Hep E in Israel

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Hep E -history

• 1955-the biggest flood in Delhi, 29,000 hepatitis cases.
• 1970’-Serological tests for Hep A+B, were developed
• ET-NANB
• 1983 – Mikhail Balayan visualized HEV using immune electron microscopy to examine his own stool samples, which he collected prospectively after self-administration of infectious material.
• 1991- Discovery of Hep E
HEV

• HEV is a small non-enveloped RNA virus with a size of 27-34nm.

• Globally, HEV is the most common cause of acute viral hepatitis.
The CIWEC clinic
Viral Hepatitis diagnosed at CIWEC clinic Kathmandu

Schwartz, Innis, Shlim and Snitbhan

HEV -Israel

- Travelers
- Autochthonous
Sero-Survey Israel
n=1416

Seroprevalence by EIA + immunoblot-2.6%

• Jewish populations-2.81% (=1,139)
• Arab population- 1.81% (N=277)

• No acute disease
• one patient with chronic hepatitis was positive for both IgG and IgM

Populations with high prevalence of antibody against hepatitis E virus in Israel

- Beduim \((n=201)\) - 8.0%
- Ethiopian Immigrants \((n=555)\) - 9.6%
- Kibutz Izrael \((n=48)\) - 14.5%
- None had IgM+

Figure 2  Seroprevalence of antibody to hepatitis E virus (HEV) among healthy blood donors in industrialized countries.\textsuperscript{14,26-31}
Hepatitis E Virus Infection in Travelers

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Clinical Infectious Diseases   1999; 29:1312–4
Hep E in Israeli Travelers

- Nation-wide survey.
- 5 cases identified
- All from India & Nepal

E. Schwartz et al; *Clinical Infectious Diseases* 1999;29:1312–4
Hep E in Israeli Travelers

- Hep E; Risk for Israeli travelers < 1:100,000
- Hep A; Risk ~ 300-2,000:100,000

E. Schwartz et al; *Clinical Infectious Diseases* 1999;29:1312–4
# Hep E-Seroconversion in Travelers

<table>
<thead>
<tr>
<th>Year of study</th>
<th>Group</th>
<th>Number</th>
<th>Seroconversion</th>
</tr>
</thead>
<tbody>
<tr>
<td>1967-84</td>
<td>US missionaries</td>
<td>328</td>
<td>0%</td>
</tr>
<tr>
<td>1993</td>
<td>US travelers (&lt;3mo.)</td>
<td>104</td>
<td>0%</td>
</tr>
<tr>
<td>1998</td>
<td>Israeli travelers (6mo.)</td>
<td>84</td>
<td>0%</td>
</tr>
<tr>
<td>1997-8</td>
<td>Nepal, expatriate (12 mo.)</td>
<td>373</td>
<td>0.3% 1 case</td>
</tr>
</tbody>
</table>
HEV in Int’l Travelers

- 1986-1999
- 161 reported cases
- 6 – Fulminant hepatitis
- 2 – Death

*Based on reported cases, the risk:*

1: 300,000,000

Safety and Efficacy of a Recombinant Hepatitis E Vaccine

Mrigendra Prasad Shrestha, M.B., B.S., Robert McNair Scott, M.D., Durga Man Joshi, M.D., Mammen P. Mammen, Jr., M.D., Gyan Bahadur Thapa, M.B., B.S., Narbada Thapa, Ph.D., Khin Saw Aye Myint, M.B., B.S., Marc Fourneau, B.S., Robert A. Kuschner, M.D., Sanjaya Kumar Shrestha, M.D., Marie Pierre David, M.S., Jitvimol Seriwatana, M.S., David W. Vaughn, M.D., Assad Safary, M.D., Timothy P. Endy, M.D., and Bruce L. Innis, M.D.

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Volume 356(9):895-903
March 1, 2007
Acute hepatitis in Israeli travelers

Tamar Lachish, Eli Schwartz

J. Travel Med. 2013 in press
Acute hepatitis in Israeli travelers

- Hepatitis =1.3% of all travel related illness (Harefuah 2010).
- 1% of all travel related hospitalization (JTM 2005).
- In the current literature, data regarding the etiology of acute hepatitis in travelers is scarce and indirect.
Methods

• A prospective observational study.
• Study period: 1997 - 2012
• Patient population: Travelers that presented with acute hepatitis at two travel medicine clinics.

