Training workshop on screening, diagnosis and treatment of hepatitis B and C

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Session 13

Testing and serological markers for hepatitis C virus infection

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Learning objectives

At the end of this session, participants would be able to understand the following:

- Various serological markers of HCV infection
- The significance and interpretation of these tests and their role in patient care
- Whom to test for HCV infection and how.

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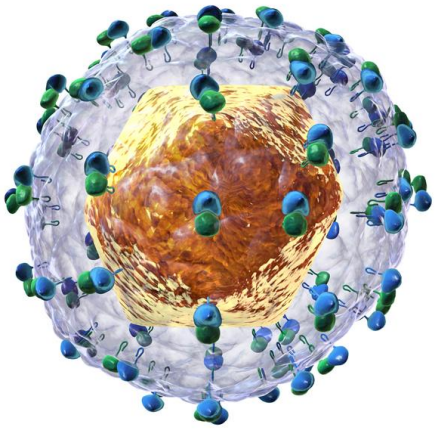
In this session, we will learn the various serological markers used in the diagnosis and management of HCV. We will also learn about how to interpret these reports and draw a conclusion from them.

Hepatitis C virus



https://commons.wikimedia.org/wiki/File:HCV.png

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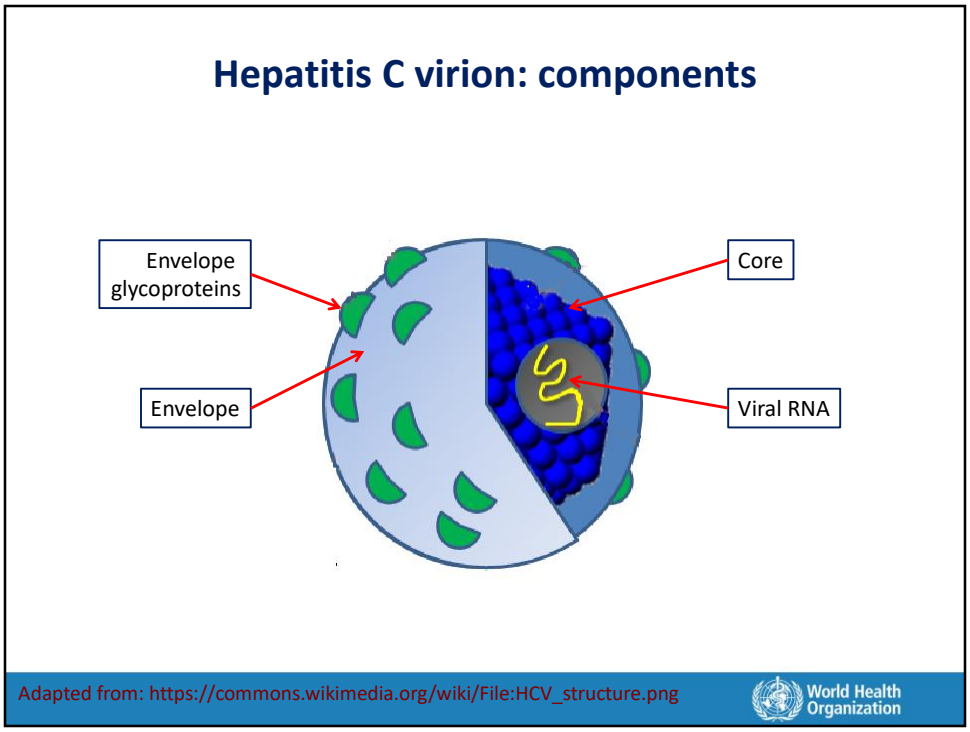
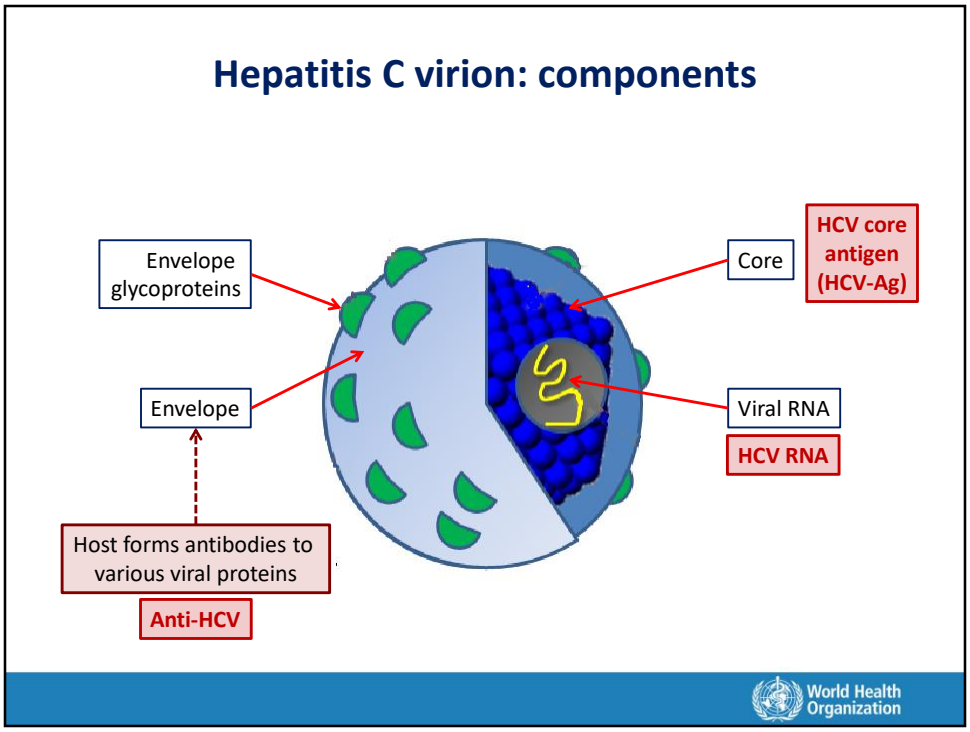
This is a picture of HCV.



