New HCV Virological Tools for Elimination

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Conflict of Interest Disclosure

- **Research grants**: Abbott, Gilead and Abbvie
- **Advisor**: Abbott, Abbvie, Gilead, GSK, Merck and Siemens Healthcare
HCV Cascade of Care (BC)

(Janjua et al., EBioMedicine 2016;12:189-195)
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Point-of-Care Tests

- Point-of-care (POC) testing is defined as testing performed close to or near the patient, i.e., where healthcare is provided and outside of traditional centralized biology laboratories.
Rapid Diagnostic Tests (RDT)

Example of the Oraquick Test (Orasure)
Rapid Diagnostic Tests (RDT)

- RDTs are simple to perform at room temperature, without specific instrumentation or extensive training.
- RDTs use various matrices, including:
  - serum or plasma
  - fingerstick capillary whole blood
  - oral fluid
- No need for venipuncture, tube centrifugation, freezing and skilled labor.
Dried Blood Spots (DBS)
Advantages of DBS

• Advantages
  
  • “Universal” access to care in particular situations, such as geographical remoteness, difficult venous access, prisoners, etc
  
  • Easy to collect, painless and mail at room temperature
  
  • Good stability of the biological matrix
  
  • A second spot on the same card can be used to test for NAT, allowing for reflex testing to be performed in anti-HCV antibody- or HBsAg-positive samples

(WHO Guidelines on Hepatitis B and C Testing 2017; EASL Recommendations on Treatment of Hepatitis C 2018)
Disadvantages of DBS

- Disadvantages
  
  - Lower analytical sensitivity as compared to classical biological matrices (serum or plasma), particularly when storing for prolonged durations (>14 days)
  
  - Lack of standardized procedures, resulting in variability of the results (quality and volume of blood, method used for detection, quality of filter paper, buffer used for extraction, etc)
  
  - No immediate results

(WHO Guidelines on Hepatitis B and C Testing 2017; EASL Recommendations on Treatment of Hepatitis C 2018)
Xpert (Cepheid)
Point-of-care NAT test
HCV Cascade of Care (BC)

(Janjua et al., EBioMedicine 2016;12:189-195)
EASL Recommendations 2018

• Screening for HCV infection should be based on the detection of anti-HCV antibodies in serum or plasma by means of enzyme immunoassay

• Whole blood sampled on dried blood spots can be used as an alternative to serum or plasma obtained by venipuncture for anti-HCV testing, after shipment to a central laboratory where the enzyme immunoassay will be performed

• Rapid diagnostic tests (RDTs) using serum, plasma, fingerstick whole blood or saliva as matrices can be used instead of classical enzyme immunoassays at the patient’s care site to facilitate anti-HCV antibody screening and improve access to care

(EASL Recommendations on Treatment of Hepatitis C 2018)
Anti-HCV Antibodies from DBS

Meta-analysis (2017)

- 19 studies in a pooled quantitative meta-analysis
- Similar sensitivity and specificity after stratification based on:
  - Amount of blood (≤50 μl versus >50 μl)
  - Sampling method (venous blood vs capillary blood)

<table>
<thead>
<tr>
<th>Anti-HCV on DBS</th>
<th>Specificity</th>
<th>Sensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>99% (95%CI: 98-100%)</td>
<td>98% (95%CI: 95-99%)</td>
</tr>
</tbody>
</table>

(Lange et al., BMC Infect Dis 2017;17(suppl):700)
Performance of HCV RDTs
Meta-analysis (2017)

- >52,000 individuals included until May 2015
- Stratification according to matrix specimen

<table>
<thead>
<tr>
<th>Specimen</th>
<th>Specificity</th>
<th>Sensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whole blood (n=90,008)</td>
<td>98%</td>
<td>98%</td>
</tr>
<tr>
<td>Oral fluid (n=12,370)</td>
<td>100%</td>
<td>94%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>98% for Oraquick</td>
</tr>
</tbody>
</table>

(Tang et al., BMC Infect Dis 2017;17(suppl):695)
HCV Cascade of Care (BC)

(Janjua et al., EBioMedicine 2016;12:189-195)
EASL Recommendations 2018

- If anti-HCV antibodies are detected, HCV RNA should be determined in serum or plasma to identify patients with ongoing infection.

