNA method that can detect a low level of virus. Another option would be to obtain a branched DNA assay first. If this is negative, a qualitative PCR test can be done to confirm it.

Using HCV RNA tests to monitor therapy

As noted above, RNA tests are used to follow up positive or questionable results of antibody tests. These tests are also useful in monitoring the response to treatment. For example, a negative HCV RNA test after 3 months of interferon monotherapy is the best indicator of response and suggests that therapy should be continued for a full 12-month course. In addition, if the HCV RNA test is negative 6 to 12 months after discontinuing therapy, the virus is most likely eradicated and the patient has achieved a sustained virologic response.

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CME ANSWERS

Answers to the credit test on page 575 of this issue

1 **C** 2 **C** 3 **C** 4 **B** 5 **B** 6 **B** 7 **E** 8 **C** 9 **B**