Virological Tests for Improved Access to Cure

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Worldwide HCV RNA Prevalence

The Global Burden of HCV Infection

- HCV is responsible for >350,000 deaths a year worldwide (195 000 HCC)
- Up to 50% of HCV-infected patients are unaware of their infection
- Less than 10% of the HCV-infected population has received treatment in the US

Global control of HCV infection is now a realistic objective

Chronic HCV infection is curable by DAAs

large-scale screening of HCV infection is now needed to identify infected patients and provide them with efficacious therapies.
Alternative Tests

• Point-of-care tests (POCT)
  – Rapid diagnostic tests
  – Molecular tests

• Dried blood spot (DBS)
Advantages and Disadvantages of DBS

• **Advantages**
  – Low volume required (50-70 µL)
  – Good stability of the biological matrix
  – Easy to collect and mail at room temperature
  – Serological, molecular and pharmacological analysis can be performed

• **Disadvantages**
  – Lower analytical sensitivity than classical biological matrices (serum or plasma)
  – No standardized procedures
  – Storage at -20°C required for long-term conservation
Detection of anti-HCV Ab in Whole Blood from DBS by 3rd-generation EIA (Vitros)

Samples from DBS can be confidently used for anti-HCV antibody detection by means of standardized, commercially available methods.

Sensitivity = 99.1%
Specificity = 98.2%

Soulier et al., J Infect Dis 2015
HCV RNA Quantification by the RealTime HCV Assay in Whole Blood from DBS

Absolute amount of HCV RNA should not be considered when quantification is performed on DBS. The HCV RNA levels are usually high in patients who do not eradicate infection. The DBS result, if negative, can be trusted as indicative of a sustained virological response.

Soulier et al., J Infect Dis 2015
HCV Core Ag Quantification

• Attractive alternative to molecular methods

• Advantages over molecular methods
  – Cheap (50% to 70% less expensive)
  – Stability of the marker at RT for 96 hours
  – Easy to perform through automated EIA

• New HCV treatment monitoring tool, well suited to IFN-free regimens
Relationship between HCV Core Ag and HCV RNA Levels

HCV Core Ag Quantification by the Architect HCV Assay in Whole Blood from DBS

When whole-blood specimens from DBS are used, HCV RNA testing should be preferred to HCV core Ag testing

Soulier et al., J Infect Dis 2015
POCT: Benefits to Patients

- Reduced waiting times
- Immediate discussion of results
- Fewer or no follow-up visits
- Improved healthcare accessibility
Rapid Diagnostic Test (RDTs)

- Can be used at the site of patient care
  - Physician’ office
  - Emergency room, ICU
  - Outpatient clinics, rural areas

- Can use original specimen matrices in addition to serum or plasma
  - Oral fluid
  - Fingerstick whole blood
Interest of Oral fluid as an Alternative Matrix

- Simple, safe, painless, cheap to collect
- Contains lower amount of immunoglobulins (and viral markers) than whole blood

<table>
<thead>
<tr>
<th>Specimen</th>
<th>IgG (mg/L)</th>
<th>IgM (mg/L)</th>
<th>IgA (mg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasma</td>
<td>14730</td>
<td>1280</td>
<td>2860</td>
</tr>
<tr>
<td>Whole saliva</td>
<td>14.4</td>
<td>2.1</td>
<td>19.4</td>
</tr>
<tr>
<td>Parotid saliva</td>
<td>0.36</td>
<td>0.43</td>
<td>39.5</td>
</tr>
<tr>
<td>Crevicular fluid</td>
<td>3500</td>
<td>250</td>
<td>1110</td>
</tr>
</tbody>
</table>

Performance of a RDT to detect anti-HCV Ab in Oral Fluid

Sensitivity = 97.1% (94.7%-98.6%)
Specificity = 97.1% (93.3%-99.0%)

ROC curve analysis

Chevaliez et al., Clin Microbiol Infect 2016 Jan S1198-743X(16)00025-2
Performance of RDTs: Meta-Analysis

- More than 13,000 individuals included in 18 studies between 1994 and 2011
  - Stratification according to matrix specimens
    - Whole blood (venous and capillary): 4,259 specimens
    - Saliva: 3,994 specimens

