Hepatitis E Prevalence in North American Blood Donors

IPFA May 16 - 17, Athens
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Canadian Blood Services
Disclosures

• Funding for all laboratory support and reagents provided by:
  – Roche Molecular Diagnostics
  – National Microbiology Laboratory (NML), Public Health Agency of Canada (Canadian Study #1)

• Testing performed by:
  – Screening: American Red Cross Scientific Affairs
  – Confirmatory: Sanquin, The Netherlands
  – Sub-population antibody screening: CDC
  – NML (Canadian Study #1)

• Samples provided by
  – American Red Cross
  – Hema-Quebec and Canadian Blood Services
Hepatitis E Prevalence
Geographical Distribution of Hepatitis E virus Genotypes

> 3 million cases/year, mainly in developing countries
Seroprevalence 2 – 50% in developed countries

Hepatitis E: Current Status Perez-Gracia et al. Reviews in Medical Virology 2013;23(6)
Clinical Presentation

Most cases asymptomatic

• **Acute hepatitis**
  – more common in males > 65 yrs. and in pregnant women
  – Incubation period 2 weeks – 2 months
  – Jaundice, fever, malaise, anorexia
  – Viremia is transitory – disappears with symptom onset

• **Chronic hepatitis**
  – Chronic HEV infection reported in liver and kidney transplant recipients (SOT), those with non-Hodgkins lymphoma, in HIV/AIDS patients, stem-cell transplant (SCT) patients. (all immunosuppressed patients)
  – Almost all cases represent autochthonous HEV gt3
  – Persistent viremia with titers $10^5$-$10^7$ IU/mL
  – Evolution to cirrhosis occurs in up to 50%; liver failure
Risk Profile of Hepatitis E Virus from Pigs or Pork in Canada.
Wilhelm B¹, Fazil A², Rajić A¹, Houde A³, McEwen SA¹.
Send to

Survey of Canadian retail pork chops and pork livers for detection of hepatitis E virus, norovirus, and rotavirus using real time RT-PCR.
Wilhelm B¹, Leblanc D², Houde A², Brassard J², Gagné MJ², Plante D³, Bellon-Gagnon P³, Jones TH⁴, Muehlhauser V⁴, Janecko N⁵, Avery B⁶, Rajić A⁷, McEwen SA⁷.
Hepatitis E and Transfusion Transmission

• Over 30 cases of reported cases of transfusion transmission.
• Cases reported in Japan, U.K., France, Saudi Arabia.
• To date, no reported cases of TT HEV in North America
North American Donor Prevalence Studies 1

In 2013 **CBS and Hema Quebec** in collaboration with the National Microbiology Lab, carried out a geographically limited HEV prevalence study on approximately **14,000** Canadian blood donors.

- Antibody prevalence of 5.8%
- 0 HEV NAT positive donors (pooled testing 48-100)

*Fearon M, O’Brien S. et al Hepatitis E in Canadian Blood Donors. Transfusion 2017;57:1420-142*

Also in 2013 the **American Red Cross** surveyed approximately **19,000** U.S. blood donors

- 2 HEV NAT positive donors out of 18,829 tested (ID NAT).
- Antibody prevalence of 7.7% of 4,499 tested donors.

North American Donor Prevalence Studies 2

• Two independent RNA prevalence studies – target 100,000 donations total
  – Canadian - between October 2016 - June 2017
• **50,000 US (ARC)** donations throughout US but focus in Midwest
  – Unlinked
• **50,000 (30,000 CBS and 20,000 HQ)** donations from every province
  – Linked, tested following product release
• Donations tested for HEV RNA by ID-NAT at the ARC, using the Roche **cobas®** HEV test, and the **cobas®** 6800/8800 System (assay not approved for use in the US or Canada)
  – Hemi-nested PCR from amp/detection plates at Roche
• Additional testing on reactive samples performed at Sanquin and included
  – HEV RNA quantitative PCR (74 bp ORF-3; LOD 10.3 IU/mL)
  – HEV genotyping (ORF-1, ORF-2)
  – HEV antibody testing (Wantai)
• Comparative antibody studies done on a subset of US samples at CDC
The **cobas®** HEV test is not approved in the US or Canada but is available in countries that accept the CE mark.
# US Results

