Hepatitis E in developing countries

- **Forms**
  - Epidemic
  - Sporadic

- **Transmission**
  - Water-borne
  - Human-to-human

- **Genotypes**
  - Genotype 1
  - Genotype 2

- **Clinical forms**
  - Asymptomatic
  - Acute hepatitis
  - Acute liver failure

- **Transmission**
  - Water-borne
  - Human-to-human

- **Special situations**
  - During pregnancy
  - In persons with chronic liver disease

**Hepatitis E outbreaks: HEV genotypes**

**Hepatitis E: Outbreaks (1980-2007)**

- Reported from 29 countries

**Hepatitis E: Outbreaks in India affecting >1000 persons**

- Sample (n = 3,666) vs Population (n = 2.1 million)

- Mortality
  - Healt: 3.76%
  - Deaths: 0.7%

**Hepatitis E epidemic: Kanpur, India, 1991**

- Sample (n = 3,666) vs Population (n = 2.1 million)

- Mortality: 0.06% (13 pregnant women)
Hepatitis E epidemic: Kanpur, India, 1991

Another hepatitis E outbreak in India

A hepatitis E outbreak caused by a temporary interruption in a municipal water treatment system, Baripada, Orissa, India, 2004


Epidemic hepatitis E: Transmission

- Fecal-oral transmission, often via contaminated water supply systems
- Person-to-person transmission rare
- Food borne?

- Vertical transmission
- Transmission through blood transfusions
- Zoonotic transmission?

HEV outbreaks: Associated factors

- Flooding, heavy rainfall
- Failure of water treatment systems
- Use of untreated water from river or spring
- Hot summer >> reduced river water >> increased contaminants
- Leaking water pipes, with interrupted water supply
- Leakage of sewage pipes

HEV outbreaks: Control measures

- Chlorination of water
- Water boiling
- Repair of water pipelines
- Alternative safer water supply
- Improving hygiene (e.g., handwashing practices)
- Improving sewage disposal
Africa: Outbreaks in humanitarian emergencies

- Outbreaks: In refugee camps (humanitarian emergency/conflict zones)
  Waterborne infection
  Large, affecting several persons
  Mainly adults
  Pregnant women particularly affected

- Special features: High disease attack rates
  Prolonged, lasting several months
  ? Person-to-person (intra-familial) transmission


Sporadic hepatitis E (1980-2007)

Hepatitis E as percent of sporadic acute viral hepatitis

Sporadic hepatitis E in endemic areas

- Cases with acute hepatitis E in the absence of outbreak
- Similar to epidemic hepatitis E in
  - Epidemiologic features
    - Age, gender distribution
    - Exposure to unclean water
    - Relationship with pregnancy
    - Seasonal occurrence
  - Clinical features
  - Outcomes
- ? Micro-outbreaks – not recognized as outbreaks

Epidemic hepatitis E: Clinical spectrum

- Acute icteric viral hepatitis
- Asymptomatic infection
- Anicteric hepatitis
- Fulminant hepatic failure
- Acute worsening of chronic liver disease

Table 1: Number (%) of animals testing positive for IgG anti-HEV

<table>
<thead>
<tr>
<th>Animal species</th>
<th>Modified Genelabs assay n</th>
<th>ORF 2.1 assay n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pig</td>
<td>200 (100)</td>
<td>193 (97)</td>
</tr>
<tr>
<td>Goat</td>
<td>98 (100)</td>
<td>98 (100)</td>
</tr>
<tr>
<td>Chicken</td>
<td>86 (98)</td>
<td>84 (98)</td>
</tr>
<tr>
<td>Sheep</td>
<td>58 (100)</td>
<td>45 (78)</td>
</tr>
<tr>
<td>Buffalo</td>
<td>30 (100)</td>
<td>30 (100)</td>
</tr>
</tbody>
</table>


Animal HEV infection in India


Animal and human HEV in India

Aggarwal R. J Gastroenterol Hepatol 2009; 24: 1484-93.
Asymptomatic infection

Acute hepatitis (Jaundice)

Liver function (%)

Time (wk)

0 4 8 12 16 20 24

Liver failure

Jaundice

Liver function (%)

Time (wk)

0 4 8 12 16 20 24

Liver failure

Jaundice

Acute liver failure

HEV superinfection in cirrhosis

Liver function (%)

Time (wk)

