

# Sensible screening

**Dr Ali H Hajeer** head of the immunology laboratory at the King Fahd National Guard Hospital Saudi Arabia, looks at how to deal with false positive results when carrying out laboratory testing of HCV antibody status

**YOU ARE AN** employee health practitioner at a local hospital. Test results of a new employee (expatriate, family doctor) are referred to you showing the following: HCV antibody screening positive, Recombinant Immunoblot Assay (RIBA) test indeterminate and HCV PCR below detectable limits. What would you do? Is the employee positive for HCV, which means send him home, or do you accept them but repeat the test at a later stage. The problem is, they also did the test back home and the results were negative. Who is right?

Recent advances in HCV diagnosis have lead to the development of new assays using recombinant proteins. These assays are highly sensitive in detecting HCV antibodies. However, they can have low specificity, depending on the prevalence rate of HCV antibodies in the population. More recent anti-HCV screening tests results are reported as signal/cutoff ratio (S/Co). A reading of > 1.0 is usually considered positive. Any positive is usually confirmed by RIBA or PCR.

HCV is an RNA virus that can infect humans mainly through blood. The transmission route includes shared needles for drugs, tattooing, body piercing and acupuncture. Sharing personal items such as razors and toothbrushes also carry a risk of HCV transmission. Sexual and perinatal transmission risks are very small. Healthcare workers are also at risk of infection from needlestick injuries.

HCV infection usually passes unnoticed. The majority of cases will develop chronic HCV infection, which is usually intermittent and goes into phases. This manifests itself in the liver enzymes profile and HCV RNA levels. It is interesting to note that there is no protective immunity to HCV.

Recently the Centers for Disease Control Protection (CDC) published new guidelines for laboratory testing of HCV antibody status. The need for these guidelines stemmed from the fact that a cutoff of 1.0 S/Co is not highly specific and can lead to false positive results. We have modified these guidelines

based on results from the King Abdulaziz Medical City, National Guard Health Affairs, Riyadh. We have evaluated these guidelines and found that a S/Co ratio of 16 is highly specific and sensitive in detecting true positive cases (Using Abbott HCV v3.0 on the AxSYM)

We found that using this cutoff, the true positive HCV blood donors are on average 1-2 per 1000. Suggesting that the rate of HCV in this region is much less than what is being used based on screening assays.

So what to do? It is suggested that each centre defines its own cutoff S/Co based on their test on blood bank donors. Defining this cutoff can cut costs, as those with S/Co more than the established cutoff will most likely be HCV positive and do not need a confirmatory testing. They will therefore have to be referred to a specialist to confirm the stage of their infection and treatment.

To go back to our earlier example, the employee presenting with screening test result positive, RIBA indeterminate, PCR negative; this suggests that HCV antibody status is indeterminate, most probably false positive, therefore no HCV infection.

However this is an issue that comes up again and again. Can we depend on one assay to diagnose HCV? and if so which one? A screening test is a very useful marker in true HCV infected people, but can be misleading in cases of false positive results. RIBA cannot be used as a screening test as it is expen-

sive and the results can be misleading when they come up as indeterminate. PCR is very valuable test, however it is expensive and can give false negative results, especially in dialysis patients, and due to the nature of the disease, when the virus is inactive, viremia can be at its lowest level.

- To summarise:
- If results show – low positive (low S/Co) screening. Carry out both RIBA and PCR testing.
  - If they show strong positive, there is no need for a confirmatory and an HCV positive code can be given. The patient should then be referred to a specialist for further testing and treatment.
  - HCV screening results should not be reported as positive/negative but as S/Co, with a locally established cutoff.

**Selected references**

- 1 Alter MJ, Kuhnert WL, Finelli L, Guidelines for laboratory testing and result reporting of antibody to hepatitis C virus. Centers for Disease Control and Prevention. MMWR Recomm.Rep. 2003;52:1-13, 15.
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INTERPRETING LABORATORY RESULTS OF HCV INFECTION				
Screening Test	RIBA	HCV RNA	Anti-HCV Status	HCV Infection Status
Negative	NA	NA	Negative	Not infected unless recent infection is suspected
Positive	Negative	NA	Negative	Not infected unless recent infection is suspected
Positive (high S/Co)	ND	ND	Positive	Past or Present infection
Positive	Positive	ND	Positive	Past or present infection
Positive	ND	Negative	Unknown	Unknown*
Positive	Positive	Negative	Positive	Past or present infection**
Positive	Positive/ND	Positive	Positive	Active infection
Positive	Indeterminate	Negative	Indeterminate	Probably false positive screening test, no HCV infection

NA Not Applicable ND Not Done \* Single negative HCV result cannot determine infection status \*\* HCV RNA can be intermittent, repeat HCV RNA