

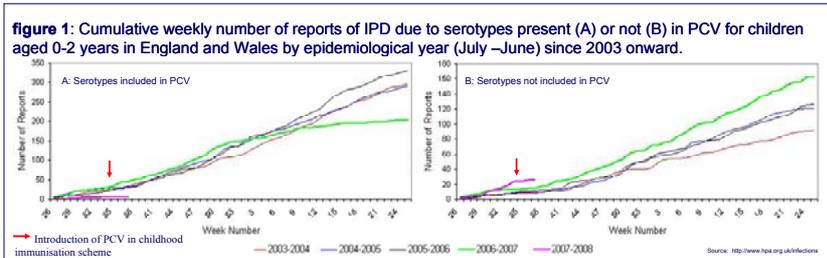
Effect of the introduction of the Pneumococcal Conjugate Vaccine in the UK childhood immunisation scheme on the genetic structure of paediatric invasive pneumococci

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In September 2006, the UK Department of Health launched a pneumococcal immunisation campaign offering the Pneumococcal Conjugate Vaccine (PCV) to all 0-2 years old children as a preventive measure against Invasive Pneumococcal Diseases (IPD). An accompanying surveillance programme has been developed to monitor the effect of the new immunisation scheme on IPD in England and Wales. Soon after the introduction of the PCV (**Figure 1**), a decrease of IPD caused by pneumococci of serotypes included in PCV was observed in children. However a small increase of IPD due to pneumococcal serotypes not included in PCV was observed during the same period. The recent introduction of PCV raises many questions:

- What is the effect of PCV on the genetic structure of the pneumococcal population?
- Are particular virulent clones associated with PNC-7 vaccine failures?
- Will any increase in IPD due to non-PCV serotypes be caused by emergent genotypes, expansion of existing clones or capsular switching or a combination of these phenomena?

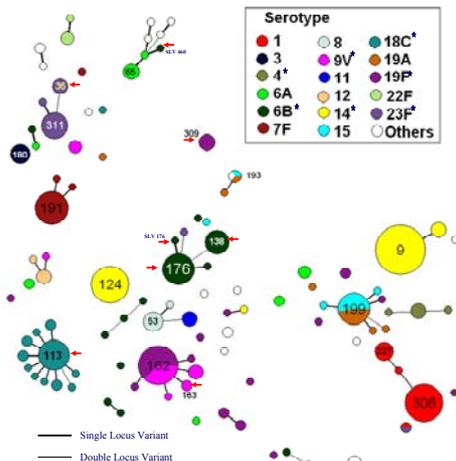


This report focuses on the genetic characteristics of invasive pneumococci isolated from PCV eligible children in England & Wales during epidemiological year 2006/07 (July 2006 – June 2007, the first 10 months of the programme).

Methods

During epidemiological year 2006/07, 360 invasive pneumococci from paediatric cases (0 – 2 years) collected in England and Wales and referred to RSIL for serotyping were analysed by MLST regardless of their serotype. To date, MLST characterization is completed for 290 pneumococci.

Figure 2: Genetic relatedness and serotypic variability of pneumococcal clones collected in England and Wales – Epidemiological year 2006/07



Minimal spanning tree analysis of 290 invasive pneumococci : 70 ST clustered in 41 clones and Clonal Complexes.
Setting : no hypothetical link, neighbour distance = 1.
The size of the circle corresponds to the number of isolates; → ST associated with vaccine failure; * serotypes included in PCV

Findings

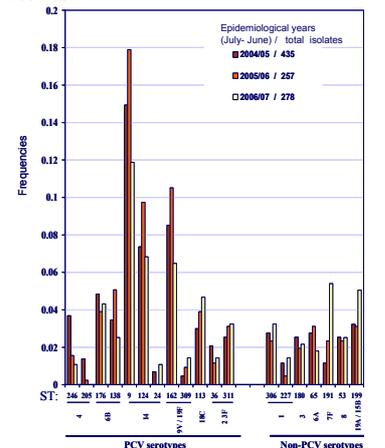
- MLST has identified 70 distinct sequence types (ST) from the international MLST database (<http://spneumoniae.mlst.net>). 18 ST were new clones: 11 new ST associated with vaccine serotypes (6B: n=6; 18C: n=1, 19F: n=4) and 7 new ST associated with non vaccine serotypes (7F: n=2; 8, 15C, 16F, 19A and 24F: n=1).
- The pneumococcal population is polyclonal and there is a high genetic variability within serotypes (**Figure 2**).
- As of 23 October 2007, MLST was carried out on 13 out of 18 vaccine failures observed in England and Wales (**Table 1**). Interestingly, ST163 (9V vaccine failures) is not common in England and Wales. Two clones associated with 6B vaccine failure are new entrants in the MLST database.
- Overall, the distribution of ST did not vary significantly ($p=0.227$) from 04/05 to 06/07. However changes may have occurred for some ST after PCV introduction (**Figure 3**) in particular for ST9, ST124, ST162, (commonly observed in serotypes 14 and 9V/19F) and ST191 and ST199 (serotypes 7F and 19A/15B).
- Increase of non-vaccine serotypes in 06/07 was caused by clones already existing in the pneumococcal population.

Table 1: Genetic characteristic of invasive pneumococci causing PCV failure* in children in England and Wales since 09/2006**

| SEROTYPE | ID | ST | Dose | DATE | REGION |
|----------|-----------|---------|------|--------|--------------------|
| 6B | H05520045 | 138 | 1 | Dec-06 | South West |
| | H07140214 | 176 | 1 | Mar-07 | London |
| | H07134052 | 176 | 2 | Mar-07 | North West |
| | H07154040 | 176 | 1 | Apr-07 | South West |
| | H07284037 | 176 | 2 | Jul-07 | North West |
| 9V | H07080162 | SLV_460 | 1 | Feb-07 | Wales |
| | H07180070 | SLV_176 | 2 | Apr-07 | East of England |
| 18C | H07060003 | 163 | 1 | Jan-07 | South East |
| | H07180103 | 163 | 1 | Apr-07 | Yorkshire & Humber |
| 19F | H07040008 | 113 | 2 | Jan-07 | East of England |
| | H07014078 | 309 | 1 | Dec-06 | Wales |
| 23F | H07200038 | 162 | 2 | Jul-07 | Wales |
| | H07120057 | 36 | 1 | Mar-07 | London |

* Vaccine failure are defined as: IPD due to a PCV serotype (i) in a child with at least 2 doses of PCV before 12 months of age but no subsequent booster and with onset more than 14 days after the second dose or (ii) in a child who had received at least one dose after 12 months of age and with onset more than 14 days after the last dose or (iii) in a child with at least 2 doses in the first year of life and a booster dose after 12 months of age and with onset more than 7 days after the booster dose.

Figure 3: Distribution of major ST of invasive pneumococci causing IPD in children (0-2 years) in England and Wales since epidemiological year 2004/05.



Conclusions

- Changes in the phenotypic and genotypic structure of pneumococci causing IPD may already have occurred after only one year since the introduction of PCV.
- To date, potential serotype replacements are caused by the expansion of existing clones rather than capsular switches or emergence of new clones.
- Ongoing analyses of invasive pneumococci being collected over the next two years should provide meaningful data to assess the short term impact of the PCV on the genetic structure of the pneumococcal population.
- To date, vaccine failures have been caused mostly by common STs associated with vaccine serotypes.

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