This is the schematic diagram of the hepatitis C virus. The virus has a “envelope” on the outermost aspect. This envelope contain surface glycoproteins, which induce host immunity for the development of antibodies. Inside the envelope, the virus has a protein core made up of core proteins. This protein core encloses the virus genome RNA.



The envelope protein induces host immunity for antibody formation (anti-HCV antibody). In the diagnosis and management of HCV, anti-HCV antibody, HCV core antigen and HCV RNA are used to determine the type of intervention

HCV markers

Test	Clinical interpretation
Anti-HCV (anti-hepatitis C virus antibody)	• Indicates exposure to HCV • Does not differentiate between active or resolved infection • Remains positive even after successful treatment and clearance of HCV infection • Cheap, easy, scalable • A very good screening test for HCV infection
HCV RNA (quantitative or qualitative) (nucleic acid test)	• Qualitative tests: whether HCV RNA is detectable (positive) or not • Quantitative tests: amount of HCV RNA per unit of blood • Positive test indicates the presence of active virus replication • Becomes negative after successful HCV treatment • Costly, time-consuming and require expertise • Differentiates between active and resolved infection • Used for monitoring treatment and its efficacy

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Anti-HCV antibody test indicates prior exposure to the virus but it does not differentiate between active or resolved HCV infection. Anti-HCV antibody does not have a protective effect. Anti-HCV antibody, after successful HCV treatment, persists for life but does not provide immunity against reinfection.
It is the detectable HCV RNA, regardless of its quantitative value, which indicates active HCV infection. All those with detectable HCV RNA should be treated.

