

Invasive methicillin-resistant *Staphylococcus aureus*: French epidemiological dynamics from 2006 to 2011

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Objectives: The aim of this study was to characterize invasive methicillin-resistant *Staphylococcus aureus* (MRSA) isolates collected during a 2011 six-month period in France and compare data with those obtained in 2006 using the same protocol. **Methods:** We conducted a prospective multicenter study of invasive (bacteraemia) MRSA strains, including the first five consecutive blood culture isolates, collected between January and July 2011 in 29 hospitals located throughout France. The strains were extensively characterized using antibiotic susceptibility patterns, *agr* typing, *spa* typing, SCCmec typing, toxin profiling and DNA microarrays (StaphyType, Alere). Clones were designated by their sequence type (ST) followed by their SCCmec type (I to VI). **Results:** A total of 127 isolates were included (see Figure 1). Five main clones were identified: the ST8-IV Lyon clone (or UK-EMRSA-2, n=74, 58.3%), the ST5-VI New Paediatric clone (n=22, 17.3%), the ST5-IV old Paediatric clone (n=10, 7.9%), the ST22-IV (or UK-EMRSA-15, n = 8; 6.3%), the ST5-I Geraldine clone (n = 3; 2.4%) and the ST80-IV European CA-MRSA clone (n = 3, 2.4%). The seven remaining isolates were related to six other clones. The Lyon clone remains the most prevalent MRSA clones in France compared to a similar previous study in 2006. Since 2006, the evolution is marked by the significant increased rate of the ST5-MRSA-VI New Pediatric clone (p=0.015) and the concerning emergence of the ST22-IV clone (p=0.006). Besides, this latter has been involved recently in several outbreaks within French neonatal units. Data from DNA microarrays provide a accurate picture of virulence and resistance profiles of the various invasive clones circulating in France and their genetic plasticity. **Conclusion:** Our results highlight i) the interest of epidemiological surveillance of MRSA circulating in each European country to be able to follow the dynamic of the various clones and adapt the management of invasive MRSA infections, ii) the dynamic of MRSA clones demonstrating the potential dissemination and/or emergence of specific MRSA clones at country scale in a short period of time.

| Clone | <u>spa-type</u> | Features: <u>toxin genes;</u> <u>antimicrobial susceptibility patterns</u> | 2006 n=111 | 2011 n=127 | P value* |
|----------------------|-------------------------|---|---------------|---------------|----------|
| ST8-IV Lyon | <u>t008 and related</u> | R to Pen, Met, <u>Flq</u> | 69.4% | 58.3% | 0.050 |
| ST5-VI New Pediatric | <u>t777</u> | <u>sed, sej, ser, egc operon;</u> R to Pen, Met, <u>Flq</u> | 7.2% | 17.3% | 0.015 |
| ST5-IV Old Pediatric | <u>t002 and related</u> | <u>egc operon;</u> R to Pen, Met, <u>Flq</u> | 8.1% | 7.9% | 0.567 |
| ST22-IV UK-EMRSA 15 | <u>t032 and related</u> | <u>sec, sed, sej, ser, sel, egc operon;</u> R to Pen, Met, <u>Flq</u> | 0% | 6.3% | 0.006 |
| ST5-Geraldine | <u>t002 and related</u> | <u>tst, sec, sed, sej, ser, sel, egc operon;</u> R to Pen, Met, <u>Fus</u> and variably R to <u>Kan, Tobra</u> | 6.3% | 2.4% | 0.117 |
| ST80-IV European | <u>t044</u> | <u>luk-PV, etd, edin;</u> R to Pen, Met, Kan, Fus | 3.6% | 2.4% | 0.426 |
| Others | - | - | 5.4% | 5.4% | 0.600 |

spa, staphylococcal protein A; tst, toxic shock syndrome toxin 1 gene; sec, sed, sej, ser, sel, staphylococcal enterotoxin; egc, enterotoxin gene cluster containing seg, sej, sem, sen, seo and seu genes; luk, staphylococcal leukocidin; edin, epidermal cell differentiation inhibitor; etd, exfoliatin D; Pen, penicillin; Met, methicillin; Kan, kanamycin; Tob, tobramycin; Flq, fluoroquinolone; Fus, fusidic acid. *P value for differences between percentages found in 2006 and 2011 were calculated using Fisher's exact test.

Table 1. Characteristics and dynamic of the most frequent invasive MRSA clones isolated in France in 2006 and 2011.