A guide to diagnosing hepatitis C

Hepatitis C antibody test

Negative antibody test
Indicates a person has never been infected with hepatitis C
No further testing required
Except in the case of recent risk (within 6 months as it takes 6–24 weeks for a person to make antibodies) or those within weakened immune systems

Positive antibody test
Antibodies are present indicating a person has been infected with hepatitis C. 15-30% of HCV-infected individuals spontaneously clear the virus following infection but retain HCV antibodies and so further testing is required to confirm chronic hepatitis C.

Viral load – HCV RNA or core antigen – test

Undetectable
The person does not have chronic hepatitis C (either have never had it or once had it but have now been cured)

Detectable
The person has chronic HCV

Test to determine treatment type

Liver disease staging
Used to determine type and length of HCV treatment (those with cirrhosis can be more difficult to cure and so require different or longer treatment)

Genotyping
WHO 2018 guidelines recommend eliminating genotyping when pangenotypic DAAs are used
There are 6 known genotypes of hepatitis C but with the advent of DAAs that treat all genotypes (pangenotypic) this step is no longer necessary

Invasive
Liver biopsy: takes blood or tissue sample with a needle

Non invasive
Using Fibroscan, FIB-4 or APRI tests
Confirmatory testing

The largest drop off in the HCV continuum of care occurs between antibody screening and confirmatory HCV RNA testing (or core antigen testing) and then again between diagnosis and attendance at the first appointment.

Innovations

Reflex testing

To improve the testing process, and so minimise the number of people lost to follow up, reflex testing could be employed. Reflex testing occurs when an RNA test is done immediately after a positive antibody test so that there is no patient recall. Reflex testing can be done using venous blood and could also be done using dried blood spot sampling.

Dried Blood Spot Sampling

This is an alternative to collecting whole blood specimens which has the potential to expand access to screening and diagnosis. It enables the use of finger stick whole blood while the stability of the specimen means that it can be transported without the need for an intact cold chain – it can be posted by regular mail if needed. Once they have reached laboratories they can also be stored for long periods of time. It also supports reflex testing for hepatitis C as multiple spots can be taken and then tested. It also enables testing to be done by peer workers.

The testing itself is done by traditional laboratory based enzyme immunoassays (EIAs) and so a central laboratory is required. This means that there is a longer wait for results.

Manufacturers have not yet sought stringent regularity approval to use dried blood spot sampling with their existing assays and so the use of DBS is currently limited to research.
One-step test

A long term solution to improve the continuum of care would be a one-step test. Currently HCV RNA testing is not used to determine exposure to hepatitis C, primarily because of cost, as unless there is exceptionally high prevalence it is not cost effective to use HCV RNA tests as part of a screening campaign. A hepatitis C core antigen test is a good alternative here as it is less costly then HCV RNA testing, studies in the UK and Egypt have found:

<table>
<thead>
<tr>
<th>Country</th>
<th>Cost of HCV RNA test (USD)</th>
<th>Cost of HCV core antigen test (USD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>United Kingdom</td>
<td>$108</td>
<td>$23.40</td>
</tr>
<tr>
<td>Egypt</td>
<td>$141</td>
<td>$19.80</td>
</tr>
</tbody>
</table>

Costs include equipment and personnel expenses

Currently HCV core antigen tests require centralised laboratory equipment and to date only one highly sensitive core antigen test exists which is the Abbott ARCHITECT HCV antigen assay, which requires a laboratory based analyser which is not widely available in low and middle income countries.

A highly sensitive point-of-care HCV core antigen test that could be used in decentralised settings has the potential to be a one-step test solution and at least one of these tests is currently in development.

HCV self-testing

There is currently no HCV self-test on the market but the experience gained from HIV self-testing could be applied to hepatitis C and the 2017 WHO guidelines note that self-testing represents a potentially important approach to expand testing in the future. A hepatitis C self-test would test for antibodies only and a follow-up confirmatory test, either HCV RNA or core-antigen, would still be required. Currently WHO and the Foundation for Innovative New Diagnostics (FIND) are working with partners to assess the feasibility and acceptability of using HCV self-testing in different populations. Importantly, this will include in-depth interviews with patients to ensure the patient experience is fully understood.