Epidemiology of human MRSA in Europe and public health importance of animal strains

Carl Suetens, ECDC, 08/04/2008
Why was ECDC established?

- Emerging and re-emerging communicable diseases revitalised through globalisation, bio-terrorism, interconnectivity, and EU without internal borders
- Health implications of enlarging EU
- Strengthen EU public health capacity to help meet EU citizen's concerns
What is the role of ECDC?

Identify, assess & communicate current & emerging health threats to human health from communicable diseases (ECDC Founding Regulation (851/2004), Article 1)

- EU level disease surveillance
- Scientific opinions and studies
- Early Warning System and response
- Technical assistance and training
- Epidemic intelligence
- Communication to scientific community
- Communication to the public
Evolution of resistance in *S. aureus*

- **1940s**: Penicillin
- **1942 – 1950s**: Methicillin
- **1980s**: Vancomycin
- '97 VISA, => 2002: Vancomycin-Resistant Enterococci (VRE)

**S. aureus** → **PRSA** → **MRSA** → **VRSA**

![Diagram showing increasing genome complexity and evolutionary timeline](whyfiles.org/shorties/085/fast_evolution)
Impact of MRSA infections

• *S. aureus* bacteremia before 1940: 80% associated mortality => 20-30% after introduction of penicillin

• Mortality MRSA bacteremia vs MSSA bacteremia
  – Cosgrove et al., *Clin Infect Dis*, 2003, 36, 53-59 (metaanalysis): Pooled OR 1.9 (95% CI 1.5-2.4)

• Morbidity & mortality MRSA vs MSSA in pneumonia
  – Shorr. Morbidity and cost burden of MRSA in early onset VAP. Critical care 2006, 10:R97
  – Most mortality studies negative, eg Combes et al. Impact of Methicillin Resistance on Outcome of S. aureus VAP. *Am J Respir Crit Care Med*, 2004, 170, 786-792
European Surveillance of MRSA: EARSS 1999-2007

• Number of samples per species per year

![Graph showing number of samples per species per year from 1999 to 2006.](image)
Evolution of MRSA resistance rates in blood isolates in Europe, 2001-2006 (EARSS)

Proportion of MRSA isolates in participating countries in 2006
(c) EARSS

Legend:
- No Data
- < 1%
- 1-5%
- 5-10%
- 10-25%
- 25-50%
- > 50%
MRSA: trends, 1999-2006
MRSA: 3 epidemiological patterns

Healthcare-associated MRSA

Community-associated MRSA

Animal MRSA
Healthcare-associated MRSA

• First described in UK, 1961 – clonal waves, MDR in ’80s
• Infections: Bloodstream infections, Hospital-acquired Pneumonia, Surgical site infections, Urinary tract infections, ...
• Risk factors: hospitalisation, invasive devices, underlying illness, AB use => later also LTCF (nursing homes...)
• ± 4% of all nosocomial infections in the EU (\textit{S. aureus} 15% (prevalence surveys), 24% mean %MRSA (EARSS))

=> ± 1-200,000 nosocomial MRSA infections per year in EU27

• Major clones < 4 MRSA lineages (CC5, CC8, CC22, CC45), e.g. UK E-MRSA-15&16, Iberian... (SCC\textit{mec} types I,II, III + IV)
Community-associated MRSA

- First described in Australia, 1993 (indigenous population)
- Frequent Panton-Valentine Leukocidin (PVL) positive, less MDR
- Infections: Skin and soft tissue infections, septic arthritis, TSS, necrotising pneumonia
- Main risk factor: high intensity physical contact (jailed inmates, MSM, military recruits, sportsmen, children in day care centres), younger patients
- Major clones: USA300 (ST8-SCC\textit{mec} IV), ST30 (Australia, Europe), ST80 (Mediterranean clone), ST-8 (French clone), …
- Emergence in hospitals, mainly US (e.g. King MD et al. Emergence of community-associated methicillin-resistant \textit{Staphylococcus aureus} USA300 genotype as a major cause of health care-associated blood stream infections. Clin Infect Dis. 2006 Mar 1;42(5):647-56)
- More sensitive to antibiotics (fluoroquinolones, tetra, ctmx)
Animal MRSA in humans: occurrence