• Laboratory diagnostic tools
  – Acute HAV - IgM anti HAV ELISA.
  – Acute HEV - PCR for HEV-RNA.
  – Acute HBV - anti-HBc IgM and HBsAg.
  – Acute HCV - HCV RIBA or PCR for HCV-RNA.

• Unspecified hepatitis: confirmed acute hepatitis with a negative viral workup and no other obvious etiology by the end of follow up.
Results

• Among 4970 ill returning Israeli travelers who were seen during the years 1997 to 2012, 49 (1%) were diagnosed with acute hepatitis.
Results - Etiology of Acute Hepatitis

- HEV – 19 cases (39%).
- HAV – 13 cases (27%).
- HBV – 2 cases (4%).
- HCV – 1 case (2%).
- Unspecified hepatitis – 14 (29%).
Cases of acute hepatitis A & E per year

[Graph showing cases of acute hepatitis A (HA) and E (HEV) per year from 1998 to 2012.]
Discussion

- 1% of ill returning Israeli travelers were diagnosed with acute hepatitis.
- 65% of all acute hepatitis cases were enterically-transmitted.
- HEV is an emerging disease and is becoming the most common hepatitis among Israeli travelers.
- 84% of HEV cases were imported from the Indian subcontinent. The estimated risk of acquiring HEV in India, which is highly endemic, is at least 3.2/100,000 travelers.
HEV diagnosis in Israel

• HEV RNA - available since 1997, at the Liver Unit, Hadassah Medical Center.

• Serology – available since 2012 - Hadassah Medical Center, Sheba Medical Center.
Total samples

Total N. of Sera
N=580

- PCR pos.
  53=51 pts.
  (8.8%)

- PCR neg.
  527
Sera available
N=291

Negative
N=262

IgM+/IgG +
N=10

IgM+
N=9

IgG+
N=10

9.9%
(29/291)
Positive HEV PCR cases

- Travelers: 21 Cases
- Foreign workers: 7 Cases
- Acquired in Israel: 8 Cases [15%]
- Unknown: 15 Cases
Combined positive PCR + IgM

- Travelers: 22 Cases
- Foreign workers: 9 Cases
- Acquired in Israel: 10 Cases [14%]
- Unknown: 29 Cases
Combined positive data (PCR + IgM)

14 Samples

- Travelers: 10 Cases
- Foreign workers: 0 Cases
- Acquired in Israel: 1 Case
- Unknown: 3 Cases
## HEV in Pregnancy

<table>
<thead>
<tr>
<th></th>
<th>Age</th>
<th>Age of pregnancy</th>
<th>Country of acquisition</th>
<th>Outcome</th>
<th>PCR</th>
<th>IgM</th>
<th>IgG</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>41</td>
<td>31W</td>
<td>NA</td>
<td>NA</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>2</td>
<td>30</td>
<td>Post partum</td>
<td>NA</td>
<td>Acute disease (resolved)</td>
<td>-</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>30</td>
<td>Post partum</td>
<td>Israel</td>
<td><strong>Liver transplantation</strong></td>
<td>+</td>
<td>NA</td>
<td>NA</td>
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<tr>
<td>4</td>
<td>27</td>
<td>29W</td>
<td>NA</td>
<td>Very mild disease</td>
<td>+</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>5</td>
<td>28</td>
<td>36W</td>
<td>Israel</td>
<td>Acute disease (resolved)</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>6</td>
<td>27</td>
<td>12W</td>
<td>Israel</td>
<td>Acute disease (resolved 5 mo.)</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>7</td>
<td>37</td>
<td>28W</td>
<td>India</td>
<td>Acute disease (resolved)</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

NA- Not Available
HEV - Immunocompromised

• Only 1 case:
  – s/p Liver and kidney transplantation.
  – PCR negative, IgG negative, IgM positive twice - two years apart → chronic infection.
HEV outcome
PCR pos.=51 pts.

- Death-2
- Liver Transplantation-1
Conclusion

• HEV is endemic in Israel
• HEV accounts for ~ 15% of Non-ABC hepatitis

• It is the most common form among Israeli Travelers
• HEV vaccine should be considered for travelers, mainly to the Indian-Sub Continent