<table>
<thead>
<tr>
<th>Specimen</th>
<th>Specificity</th>
<th>Sensitivity</th>
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</thead>
<tbody>
<tr>
<td>Whole blood</td>
<td>99.5%</td>
<td>98.9%</td>
</tr>
<tr>
<td>Saliva</td>
<td>98.2%</td>
<td>97.1%</td>
</tr>
</tbody>
</table>

## Available RDTs for anti-HCV Detection (CE-marked)

<table>
<thead>
<tr>
<th>Manufacturer</th>
<th>Oraquick® HCV</th>
<th>Toyo® HCV</th>
<th>Labmen® HCV</th>
<th>Multisure HCV</th>
<th>Assure® HCV</th>
<th>First Response HCV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Specimen type</td>
<td>oral fluid, whole blood, serum, plasma</td>
<td>whole blood, serum, plasma</td>
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</tr>
<tr>
<td>Volume required (µL)</td>
<td>40 (oral fluid)</td>
<td>30</td>
<td>10</td>
<td>25</td>
<td>50</td>
<td>35</td>
</tr>
<tr>
<td>Time to read (min)</td>
<td>20</td>
<td>15</td>
<td>15</td>
<td>15</td>
<td>15</td>
<td>20</td>
</tr>
</tbody>
</table>

- **Orasure**
- **Turklab**
- **Turklab**
- **MP Diagnostics**
- **MP Diagnostics**
- **Premier Medical Corporation Ltd**
Principle of an RDT

Example of OraQuick®
Performance of RDTs for anti-HCV Ab Detection from Fingerstick Whole Blood

- 318 patients with chronic HCV infection, 25 patients with resolved HCV infection and 170 HCV-seronegative subjects (N=513)

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<tr>
<th>Tests</th>
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<th>Sensitivity</th>
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</thead>
<tbody>
<tr>
<td>OraQuick® HCV Rapid Ab Test</td>
<td>100%</td>
<td>99.4%</td>
</tr>
<tr>
<td>TOYO® anti-HCV test</td>
<td>98.8%</td>
<td>95.8%</td>
</tr>
<tr>
<td>Labmen® HCV test</td>
<td>100%</td>
<td>63.1%</td>
</tr>
</tbody>
</table>

Chevaliez et al., Clin Microbiol Infect 2016 Jan S1198-743X(16)00025-2
Performance of RDTs for anti-HCV Ab Detection from Oral Fluid

- 318 patients with chronic HCV infection, 25 patients with resolved HCV infection and 170 HCV-seronegative subjects (N=513)

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Chevaliez et al., Clin Microbiol Infect 2016 Jan S1198-743X(16)00025-2
Performance of RDTs for anti-HCV Ab Detection from Whole Blood Collected on DBS

- 129 patients with chronic HCV infection, 10 patients with resolved HCV infection and 68 HCV-seronegative subjects (N=207)

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<td>100%</td>
</tr>
<tr>
<td>First Response® HCV Card test</td>
<td>100%</td>
<td>99.3%</td>
</tr>
<tr>
<td>Assure HCV Rapid Test</td>
<td>100%</td>
<td>98.6%</td>
</tr>
<tr>
<td>MultiSure HCV</td>
<td>100%</td>
<td>98.6%</td>
</tr>
</tbody>
</table>

Poiteau et al., J Viral Hepat 2016 Feb
Molecular POCT

Alere™ q

GeneXpert® I
HCV RNA Quantification by means of GenXpert

Genotypes 1 to 4 (n=46)

Unpublished data.
Summary

• RDTs and DBS are reliable tools for the screening and diagnosis of HCV infection

• Treatment monitoring can be simplified by the use of DBS, ideally as qualitative tests due to their altered ability to accurately quantify HCV RNA or core antigen

• HCV core Antigen quantification may be an attractive alternative tool to monitor patients receiving IFN-free regimens
Conclusions

• The advent of new, highly effective therapies, makes it possible to control HCV infection globally

• Such control will be possible only if infected patients are diagnosed and provided access to affordable therapies in an organized healthcare system

• Alternative virological tools exist, including RDTs, molecular POCTs, core antigen detection and DBS, that will help improve global access to care and control of HCV infection worldwide
Thank you for your attention