Diagnostics: Present and Future

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Viral Hepatitis: Diagnostic Landscape

- **A**: Total anti-HAV, IgG anti-HAV, IgM anti-HAV, HAV RNA
- **B**: HBsAg, HBeAg, IgM anti-HBc, Total anti-HBc, Anti-HBs, Anti-HBe, HBV DNA
- **C**: IgG anti-HDV, IgM anti-HDV, HDV Ag, HDV RNA
- **D**: IgG anti-HCV, HCV core Ag, HCV RNA
- **E**: IgG anti-HEV, IgM anti-HEV, HEV Ag, HEV RNA
Present Diagnostic Methodologies

**Serology**
- EIA (Enzyme immunoassay)
- CIA (Chemiluminescence immunoassay)
- CMIA (Chemiluminescent microparticle IA.)
- MEIA (Microparticle enzyme immunoassay)
- ICA (Immunochromatographic assay)

**Nucleic Acid Tests**
- RT-PCR (Reverse-transcription polymerase chain reaction)
- qPCR (Quantitative polymerase chain reaction)
- bDNA (branched DNA)
- TMA (transcription-mediated amplification)
Hepatitis C: Diagnostic Landscape
Challenges

Screening assays
  • Unregulated; unknown performance

Diagnoses of current infection
  • Limited markers

NAT
  • Laboratory set up; equipment
  • Technical expertise

QA/QC
  • Internal and external quality control
## “Diagnostic burn-out”

<table>
<thead>
<tr>
<th>Country</th>
<th>HCV Epidemic</th>
<th>Diagnosed Before 2016</th>
<th>New HCV Diagnoses</th>
<th>Cures in 2016</th>
<th>Outcome Dx Burn-out</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brazil</td>
<td>1.8M</td>
<td>235,000 (13%)</td>
<td>10,000 (0.6%)</td>
<td>43,000 (2.4%)</td>
<td>2025</td>
</tr>
<tr>
<td>Spain</td>
<td>328,000</td>
<td>140,000 (43%)</td>
<td>5500 (1.7%)</td>
<td>25,000 (8%)</td>
<td>2022</td>
</tr>
<tr>
<td>Portugal</td>
<td>96,000</td>
<td>37,000 (39%)</td>
<td>1300 (1.3%)</td>
<td>4400 (4.6%)</td>
<td>2026</td>
</tr>
</tbody>
</table>

*potential outcomes, based on 2016 data*

AASLD 2017, Abstract #205
Andrew Hill, University of Liverpool
Point-of-care HCV RNA Test – Xpert System

**Evaluation of the Xpert HCV Viral Load point-of-care assay from venepuncture-collected and finger-stick capillary whole-blood samples: a cohort study.**

Grebelky J¹, Lamouny FMJ², Hajjarizadeh B², Mowat Y², Marshall AD², Balsis S², Marks P², Amini P³, Smith J⁴, Edwards M⁵, Gorton C⁶, Fizard N⁷, Persing D⁸, Kieman M⁹, Cunningham P¹⁰, Cattell B¹⁰, Dore G¹², Applegate TL¹², LiveRiLife Study Group.
HCV core Antigen Test
ARCHITECT (Abbott)

**Eval. panel: 551 serum samples**
- Pre-seroconversion: Anti-HCV - / HCV RNA +
  - **Sensitivity 100%**
- Post-seroconversion: Anti-HCV and HCV RNA +
  - **Sensitivity ~ 94%**


Innovative Methodologies

- Microfluidics
- Nanotechnology

Nano Lett. 2007;7:2812-2818

OPKO platform
POC Diagnostics: Smartphone dongle

Cost of testing
Typical EIA set up: $18K
Smartphone dongle: $34 + smartphone

Tassaneewon L et al., Sci Transl Med 2015;7:273re1
Lab-on-a-drone

Lab-on-a-drone
CRISPR for Diagnostics

SHERLOCK
Specific High Sensitivity Enzymatic Reporter UnLOCKing

Nucleic acid detection with CRISPR-Cas13a/C2c2

**Global Hepatitis Outbreak and Surveillance Technology (GHOST)**

*Cyber-Molecular Detection of Hepatitis C Outbreaks*

- Clinical samples
- Deep sequencing: E1/E2 (HVR1) amplicon
- FASTQ/FASTA

**Outbreak**

- Upload
- Web-based Software
- Transmission cluster
- Source?

**Surveillance**

GHOST

- A node represents all HCV quasispecies from a single individual
- Two nodes are linked if individuals share HCV strain
- Node size is proportional to HCV quasispecies heterogeneity
Summary

• Evaluation of performance characteristics of rapid diagnostic tests for HBsAg and anti-HCV is needed

• Development of global proficiency panels for evaluation of diagnostic assays is the key to ensuring reliable diagnostics

• Assays for the diagnosis of current HCV infection, the HCV core antigen and HCV RNA, in a point-of-care format need to be urgently developed

• Accurate, Affordable and Accessible assays for diagnosing current infections key to any elimination programs
Thank you!

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The findings and conclusions in this report are those of the author and do not necessarily represent the official position of the Centers for Disease Control and Prevention.