HCV markers

Test	Clinical interpretation
HCV genotype	• HCV has several strains that vary from each other genetically • Classified based on genomic sequences into genotypes 1 to 6 • Virus genotypes vary in sensitivity to some drugs • Costly to test, needs specialized equipment and personnel • Can help in deciding appropriate treatment in some situations • No use if treatment does not depend on genotype
HCVcAg (hepatitis C core antigen)	• A viral protein produced only when the virus is replicating • Positive in unresolved chronic infection • Becomes negative after successful HCV treatment • Cheaper and easier than HCV RNA, should be scalable • Reasonable and cheaper alternative of the HCV RNA test • However, may be negative in those with very low HCV RNA (lower sensitivity)

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Hepatitis C virus has 7 major genotypes. The therapeutic response of these genotypes to different drugs varies. Earlier, it was common practice to test all those with detectable HCV RNA for the HCV genotype to select the appropriate treatment regimen. HCV genotype is a costly investigation that has limited availability; further, it needs time, facilities and expertise.
In the present era, we have drugs that are equally effective against all the genotypes. These drugs are called pangenotypic drugs and they obviate the need for genotyping.

HCV core antigen (HCVcAg) is produced on replication of HCV. This antigen is released in the circulation and can be detected with simple tests. Recently, HCVcAg has emerged as an affordable and acceptable alternative to HCV RNA. HCVcAg testing, as compared to HCV RNA, has several advantages, such as lower cost, easy to test, less labour-intensive, and obviates the need for immediate testing after sample collection. HCVcAg can even be detected in dried blood spots.
HCV antigen test gives the same information as HCV RNA. It has the potential to replace the RNA test – currently not widely accepted, but is likely to do so in future.

Interpretation of HCV serological test results

Anti-HCV	HCV RNA	HCV Ag	Interpretation
–	–	–	

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Let us recapitulate our understanding of HCV infection and interpretation of its diagnostic tests.

What is the condition shown here?

Interpretation of HCV serological test results

Anti-HCV	HCV RNA	HCV Ag	Interpretation
–	–	–	Never infected

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Interpretation of HCV serological test results

Anti-HCV	HCV RNA	HCV Ag	Interpretation
–	–	–	Never infected
–/+	+	+	

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What about this scenario?

Interpretation of HCV serological test results

Anti-HCV	HCV RNA	HCV Ag	Interpretation
–	–	–	Never infected
–/+	+	+	Recent infection

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Interpretation of HCV serological test results

Anti-HCV	HCV RNA	HCV Ag	Interpretation
–	–	–	Never infected
–/+	+	+	Recent infection
+	+	+	

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Interpretation of HCV serological test results

Anti-HCV	HCV RNA	HCV Ag	Interpretation
–	–	–	Never infected
–/+	+	+	Recent infection
+	+	+	Persistent (chronic) infection

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Interpretation of HCV serological test results

Anti-HCV	HCV RNA	HCV Ag	Interpretation
–	–	–	Never infected
–/+	+	+	Recent infection
+	+	+	Persistent (chronic) infection
+	–	–	

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Interpretation of HCV serological test results

Anti-HCV	HCV RNA	HCV Ag	Interpretation
–	–	–	Never infected
–/+	+	+	Recent infection
+	+	+	Persistent (chronic) infection
+	–	–	Previously infected (infection resolved or cured)

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Approaches to detect HCV infection

- Mass screening
  (unselected testing of the general population)

- Targeted screening
  - Birth cohort testing
  - Specific high-risk groups
  - Blood donor screening (primarily done for blood safety)

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Approach to testing for HCV infection

Testing approach	Recommendations
General population testing	In a setting with anti-HCV seroprevalence ≥2% or ≥5%, all adults should have access to HCV serological testing and linkage to care
Birth cohort testing	Used if "specific identified birth cohorts" (e.g. older persons) are at a higher risk of HCV infection
Focused testing in most affected populations	In all settings, testing for anti-HCV antibody should be offered to: • adults and adolescents from populations most affected by HCV infection • those from high-prevalence areas: migrants, high/intermediate prevalence, specific tribes • those with a history of exposure • people with high-risk behaviours • adults and children with a clinical suspicion of chronic viral hepatitis.

WHO. Guidelines on hepatitis B and C testing, 2017. P37.