- HCV RNA detection and quantification should be made by a sensitive assay with a lower limit of detection of ≤15 IU/mL.

(EASL Recommendations on Treatment of Hepatitis C 2018)
HCV RNA Assays (rtPCR or TMA)

- RealTime™ HCV (Abbott)
- Cobas TaqMan HCV v2.0 (Roche)
- VERIS HCV (Beckman)
- APTIMA® HCV Quant Dx (Hologic)
- Xpert® HCV (Cepheid)
- Xpert® HCV FS (Cepheid)

(Updated from Chevaliez et al., Gastroenterology 2012;142:1303-13)
Improving the Cascade of Care

- Reflex testing
- DBS
- Point-of-care test (POCT) for HCV RNA
- HCV core Ag test
- POCT with HCV RNA LOD ≤1000 IU/mL
## Reflex HCV RNA Testing

- HCV-infected patients in 5 health centers, Philadelphia, Pennsylvania

<table>
<thead>
<tr>
<th>Year</th>
<th>Testing Method</th>
<th>Proportion (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;2013</td>
<td>HCV RNA testing performed on second blood specimen</td>
<td>84%</td>
</tr>
<tr>
<td>July 2014</td>
<td>Reflex HCV RNA testing</td>
<td>96%</td>
</tr>
</tbody>
</table>

(Coyle et al., MMWR Morb Mortal Wkly Rep 2015;64:459-63)
HCV RNA from DBS

CAP/CTM (Roche)

m2000 (Abbott)

(Soulier et al., J Infect Dis 2016;213:1087-95)
Relationship Between HCV Core Ag and HCV RNA Levels

Analytical sensitivity equivalent to **500-3000** HCV RNA IU/mL

Rare false-negatives (core Ag-negative, HCV RNA-positive)

(Chevaliez et al., J Clin Virol 2014;61:145-8)
Xpert HCV Viral Load (Cepheid)

*Point-of-care HCV RNA test (serum)*

(McHugh et al., J Clin Microbiol 2017;55:1550-6)
Xpert HCV Viral Load (Cepheid)

*Fingerstick capillary whole blood*

- 150 individuals tested, 45 HCV-infected (comparator: Abbott RealTime)

<table>
<thead>
<tr>
<th>Xpert specimen</th>
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<th>Sensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasma</td>
<td>99%</td>
<td>100%</td>
</tr>
<tr>
<td>Fingerstick capillary whole blood</td>
<td>98%</td>
<td>95%</td>
</tr>
</tbody>
</table>

- 167 individuals tested, 59 HCV-infected

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<th>Xpert specimen</th>
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<th>Sensitivity</th>
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<tbody>
<tr>
<td>Fingerstick capillary whole blood</td>
<td>100%</td>
<td>100%</td>
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(Grebely et al., Lancet Gastroenterol Hepatol 2017;2:514-20; Lamoury et al., J Infect Dis 2018; epub ahead of print)
EASL Recommendations 2018

- In low- and middle-income countries and in specific settings in high-income countries, a qualitative HCV RNA assay with a lower limit of detection of ≤1,000 IU/ml can be used if more sensitive quantitative assays are not available and/or not affordable.
HCV Cascade of Care (BC)

(Janjua et al., EBioMedicine 2016;12:189-195)
Simplified Treatment

**Pretreatment assessment:**
- Proof of HCV replication
- APRI or FIB-4 for liver disease severity (if treatment for HCC available)
- Assessment of drug-drug interactions

**Treatment**
- **Sofosbuvir/velpatasvir** for 12 weeks
- **Glecaprevir/pibrentasvir**
  - For 8 weeks in patients without cirrhosis
  - For 12 weeks in patients with cirrhosis
- Generic drugs possible if quality controls met and guaranteed

(EASL Recommendations on Treatment of Hepatitis C 2018)
HCV Cascade of Care (BC)

(Janjua et al., EBioMedicine 2016;12:189-195)
Treatment Monitoring

Weeks

Baseline

Treatment

SVR12
Conclusion

• New virological assays, including point-of-care tests, are now available for HCV screening, diagnosis and monitoring.

• Their appropriate use, together with the implementation of simplified treatment procedures, is likely to substantially improve global access to diagnosis and linkage to care.

• These aspects must be reflected in international clinical practice guidelines.

• Further technical improvements are needed to address specific issues (POC qualitative NAT testing).
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