

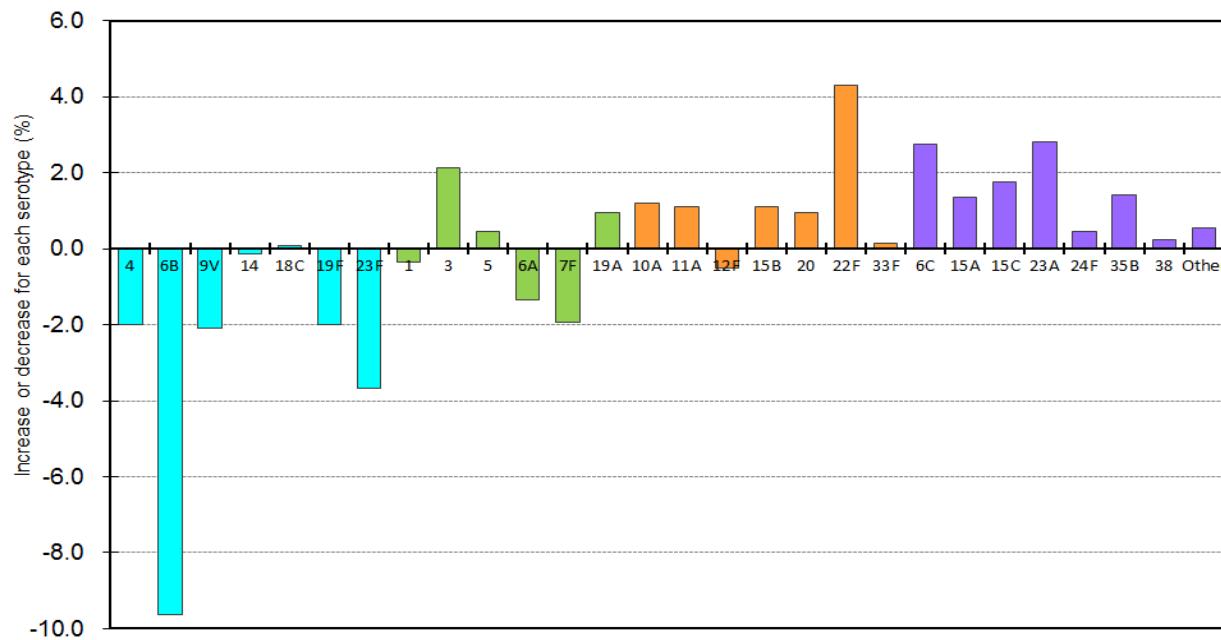
Serotype Changes and Drug Resistance in Invasive Pneumococcal Diseases in Adults after Vaccinations in Children, Japan, 2010–2013

Technical Appendix

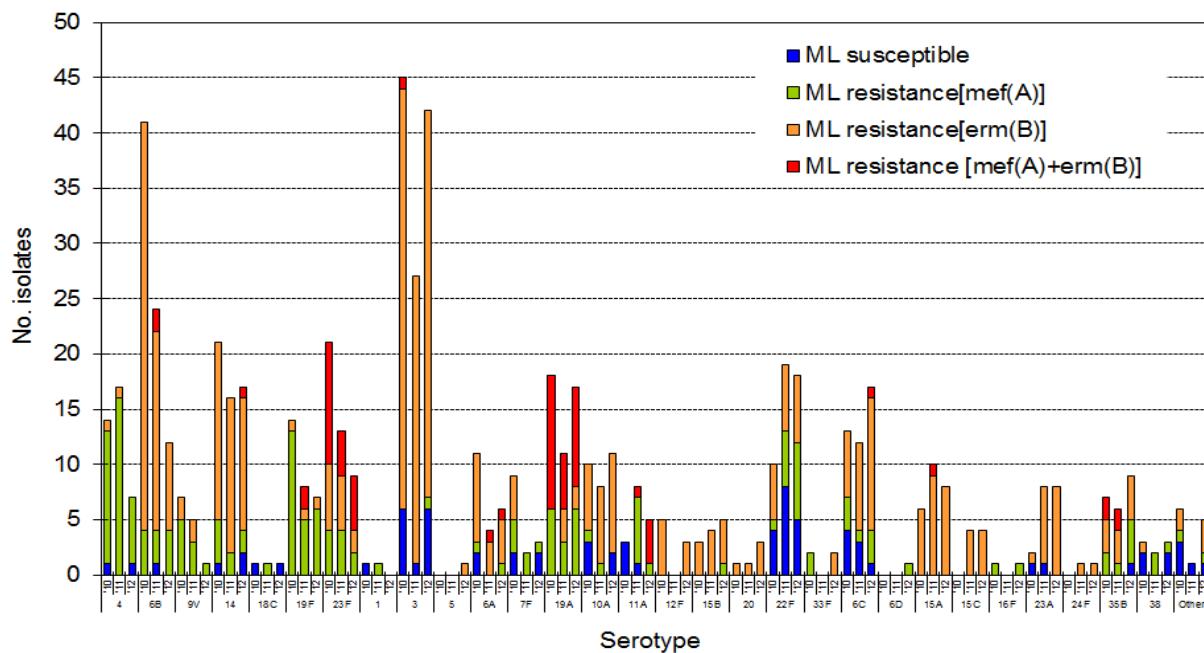
Technical Appendix Table. Susceptibility to 6 parenteral β -lactam antimicrobial agents by genotype class in isolates from adults with invasive pneumococcal diseases, Japan, April 2010–March 2013.