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In a setting of a public health programme, we can adopt any one of the following approaches. The approach selected is determined by several factors such as disease prevalence, cost of treatment in a given country, risk factors for HCV transmission in a given setting, etc.

First, we can consider screening all the population if the HCV prevalence in community is more than either 2% or 5%.

Second, we may restrict screening to high-risk groups only, which will increase the yield of the screening activity.

Third, we may focus on screening of people born in a certain specified period of time in the past; this approach is usually adopted when we know that most of the people were exposed to HCV during that specific period, such as people during World War II were exposed to HCV because of blood transfusion or promiscuity, etc.

High risk-groups for HCV infection

The following groups of people are at high risk for acquiring HCV infection:

- People living with HIV
- Those who are transfusion-dependent (haemophilia, thalassaemia)
- People who inject drugs
- Persons on maintenance haemodialysis
- Persons with high-risk sexual practices (MSM, sex workers)

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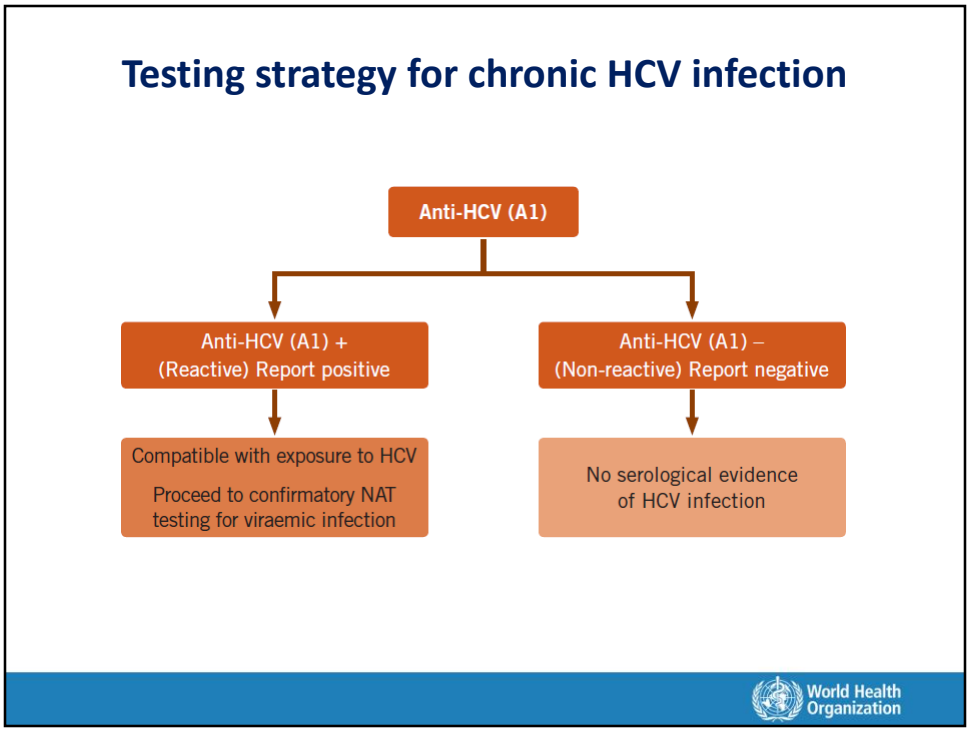
These are the universally accepted groups of people who are at much higher risk for acquiring HCV infection than the general population.



While screening a person for HCV infection, we need to use only a single anti-HCV antibody test kit. The kit used for screening should be WHO-prequalified to increase the sensitivity and specificity of the screening programme.

Summary

- A positive anti-HCV test indicates exposure to HCV, which is either active or has resolved.
- Anti-HCV remains positive following successful treatment.
- The anti-HCV antibody test can be used as a screening test for HCV infection, and has been employed in several different strategies.
- Tests for HCV RNA or HCVcAg serve as confirmatory tests. They indicate active infection and the need for treatment. These are also useful to monitor treatment and confirm cure.

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