Pertussis vaccine: does strain variation matter?

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4 questions

• Is *B. pertussis* changing?
• Are the changes in response to vaccination?
• Are these changes advantageous to the bacterium?
• How can we use this information to control pertussis?
Is *B. pertussis* changing?

• Neutral markers:
  – Multilocus variable number tandem repeats analysis (MLVA)
  – Single nucleotide polymorphism typing (SNP typing)

• Isolates from over 40 years

• Isolates from the recent epidemic
Major Australian MLVA types

SNP types

Australian isolates
Other international isolates

Japan isolates
Old isolates

Are the changes in response to vaccination?
Vaccines

- Whole cell vaccine (WCV): 1950s to 1997
- Acellular vaccine (ACV): 2000 onwards
- Transition period, WCV or ACV: 1997-1999
Frequency of SNP clusters by vaccine period in Australia
Variation in genes encoding acellular vaccine antigens

- Acellular vaccine (ACV) components:
  - Pertactin (Prn)
  - Pertussis toxin (PTX)
  - Filamentous haemogglutinin (FHA)
  - Fimbriae (Fim2 and Fim3)

- $ptxP$ – pertussis toxin promoter
Antigenic gene variation

<table>
<thead>
<tr>
<th></th>
<th>Prn</th>
<th>Ptx(A)</th>
<th>FhaB</th>
<th>Fim2</th>
<th>Fim3</th>
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<td>ACV</td>
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<td>A2</td>
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<td>2-1</td>
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<td>Cluster I</td>
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<td>A1</td>
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Strain variation in other parts of the world
UK
The Netherlands
Sweden

Distribution of *ptxP* alleles in strains collected during 1997 until 2006 in the Gothenburg area and in the Rest of Sweden.

<table>
<thead>
<tr>
<th>Area for sample</th>
<th>Gothenburg</th>
<th>Rest of Sweden</th>
<th>Total</th>
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<tr>
<td><em>ptxP</em> allele</td>
<td>1</td>
<td>109 (21)</td>
<td>998 (33)</td>
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<tr>
<td>Number (%)</td>
<td>3</td>
<td>403 (79)</td>
<td>2001 (67)</td>
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<tr>
<td>Total</td>
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<td>512 (100)</td>
<td>2999 (100)</td>
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Advani et al. Vaccine 2011 29 3438
Europe (Netherlands and Sweden)

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<tr>
<th>ST</th>
<th>ptxP1</th>
<th>ptxP3</th>
<th>ptxP4</th>
<th>ptxP6</th>
<th>continent</th>
<th>Earliest isolation year of strain</th>
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van Gent et al. (2011) PLoS ONE 6(5): e20340
Are the changes advantageous?
Prn2

- Allelic specific epitope
  - Prn type-specific antibodies (He et al. 2003)
  - Advantage

- Mouse colonisation
  - Prn1>Prn2 and Prn3 (van Gent et al. 2011)
  - Disadvantage
ptxP3 and pertussis toxin

- *ptxp3* versus *ptxp1* [Mooi et al. (2009)]
  - Increases Ptx production (PtxA1) 1.6x
  - More virulent
Mouse challenge experiments

How can we use this information to control pertussis?

Vaccine
- Prn1
- PtxA2

Strain
- Prn2
- PtxA1
- ptxP3
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