Pertussis: incidence, seroprevalence and prevention

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**PCR:** 0 – 4 weeks

**Serology:** > 3 weeks
Structure NRC

Two labs

→ UZ Brussel
  • Diagnosis on respiratory samples (PCR; culture for strain typing)
  • Most useful for young children
  • Confirmation of diagnosis/strain identification for other labs

→ WIV-ISP
  • Serological diagnosis (anti-PT IgG; not applicable if vaccine dosis < 1 year)
  • Mostly samples from adults, generally one-point > 3 weeks symptoms
Real-time PCR: which target for which species?

- **Screening assay: IS481-IS1001**
  - High sensitivity: high copy number
  - Low specificity

- **Confirmation assay: IS1002-recA**
  - Lower sensitivity
  - Specificity is high in combination with first assay

- **At first other assays were only performed after positive result in screening**
  - practical difficulties
  - performing both at the same time

<table>
<thead>
<tr>
<th></th>
<th>B. pertussis</th>
<th>B. parapertussis</th>
<th>B. holmesii</th>
<th>B. bronchiseptica</th>
</tr>
</thead>
<tbody>
<tr>
<td>IS481</td>
<td>+++</td>
<td>-</td>
<td>++</td>
<td>+/-</td>
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<tr>
<td>IS1001</td>
<td>-</td>
<td>++</td>
<td>-</td>
<td>+/-</td>
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<tr>
<td>IS1002</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+/-</td>
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<tr>
<td>recA</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>-</td>
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PCR interpretation

- **Sensitivity**
  - IS481: 3 CFU/PCR
  - IS1001: 5 CFU/PCR
  - recA: 52 CFU/PCR
  - IS1002: +/- 40 CFU/PCR

- **Possible outcomes:**
  - Positive for *B. pertussis*
  - Positive for *B. parapertussis*
  - Positive for *B. holmesii*
  - Positive for *B. species*, probably *B. pertussis* if compatible with clinical information
  - Positive for *B. species*, probably *B. parapertussis* if compatible with clinical information
  - **undetermined** (weak positive signal, which was not confirmed by repeating the test, sample should be considered as negative)
Results 2014 (January to October)

- **1201 cases of** *B. pertussis* infection
  - Serology: **808** cases
  - PCR: **385** cases
  - Serology + PCR: **6** cases
  - 2 strains for confirmation by culture

- **88** *B. parapertussis*

- **7** *B. holmesii*
NRC Bordetella: *B. pertussis* cases
Monthly reported cases of B. pertussis

© WIV-ISP | Data source: NRC
Cyclus installation? An outbreak/5 to 7 years?

2002 2007 2014
Culture & PCR cases

![Graph showing the number of cases over years for different types of Bordetella bacteria.]

- B. bronchiseptica
- B. holmesii
- B. parapertussis
- B. pertussis
Cyclus installation? An outbreak/5 to 7 years?
Evolution of virulence factors in 2013

- **Most common MLST types**

<table>
<thead>
<tr>
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<th>MLST- 3</th>
<th>MLST- 4</th>
<th>MLST- 5</th>
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<tr>
<td>ptxA</td>
<td>ptxA1</td>
<td>ptxA1</td>
<td>ptxA1</td>
</tr>
<tr>
<td>ptxC</td>
<td>ptxC1</td>
<td>ptxC1</td>
<td>ptxC2</td>
</tr>
<tr>
<td>tcfA</td>
<td>2</td>
<td>3</td>
<td>2</td>
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</table>

  → In 2013: 93/94 identified as MLST-5

- **Pertactin**

  → 80% in last 13 years was prn2

  → Before 2005: more often other types

- **PtxP**

  → ptxP3 is dominant

  → Few isolates have ptxP1 or ptxP15
SHORT REPORT

Bordetella pertussis seroprevalence in Belgian adults aged 20–39 years, 2012

In the context of the Eupert-Labnet WP6 seroprevalence study (comparing sera from 14 European member states), 1500 anonymized leftover diagnostic samples were collected randomly during the second semester of 2012 by the laboratories of clinical biology of six participating Belgian centres, equally distributed between Flanders, Wallonia and Brussels Capital region. A total of 750 samples (125/centre) were selected from subjects in the age group 20-29 years and 750 samples (125/centre) from subjects in the age group 30-39 years.
Number of sera with anti-PT IgG titer indicative of a recent or acute infection

<table>
<thead>
<tr>
<th>REGION</th>
<th>PROVINCE</th>
<th>50&lt;x&lt;100 IU/ ml&lt;sup&gt;a&lt;/sup&gt;</th>
<th>&gt; 100 IU/ ml&lt;sup&gt;b&lt;/sup&gt;</th>
<th>% Positive</th>
</tr>
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<tbody>
<tr>
<td>Flanders</td>
<td>West-Flanders (AZ Brugge)</td>
<td>13</td>
<td>16</td>
<td>11.6</td>
</tr>
<tr>
<td></td>
<td>East-Flanders (UZ Gent)</td>
<td>8</td>
<td>11</td>
<td>7.6</td>
</tr>
<tr>
<td>Wallonia</td>
<td>Liège (CHU Liège)</td>
<td>12</td>
<td>6</td>
<td>7.2</td>
</tr>
<tr>
<td></td>
<td>Hainaut (CHU Charleroi)</td>
<td>13</td>
<td>14</td>
<td>10.8</td>
</tr>
<tr>
<td>Brussels Capital</td>
<td>UZ Brussel</td>
<td>8</td>
<td>5</td>
<td>5.6</td>
</tr>
<tr>
<td></td>
<td>CHU Bruxelles</td>
<td>7</td>
<td>9</td>
<td>6.4</td>
</tr>
</tbody>
</table>

<sup>a</sup>: anti-PT IgG titre reflecting probable pertussis infection during the past 2 years

<sup>b</sup>: anti-PT IgG titre reflecting probable acute pertussis infection
Sixty-one (4%) sera were indicative of an infection in the past two years (between 50 and 100 IU/ml) and another sixty-one (4%) sera had anti-PT IgG antibodies reflecting acute infection (> 100 IU/ml).