3 positives/50,724 valid results

1:16,908 (95% CI: 1:5786-1:81,987)

<table>
<thead>
<tr>
<th>Sex</th>
<th>Age</th>
<th>State</th>
<th>cobas® HEV Test (Ct value; max = 50)</th>
<th>hn-PCR (Roche)</th>
<th>Viral Load (IU/mL) 2 reps</th>
<th>Genotype</th>
<th>IgM (S/CO)</th>
<th>IgG (S/CO)</th>
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<tbody>
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<td>Male</td>
<td>65</td>
<td>IN</td>
<td>38.54</td>
<td>Pos</td>
<td>15, 30</td>
<td>3a</td>
<td>0.02</td>
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<td>37.38</td>
<td>Pos</td>
<td>13, 58</td>
<td>3b</td>
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<td>0.02</td>
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<td>Female</td>
<td>55</td>
<td>KY</td>
<td>34.42</td>
<td>Pos</td>
<td>1440, 1400</td>
<td>n/a</td>
<td>11.03</td>
<td>&gt;15</td>
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</table>

Prior published US study (Stramer et al. Transfusion 2016):

2 positives/18,829 valid results

1:9500 (95%CI: 1:2580-1:56,180)

66 yo Male, IA (n/a IU/mL, Ab pos)
71 yo Male, IL (14 IU/mL, Ab neg)
HEV RNA Positive Donations By Donor Residence

N=3 pos/50,724 (this study)

N=2 pos/18,829 (prior study)
## Canadian Results

**11 positives/50,765 valid results**

**Total:** $1:4615$ (95% CI: $1:2579$-$1:9244$)

**HQ:** $1:2920$ (95% CI: $1:1417$-$1:7262$)

**CBS:** $1:7582$ (95% CI: $1:2961$-$1:27,825$)

<table>
<thead>
<tr>
<th>Site</th>
<th>Sex</th>
<th>Age</th>
<th>Province</th>
<th>cobas® HEV Test (Ct value; max = 50)</th>
<th>Viral load (IU/mL)</th>
<th>IgM (S/CO)</th>
<th>IgG (S/CO)</th>
<th>IgM (S/CO)</th>
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<tr>
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<tr>
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<tr>
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<tr>
<td>CBS</td>
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<td>0.1</td>
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</tr>
</tbody>
</table>

*Genotype 3 (unique)
Subset of 5040 RNA-negative samples tested for IgM/IgG by 3 Commercial HEV antibody assays (CDC; submitted)

Prevalence increases with age

11.4% prevalence (range 10.65-12.28%)
84% agreement between assays

1.8% prevalence (range 0.67-2.9%)
22% agreement between assays
Summary

- HEV RNA is present in US and Canadian donors
  – Frequency of all ID-NAT studies (Roche/Grifols)
  – 16 pos/120,318 tested, or **1:7500**
    - Wide 95% CIs; no statistical difference amongst studies
    - Highest viral load = 3080 IU/mL; most too low to genotype @ < 100 IU/mL (all gt 3)
    - Most males (13/16)
    - High performance of ID-NAT assays
  – Ab positivity suggests higher frequencies of infection
    - IgM = 1.8% vs IgG = 11.8% => this study
    - IgM = 0.58% vs IgG = 7.7% => prior study
    - IgG = 5.9% Fearon et al; Canada; all significantly different
Summary

- Absence of TT HEV in US/Canada, but clinical disease occurs - magnitude not well understood

  *“HEV infection causes chronic hepatitis in >60% recipients of solid organ transplants”

  - Hewitt et al-UK; mean viral load
    - **TT = 4.53 log₁₀ IU/mL vs**
    - **non-TT = 2.57 log₁₀ IU/mL; 95% CIs overlap**

- Decision making underway in Canada
  - RBDM

- Should screened blood be used for:
  - Solid organ, stem cell transplant recipients?