Why is HBV molecular typing important?

- Effectiveness of targeted vaccination programs
- Identification of new transmission routes
- Fast detection of central (medical) infection source
- Spread of antigenic variants
- Spread of antiviral resistance

↓

Is the current Dutch HBV control policy effective?
How different are the HBV genomes?

- 8 different genotypes are known (A – H, 8% nt difference)
- Variation is depending on the position on the genome
- Many subdivision within a genotype
  - gA1 [Africa] and gA2 [MSM]
  - gD of Intravenous Drugs Users differs from immigrants
  - Ba (recom.) and Bj in Japan
- Phenotypic and clinical differences between genotypes
Acute HBV incidence in the Netherlands

Average incidence: 1.8 / 100,000

~300 cases/y → ~1000 inf./y

Male vs. Female: 5 vs. 1
Most likely source of transmission of acute HBV

<table>
<thead>
<tr>
<th>Source</th>
<th>Database (Osiris, n=1060)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sexual</td>
<td>60%</td>
</tr>
<tr>
<td>MSM</td>
<td>34%</td>
</tr>
<tr>
<td>Heterosexual</td>
<td>23%</td>
</tr>
<tr>
<td>Other</td>
<td>3%</td>
</tr>
<tr>
<td>Vertical</td>
<td>1%</td>
</tr>
<tr>
<td>Accidents</td>
<td>2%</td>
</tr>
<tr>
<td>IDU</td>
<td>1%</td>
</tr>
<tr>
<td>Other</td>
<td>11%</td>
</tr>
<tr>
<td>Unknown</td>
<td>25%</td>
</tr>
</tbody>
</table>
Genomic organization of HBV

HBV-DNA 3220 nt

First PCR

Sequence analysis (110 – 765 nt)

Nested PCR

Polymerase

Lamivudine resistance

(L526 → M) (M550 → I,V)

A-determinant (124 -147 aa)

HBs (nt 155 – 839)

Molecular epidemiology of HBV in The Netherlands

Genotype A  Europe, North America
Genotype B  South-east Asia
Genotype D  Mediterranean
Genotype C  Asia
Genotype E  Africa
Genotype F  South America
Sexual active man from Dutch Caribbean
## Incidence of genotypes in acute HBV

<table>
<thead>
<tr>
<th>Genotypes</th>
<th>Total (acute)</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>gA</td>
<td>65%</td>
<td>309</td>
<td>55</td>
</tr>
<tr>
<td>gB</td>
<td>2%</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td>gC</td>
<td>3%</td>
<td>19</td>
<td>-</td>
</tr>
<tr>
<td>gD</td>
<td>22%</td>
<td>77</td>
<td>48</td>
</tr>
<tr>
<td>gE</td>
<td>4%</td>
<td>13</td>
<td>11</td>
</tr>
<tr>
<td>gF</td>
<td>4%</td>
<td>15</td>
<td>6</td>
</tr>
<tr>
<td>gG (+ gA)</td>
<td>0%</td>
<td>2</td>
<td>-</td>
</tr>
<tr>
<td>gH</td>
<td>0%</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

\[ n=579 \]

\[ 441 \]

\[ 125 \]
Minimal spanning tree of acute HBV isolates (2004-2007, n = 579)

Pink = MSM
Green = Heterosexual
Yellow = Other
Blue = Unknown
Genotype F
South America

Molecular epidemiology of HBV in The Netherlands
Molecular epidemiology of HBV in The Netherlands

HBV genotype F cluster (2004 – 2008)

Netherlands: 21/579 (4%)
Friesland: 4/17 (24%)
# HBV mutants

<table>
<thead>
<tr>
<th></th>
<th>HBV infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>S-region sequence</td>
<td>Acute: 583, Chronic: 312</td>
</tr>
<tr>
<td>Immune escape mutation (G145R)</td>
<td>Acute: 0, Chronic: 0</td>
</tr>
<tr>
<td>Antiviral resistance (M550V)</td>
<td>Acute: 2, Chronic: 2</td>
</tr>
</tbody>
</table>
HBV molecular typing of HBV

• Effectiveness of targeted vaccination programs:
  Reduction in number of MSM gA-isolates (non sig.)

• Identification of new infection sources:
  No new extensive transmissions have been found

• Spread of antigenic variants:
  Only associated with use of HB-immunoglobuline

• Spread of antiviral resistance:
  Low frequency among acute and chronic HBV
Molecular epidemiology of HBV in The Netherlands

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Molecular epidemiology of HBV in The Netherlands

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