These results highlight the presence of a *Bordetella pertussis* reservoir in the adult ‘healthy’ Belgian population.
Pertussis vaccination scheme

- **Children**
  - 2, 3, 4 months: 3 doses hexavalent vaccine
  - 13 to 15 months: 1 dose hexavalent vaccine
  - 5 to 6 years: 1 dose DTPa-IPV
  - 14 to 16 years: 1 dose dTpa

- **Adults**: 1 dose dTpa
  - Cocoon vaccination: young & future parents, other familial contacts of young children
  - Nursing personnel pediatric, maternity, day care centers …
  - **Pregnant women**: vaccination in third trimester (24-32 w)

- **Duration of immunity**
  - Max 5-10 years (? no correlates of protection)
Maternal Pertussis Vaccination

- An ongoing study on maternal pertussis vaccination in Flanders and Vietnam. Directed by Prof. P. Van Damme and Dr. E. Leuridan (supported by Vlir-UOS and FWO-Nafosted)

- **Eighteen** pregnant women vaccinated with a tetanus-diphtheria-acellular pertussis (Tdap) (Boostrix®) during the third pregnancy trimester

- **Sixteen** age-matched non-pregnant women received the same vaccine in the same time period

- A blood sample was taken at the moment of, but before vaccination and one month and 12 months after vaccination

- Analysis of vaccine specific CMI and IgG responses
Vaccine specific CMI responses after Tdap vaccination

Pregnant women

Non-pregnant women

Lymphoproliferative responses measured in WB (diluted 1:10) after 7 days of culture with Tetanus toxoid (TT), Pertussis Toxin (PT) or Filamentous Haemagglutinin (FHA)

- Transient stimulation of vaccine specific CMI responses
- Stimulation weaker in pregnant than control women

K. Huygen et al, submitted
Vaccine specific IgG antibodies after Tdap vaccination

Significant increase in IgG antibodies to five vaccine components in both pregnant and non-pregnant women at 1 month and 12 months after vaccination.

- Pregnant women
- Control women

K.Huygen et al, submitted
Management of infected patients

- Treatment: no or very limited influence on symptoms
- High risk for severe course (mortality)
  - Unvaccinated neonates & infants < 1 year
  - Children with severe heart or lung disease
- Incubation: 8 to 10 days, never > 21 d
- Contagiousness
  - Without antibiotics: 21 days (from start of catarrhal phase)
  - With adequate antibiotics: 5 days
Secundary prevention

- No source tracking needed: *B. pertussis* circulates in the population
- Perform some risk analysis for protection of high risk patients:
  - Household contacts:
    - Antibiotics only if child < 1 year old or pregnancy > 34 weeks
    - Vaccination check
  - Nursing home, hospital
    - Reinforced surveillance; antibiotics rarely considered
  - Day care center
    - Parents warning, vaccination check
Secundary prevention

- Antibiotics, more for prevention than treatment
  - First choice: azithromycin (5 days until age 6 months, 3 days after age 6 months)
  - Alternative: SXT (not < 2 m old or pregnancy)

- Exclusion from school, day care centers
  - Without antibiotics: 21 days (from start of catarrhal phase)
  - With adequate antibiotics: 5 days
  - Warning and surveillance in schools
Conclusions (1)

- *Bordetella pertussis* is still circulating in the population (5-10% ‘asymptomatic’ infections during the last year, particularly in adults, probably more than in children)

- Rise in number of cases, with a **multifactorial** cause?
  - Waning immunity in adults (less exposure)
  - Switch whole cell wP to acellular aP vaccines
  - Increased awareness of physicians > more analyses (no significant evolution in % of cases)
  - Easier and earlier diagnosis (PCR)
  - Changes in virulence of circulating strains
    - Higher virulence of strains with ptxP3 promoter
    - Less adequacy of vaccine to circulating strains (Prn⁻)
Conclusions (2)

- Improved vaccination strategies are needed (boosting? improved/new vaccines ?)
- Prevention has to be focused on the most vulnerable group: infants below 1 year of age
  - Pregnancy and cocoon vaccination
  - Early infant vaccination (avoid delays)
  - Chemoprophylaxis to all close contacts if case in entourage only if high risk patient present
Acknowledgements

- Sentinel laboratories sending samples
- RIZIV/INAMI for financial support
- WIV/ISP - Epidemiology of Infectious Diseases for organisational support: G. Muyldermans, A. Lizroth
- Co-authors of the serosurveillance study
  D. Govaerts (CHU Charleroi) I. Leroux-Roels (UZ Gent) P. Melin (CHU Liège) M. Reynders (AZ Sint-Jan, Brugge) S. Van Der Meeren (UZ Brussel) S. Van Den Wijngaert (CHU Saint-Pierre)
- Co-authors of the maternal vaccination study
  P. Van Damme/ E. Leuridan Vaxinfectio
- Collaborators of NRC pertussis in particular C. Rodeghiero (WIV), L. Detemmerman & O. Soetens (UZ Brussel)