| Antimicrobial agent and genotype class* | Concentration ($\mu\text{g/mL}$) | | |
|---|------------------------------------|-------------------|-------------|
| | MIC_{50} | MIC_{90} | MIC range |
| Penicillin | | | |
| gPSSP (n = 115) | 0.016 | 0.031 | 0.004–0.031 |
| gPISP (<i>pbp2x</i>) (n = 285) | 0.063 | 0.063 | 0.016–0.125 |
| gPISP (<i>pbp1a+2x</i>) (n = 73) | 0.125 | 0.25 | 0.063–1 |
| gPISP (<i>pbp2x+2b</i>) (n = 41) | 0.125 | 0.5 | 0.031–0.5 |
| gPRSP (<i>pbp1a+2x+2b</i>) (n = 184) | | 2 | 0.25–4 |
| Ampicillin | | | |
| gPSSP | 0.031 | 0.031 | 0.004–0.031 |
| gPISP (<i>pbp2x</i>) | 0.063 | 0.125 | 0.008–0.125 |
| gPISP (<i>pbp1a+2x</i>) | 0.125 | 0.5 | 0.031–1 |
| gPISP (<i>pbp2x+2b</i>) | 0.25 | 0.5 | 0.063–1 |
| gPRSP (<i>pbp1a+2x+2b</i>) | 1 | 2 | 0.125–4 |
| Cefotaxime | | | |
| gPSSP | 0.016 | 0.031 | 0.008–0.25 |
| gPISP (<i>pbp2x</i>) | 0.25 | 0.5 | 0.008–0.5 |
| gPISP (<i>pbp1a+2x</i>) | 1 | 1 | 0.125–4 |
| gPISP (<i>pbp2x+2b</i>) | 0.25 | 0.5 | 0.031–0.5 |
| gPRSP (<i>pbp1a+2x+2b</i>) | 1 | 2 | 0.125–8 |
| Ceftriaxone | | | |
| gPSSP | 0.016 | 0.063 | 0.008–0.125 |
| gPISP (<i>pbp2x</i>) | 0.25 | 0.25 | 0.016–0.5 |
| gPISP (<i>pbp1a+2x</i>) | 0.5 | 1 | 0.25–1 |
| gPISP (<i>pbp2x+2b</i>) | 0.25 | 0.25 | 0.063–0.5 |
| gPRSP (<i>pbp1a+2x+2b</i>) | 0.5 | 1 | 0.25–2 |
| Meropenem | | | |
| gPSSP | 0.016 | 0.031 | 0.008–0.063 |
| gPISP (<i>pbp2x</i>) | 0.016 | 0.063 | 0.008–0.125 |
| gPISP (<i>pbp1a+2x</i>) | 0.063 | 0.125 | 0.016–0.25 |
| gPISP (<i>pbp2x+2b</i>) | 0.063 | 0.5 | 0.016–0.5 |
| gPRSP (<i>pbp1a+2x+2b</i>) | 0.5 | 1 | 0.063–4 |
| Panipenem | | | |
| gPSSP | 0.004 | 0.004 | 0.002–0.008 |
| gPISP (<i>pbp2x</i>) | 0.004 | 0.008 | 0.002–0.016 |
| gPISP (<i>pbp1a+2x</i>) | 0.016 | 0.016 | 0.004–0.063 |
| gPISP (<i>pbp2x+2b</i>) | 0.016 | 0.031 | 0.004–0.031 |
| gPRSP (<i>pbp1a+2x+2b</i>) | 0.063 | 0.125 | 0.008–0.25 |

