Chronic hepatitis C: new diagnostic tools and therapeutic strategies
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Citation for published version (APA):

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INCORRECT DIAGNOSIS OF HEPATITIS C WITH RIBA-3

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Vox Sang 1995; 69: 358
In May 1990 anti-HCV screening was introduced in our blood bank and until January 1995, 442,789 donations were tested. Fifty-four blood donors were found to be confirmed anti-HCV positive (RIBA 2/3) of which 44 (81%) were HCV-RNA positive as shown by a validated cDNA-PCR [1]. Only one of the confirmed anti-HCV-positive donors had an acute HCV infection [2]. All others were chronically infected for a mean period of at least 3 years, as was shown in a look-back study [3]. In a recent study on 17 RIBA-3-positive donors we observed risk factors less frequently in donors with two-band reactivities than in donors with three- or four-band reactivities (18% versus 83%, \( p=0.03 \))[4].

In August and September 1994, 4 repeat donors were found anti-HCV ELISA (Ortho, 3rd generation) reactive and RIBA-3 (Chiron) positive. The 4 donors were recalled to the blood bank. Standardized interviews (including questions about risk factors for HCV infection) and physical examination revealed no signs of acute or chronic hepatitis. All 4 donors had normal liver transaminase values. Three donors had no risk factors at all, one donor (No.3) was tattooed 40 years ago. Since from every blood donation a serum sample is stored, samples of an earlier donation (3-6 months before) and of the index donation were tested in PCR (Roche Amplicor). Sera were collected 1 month and 3-4 months (3 of 4 donors) after the index donation and subsequently tested in PCR. Furthermore, all samples taken at the various points in time were tested in RIBA-3 and in another anti-HCV confirmation assay (Inno-LIA HCV Ab III, Innogenetics). HCV-RNA was negative in all donors at all points of time. Results of all anti-HCV assays are shown in table 1. Donor 1 and 2 tested positive in RIBA-3 at 1 point of time, donors 3 and 4 at 2 points of time. In Inno-LIA, donor 1,2 and 4 tested negative at all points of time and donor 3 tested positive at 2 points of time (NS3 reactivity).

Considering that acute HCV infection in our donor population is rare, that 3 of 4 cases had no risk factors and that none of the 4 donors were HCV-RNA positive, we think that the RIBA-3-positive results might be false-positives in these cases. This opinion is supported by the fact that the Inno-LIA assay was negative in donor 1, 2 and 4. In donor 3 we cannot exclude a flare-up of antibodies after an earlier HCV infection. Clinicians and laboratories should be aware that RIBA-3 might give false-positive test results. Especially two-band positive RIBA-3 results must be interpreted with caution.

**ACKNOWLEDGEMENTS:**

We thank Dr. L. Stuyver (Innogenetics) for kindly performing the Inno-LIA assay.

**REFERENCES:**

Table 1.
Results of anti-HCV ELISA, RIBA-3 and Inno-LIA in 4 repeat blood donors.

<table>
<thead>
<tr>
<th>Donor No.</th>
<th>Time period (months)</th>
<th>EIA 3.0</th>
<th>RIBA-3&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Inno-LIA&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>NS5</td>
<td>C22</td>
<td>C33</td>
</tr>
<tr>
<td>1</td>
<td>3-6 before</td>
<td>-</td>
<td>-</td>
<td>2+</td>
</tr>
<tr>
<td></td>
<td>0 index</td>
<td>+</td>
<td>1+</td>
<td>2+</td>
</tr>
<tr>
<td></td>
<td>1 after</td>
<td>-</td>
<td>-</td>
<td>2+</td>
</tr>
<tr>
<td></td>
<td>3-4 after</td>
<td>-</td>
<td>-</td>
<td>1+</td>
</tr>
<tr>
<td>2</td>
<td>3-6 before</td>
<td>-</td>
<td>1+</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>0 index</td>
<td>+</td>
<td>2+</td>
<td>1+</td>
</tr>
<tr>
<td></td>
<td>1 after</td>
<td>+</td>
<td>2+</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>2 after</td>
<td>+</td>
<td>2+</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>3-4 after</td>
<td>-</td>
<td>1+</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>3-6 before</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<tr>
<td></td>
<td>0 index</td>
<td>+</td>
<td>-</td>
<td>4+</td>
</tr>
<tr>
<td></td>
<td>1 after</td>
<td>+</td>
<td>-</td>
<td>4+</td>
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<td>3-4 after</td>
<td>+</td>
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<td>3+</td>
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<tr>
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<td>0 index</td>
<td>+</td>
<td>2+</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>1 after</td>
<td>+</td>
<td>2+</td>
<td>-</td>
</tr>
</tbody>
</table>

<sup>a</sup> Positive RIBA-3: at least 2 antigens reacting 1+ or more.

<sup>b</sup> Positive Inno-LIA: at least 1 antigen reacting 2+ or more, or 2 antigens reacting 1+ or more.
In May 1990 acute HCV screening was introduced in our blood bank and until January 1992, 185 donors with a history of intravenous drug use 
were identified as HCV-RNA positive by the second generation "first 
line" enzyme immunoassay (EIA) method (DAKO EIA, DAKO, Glostrup, 
Denmark) and/or a commercial nucleic acid hybridization test (1.2.3 
HCV, Biotrin, Ireland). The sera of these donors were also tested 
by PCR (Roche Amplicor) and/or shell vial culture. All donors 
were questioned about risk factors for HCV infection and none 
reported a history of intravenous drug use. In addition, all were 
seronegative for HBsAg and HCV Ab. In January 1992, the 
second generation "second line" enzyme immunoassay (EIA) 
method (Ortho Hepanet, Ortho Diagnostic Systems, Raritan, 
NJ, USA) was introduced. A total of 46 sera from every blood 
administration were also tested by the second generation 
second line EIA method, 44 sera were collected between July 24 and 
October 31, 1991 and 2 sera were obtained from blood samples 
of an earlier donation (1-6 months before). The sera were 
then tested by PCR (Roche Amplicor) and/or shell vial culture. 
None of the sera was found to be positive for HCV-RNA. The 
results of all serum HCV testing are shown in Table 1. Consider 
the 1 and 2 negative results in EIA and the 1, 2, 3, and 4 
method positive results in EIA and the 1, 2, 3, and 4 
multiplex positive results in PCR. Clinicians and laboratories 
should be aware that RIBA-3 might give false-positive test 
results. Especially as a second positive RIBA-3 result must be interpreted with caution.

ACKNOWLEDGEMENTS

We thank Dr. L. Stenner-Hansen for kindly performing the in-vitro EIA assay.

REFERENCES

second generation EIA with direct virus isolation. Vox Sanguinis 
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