- Non-typable by PFGE with *Sma1* restriction digest (NT-MRSA)
- MLST type ST398, major *spa* types: t011, t108, t034, t567
- Mostly PVL negative, 1 PVL+ ST398 report from China
- Netherlands, France, Denmark, Germany, Austria, Italia, Spain, Hong-Kong, Thailand, Canada, Belgium
- MRSA carriage in pigs and pig farmers:
  - NL: 11 to 39% MRSA+ pigs in farms and slaughterhouses
  - Canada (20 farms, Khanna et al, 2007): farmers 20%, pigs 25%
  - BE: representative national survey in 50 pig farms, 2007 (BAPCOC report; O. Denis et al., 2008): farmers 37.8% (95% CI 25.6-50.0%), pigs 44%
- High prevalence in veterinarians:
  - 34/272 (12.5%) from 9 countries at international conference in Denmark, 31/34 ST398 (Wulf MW et al., CMI 2008, 14, 29-34)
Animal MRSA in humans: risk factors

- NL (case-control study national MRSA database, Van Loo et al. EID 2007): contact with pigs (OR 12) and cattle (OR 20)
- BE (national prevalence survey in pig farms, cross-sectional): frequency of pig contact (OR 10), reported contact with dogs (OR 16) and horses (OR 5)
- Canada (veterinary conference): large-animal practice (OR 2.9)
- Reported protective measures (masks, gowns, gloves) often no effect => needs further research
- Resistance to doxycycline => spread facilitated by abundant use of tetracyclines in farming (De Neeling et al., Vet Microbiol. 2007)
Proportion of human MRSA isolates resistant to antibiotics, pig farmers and relatives, Belgium 2007

Source: Belgian Reference Laboratory for Staphylococci – MRSA (Struelens, Denis)
Consumption of Prescribed Antimicrobials and Growth Promoters in Animal Production and Prescribed Antibacterials in Humans, Denmark, 1990-2006

Adapted from: DANMAP2004 report.
Antibacterial Drugs for Therapeutic Use in Food Animals, Netherlands, 1997-2005

Source: MARAN 2005 report.
Animal MRSA: impact

- NT-MRSA cases found in national surveillance of MRSA in hospitals (e.g. NL, BE)
- First hospital outbreak described (Wulf et al. First outbreak of MRSA ST398 in a Dutch hospital, June 2007. Euro Surveill 2008;13(9)):
  - 5 patients (2 diabetic foot ulcers) and 5 healthcare workers (238 screened)
  - Spa type t567
  - Possible source: HCW living on grounds of pig farm
Proportion of animal MRSA in national surveillance in The Netherlands

Wannet W.J.B. et al. Infectieziekten bulletin 2007, 18 (10), 347-351
## Human infections with MRSA ST398 in Belgium

<table>
<thead>
<tr>
<th>Année</th>
<th>Sexe</th>
<th>Age (ans)</th>
<th>Source</th>
<th>Unité d’hospitalisation</th>
<th>Acquisition</th>
<th>Commune</th>
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<td>Pus</td>
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<td>NP</td>
<td>Roeselaere</td>
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</table>

Source: Belgian Reference Laboratory for Staphylococci – MRSA (Struelens, O. Denis)

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**Figure 1.** (a) Fore arm after initial debridement (7 March 2006). (b) Fore arm after final treatment (22 March 2006).
Public health importance

• Farmers, veterinarians and family:
  – *S. aureus* carriage in hospitals => risk of infection vs non-carriage x 4 (Safdar and Bradley, Am J Med, 2008, 121, 310-5)
  ⇒ increased risk of MRSA infection if hospitalized = \(0.05_{NI} \times 0.15_{SA} \times 0.6_{MRSA\%} \times 4 = 1.8\%\)
  ⇒ First line treatment of infections (e.g. skin) in this population may be ineffective

• Potential for inter-human transmission & hospital epidemics
  ⇒ New challenge for MRSA control, particularly low-prevalence countries
  ⇒ Need for adapted guidelines: MRSA screening in hospital e.g. at admission, impact on infection control procedures in hospitals (isolation, decolonization etc)

• Food hygiene (van Loo IH et al. Methicillin-resistant *Staphylococcus aureus* in meat products, the Netherlands. Emerg Infect Dis. 2007 Nov;13(11):1753-5)