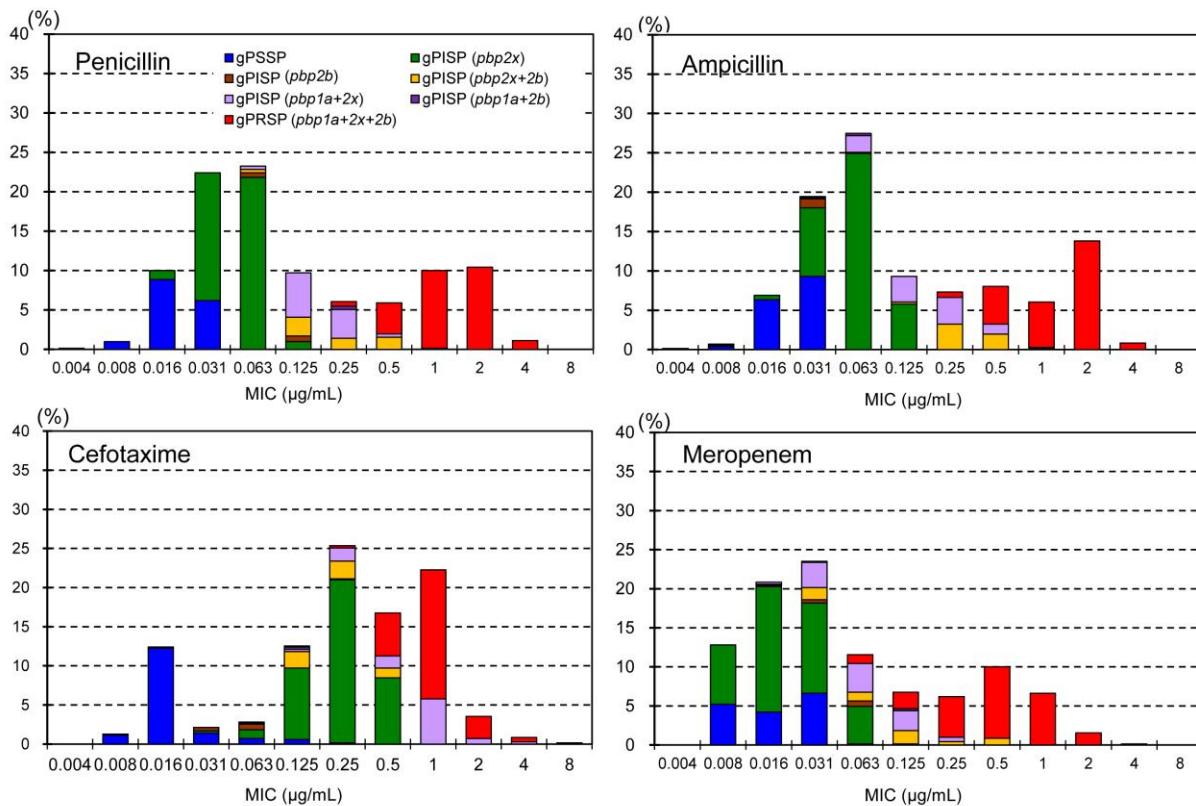
*Results of gPISP (*pbp2b*) (n = 9) and gPISP(*pbp1a+2b*) (n = 3) were omitted because of a low number of strains.



Technical Appendix Figure 1. Comparison of proportional increases and decreases in serotypes in isolates from adults with invasive pneumococcal diseases, Japan, from first surveillance period (April 2010–March 2011) to third surveillance period (April 2012–March 2013). Blue indicates serotypes included in PCV7; green indicates serotypes included in PCV13; orange indicates serotypes included in PPSV23; and purple indicates serotypes not included in PPSV23.



Technical Appendix Figure 2. Changes in number of serotypes and in macrolide (ML) resistance by genotype in isolates from adults with invasive pneumococcal diseases for 3 yearly surveillance periods, Japan, April 2010–March 2013. ML susceptible indicates not possessing any ML-resistance gene; ML resistance [*mef*(A)] indicates possessing *mef*(A) gene mediating ML-intermediate resistance to 14-membered MLs and azalide; ML resistance [*erm*(B)] indicates possessing *erm*(B) gene mediating ML-high resistance; and ML resistance [*mef*(A)+*erm*(B)] indicates possessing both resistance genes.



Technical Appendix Figure 3. Distribution of susceptibilities to 4 parenteral β -lactam antimicrobial agents (penicillin, ampicillin, cefotaxime, and meropenem) by genotype in isolates from adults with invasive pneumococcal diseases, Japan, April 2010–March 2013. gPSSP indicates genotypic penicillin-susceptible *Streptococcus pneumoniae*; gPISP indicates genotypic penicillin-intermediate–resistant *S. pneumoniae*; and gPRSP indicates genotypic penicillin-resistant *S. pneumoniae*. Parentheses enclose abnormal *pbp* genes mediating penicillin resistance.