0 4 8 12 16 20 24

Liver failure

Jaundice

Liver function (%)

Time (wk)

0 4 8 12 16 20 24

 Liver failure

Jaundice

HEV infection in cirrhosis: More often, more severe, longer duration

Hepatitis E and pregnancy

<table>
<thead>
<tr>
<th>Group</th>
<th>Sample</th>
<th>Hepatitis, n (%)</th>
<th>Acute liver failure, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td>3,822</td>
<td>107 (2.8%)</td>
<td>3/107 (2.8%)</td>
</tr>
<tr>
<td>Non-pregnant women</td>
<td>3,350</td>
<td>71 (2.1%)</td>
<td>0/71 (0%)</td>
</tr>
<tr>
<td>Pregnant women</td>
<td>208</td>
<td>36 (17.7%)</td>
<td>8/36 (22.2%)</td>
</tr>
</tbody>
</table>

Pregnancy associated with
- Higher disease attack rate
- More often severe disease
- Mortality: 15-25%


HEV superinfection in cirrhosis

Patients

(Recent worsening)

18

Controls

(Stable cirrhosis)

45

14 (43%)

(6%)

Positive Negative

Positive Negative

p<0.0001
Hepatitis E and pregnancy

Non-pregnant women

Pregnant women


Hepatitis E and pregnancy

Non-pregnant women

Pregnant women


Hepatitis E and pregnancy

Non-pregnant women

Pregnant women


Hepatitis E and pregnancy

Non-pregnant women

Pregnant women


Hepatitis E and pregnancy

Non-pregnant women

Pregnant women


Hepatitis E and pregnancy

Non-pregnant women

Pregnant women


Chronic hepatitis E: not in endemic areas of Asia and Africa

**Hepatitis E: Two different faces**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Asia and Africa (Developing countries)</th>
<th>Europe and N America (Industrialized countries)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Virus genotype</td>
<td>1, 2, (4)</td>
<td>3, (4)</td>
</tr>
<tr>
<td>Transmission</td>
<td>Waterborne, ? food</td>
<td>7, food (animal meat)</td>
</tr>
<tr>
<td>Reservoir</td>
<td>Human</td>
<td>Animal</td>
</tr>
<tr>
<td>Outbreaks</td>
<td>Small to very large</td>
<td>None to small</td>
</tr>
<tr>
<td>HEV as % of sporadic hepatitis</td>
<td>Common</td>
<td>In frequent</td>
</tr>
<tr>
<td>Age distribution</td>
<td>Young</td>
<td>Old</td>
</tr>
<tr>
<td>Co-existent diseases</td>
<td>Infrequent</td>
<td>Common</td>
</tr>
<tr>
<td>Pregnant women</td>
<td>High mortality</td>
<td>No data</td>
</tr>
<tr>
<td>Chronic infection</td>
<td>No</td>
<td>Yes (immunosuppressed)</td>
</tr>
</tbody>
</table>

**Hepatitis E in Asia and Africa: Estimated disease burden**

- Based on seroprevalence data
- Assumptions:
  - 19.9% of infections are symptomatic
  - 1.9% of non-pregnant and 19.8% of pregnant women with disease die

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Mid-estimate</th>
<th>95% credible interval</th>
<th>Upper/lower bound ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infections</td>
<td>20.1 million</td>
<td>2.8 – 37.0 million</td>
<td>13.3</td>
</tr>
<tr>
<td>Symptomatic cases</td>
<td>3.3 million</td>
<td>0.47 – 6.50 million</td>
<td>13.9</td>
</tr>
<tr>
<td>Deaths</td>
<td>69,622</td>
<td>12,490 – 133,732</td>
<td>10.7</td>
</tr>
<tr>
<td>Stillbirths</td>
<td>3,019</td>
<td>982 – 4,424</td>
<td>2.3</td>
</tr>
</tbody>
</table>

*Rein D. Hepatology 2012: 55: 988-97*

**Hepatitis E in developing countries: Take-home summary**

- Outbreaks, frequent sporadic cases with acute infection
  - Mainly waterborne, possibly food
  - Affects young people
  - Pregnant women have severe disease with frequent fatal outcome
  - Severe disease also among persons with pre-existing liver disease
- Caused by genotype 1 or 2 virus
  - Very little or no zoonotic transmission
  - No chronic infection
- Cause significant preventable human morbidity