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Epidemiology of hepatitis B in The Netherlands

Mirjam Kretzschmar

Centre for Infectious Disease Control, RIVM, and
Julius Center for Health Sciences & Primary Care
University Medical Centre Utrecht, The Netherlands
Outline

• Prevalence and incidence of notified cases by age and risk group
• Epidemiological studies
  - Seroprevalence studies
  - Modelling
  - Enhanced surveillance (BRON study)
  - Molecular epidemiology
• International dimensions
  - NL low endemic country, no universal vaccination
• Conclusions
Incidence of notified cases of acute and chronic HBV infection (1976-2007)

Source: Osiris notification system
Age distribution of notified cases

incidence per 100000

men 2006
men 2007
women 2006
women 2007

age

0-4 5-9 10- 14 15- 19 20- 24 25- 34 35- 44 45- 54 55- 64 65- 74 >75
Geographical distribution

Koedijk et al Inf Bull 2007
Numbers of notified cases of HBV infection 2003-2007

- Acute
- Chronic
- Unknown
Acute HBV infections by risk group

2007: sexual contact 65%, IDU 0.9%, needle stick injuries 1%, other 10%, unknown 23%
19% first generation migrants, 17% infected abroad

Source: Osiris
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Source: Osiris
Chronic HBV infections by risk group

2007: sexual 7%, IDU 0.6%, needle stick injury 0.6%, vertical 54%, other route 8%, unknown 29%
78% first generation migrants, 73% infected abroad

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## Fraction clinical infections

<table>
<thead>
<tr>
<th>Age</th>
<th>Numbers infected</th>
<th>Fraction clinical infections (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-4</td>
<td>21</td>
<td>9.5</td>
</tr>
<tr>
<td>5-9</td>
<td>61</td>
<td>9.8</td>
</tr>
<tr>
<td>10-19</td>
<td>58</td>
<td>10.3</td>
</tr>
<tr>
<td>20-29</td>
<td>22</td>
<td>13.6</td>
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<tr>
<td>≥ 30</td>
<td>27</td>
<td>33.3</td>
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McMahon et al. JID 1985

Underreporting?

75% of symptomatic cases reported in England (Ramsay et al. Vaccine 1998)
Seroprevalence study in representative population sample, PIENTER study 1995

Overall prevalence: 0.2% HBsAg+ and 2.1% antiHBc+

New seroprevalence study with oversampling of migrant populations conducted in 2007, results to come soon.

Van Marrewijk et al 1999
Insights from mathematical modelling

• Development of dynamic transmission model with
  - stratified by age and sexual activity
  - sexual, vertical, and horizontal transmission
  - hetero- and MSM populations
  - Age dependent probability of becoming chronic carrier

• Model used to assess effects of vaccination

• Analysis of basic reproduction number and transmission dynamics in risk groups

Williams et al. Epidemiol Infect 1996;
Kretzschmar et al Epidemiol Infect 2002;
Kretzschmar & de Wit Lancet Inf Dis 2008
Model features

probability of chronic infection

high infectivity

low infectivity

probability of chronic infection

susceptible

vaccinated

latent infection

acute infection

chronic carrier

immune

birth

probability

maximum likelihood estimate

R₀ minimal in 95% confidence region

R₀ maximal in 95% confidence region

age (years)
Estimates for $R_0$ for the heterosexual population

- Estimates in the UK:
  - Constant: 1.11
  - Age-dependent: 0.79

- Estimates in the Netherlands:
  - Constant: 0.69
  - Age-dependent: 0.53
Implications for epidemiology?

- Homosexual men $R_0 > 1$:
  - Infection persists;
  - Import of infected persons has small impact.

- Heterosexual population $R_0 < 1$:
  - Short transmission chains;
  - Import of infected persons determines prevalence.
Molecular epidemiology

Origin of hepatitis B virus in Dutch blood donors

No indigenous heterosexual strain

IDU cluster has disappeared
Effect of vaccination?

van Houdt et al Vaccine 2007
Surveillance

  - 18.8% of male, 34.3% of female patients are of non-Dutch ethnicity
  - Non-Dutch ethnicity of source: hetero men 65%, women 57%, MSM 30%

- Surveillance of chronic hepatitis B 2001-2003: 54%-76% of patients born in high or medium endemic countries (Koedijk et al. 2005)

- Chronic carriers with Dutch ethnicity mostly infected sexually, chronic carriers with non-Dutch ethnicity mostly infected perinatally (Toy et al. 2008)

- Prevalence estimate based on analysis of literature data: population prevalence is between 0.36% and 0.55% (Marschall et al. 2008)
Global immunization coverage will impact on epidemiology of low endemic countries


Conclusions

• Netherlands is a low endemic country
• Incidence of acute infections in MSM and other high risk groups
• Persistent circulation of virus in MSM but not in general heterosexual population
• Prevalence of chronic infections strongly determined by migration from high and medium endemic areas
• Epidemiology of HBV in the Netherlands will change with increasing global vaccination coverage
• Targetted screening required to increase treatment uptake of persons with chronic infection
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