MRSA: an introduction

Jaap Wagenaar, DVM, PhD

Dept. Infectious Diseases and Immunology, Faculty of Veterinary Medicine, Utrecht University, Utrecht, the Netherlands

Central Veterinary Institute, Lelystad, The Netherlands

j.wagenaar@uu.nl
Outline

- *Staphylococcus aureus* (humans, animals)

- MRSA
  - General characteristics of MRSA
  - CA-MRSA, HA-MRSA
  - Typing of MRSA
  - MRSA in farm animals
  - MRSI in companion animals

- Final remarks
**Staphylococcus aureus**

- Gram positive cocci

**Cause of several veterinary problems:**
  - bovine mastitis
  - problems in equine
  - joints problems in chickens
  - systemic disease in pigs (rare)
  - pyodermia dog (more often *S. intermedius*)

**Human:** 33% of healthy people are carrier

**Veterinary carriers**
**S. aureus** becomes MRSA.....

......by acquiring *mecA* gene

- Methicillin Resistant *Staphylococcus aureus*
- Chromosome (Staphyloccal Chromosome Cassette - SCC*mec*)
- Penicillin binding protein PBP2a
- Resistant against all beta-lactam antimicrobials - penicillines, cephalosporines

(beta-lactamase inhibitors like clavulanic acid are not active)
HA-MRSA and CA-MRSA (humans)

- **HA-MRSA:** Hospital acquired
  - emerged in the 60’s (after introduction of methicillin in 1959)
  - multi-resistant but lame
  - antibiotic usage facilitates spread
  - most important control method is prevention of cross-infection

- **CA-MRSA:** Community associated
  - emerged in the 90’s
  - in community – no relation health care settings
  - resistance moderate but often toxin (PVL+)
  - risk factors
A clone of methicillin-resistant *Staphylococcus aureus* among professional football players.
(Kazakova et al, 2005)

**BACKGROUND:** Methicillin-resistant *Staphylococcus aureus* (MRSA) is an emerging cause of infections outside of health care settings. We investigated an outbreak of abscesses due to MRSA among members of a professional football team and examined the transmission and microbiologic characteristics of the outbreak strain. **METHODS:** We conducted a retrospective cohort study and nasal-swab survey of 84 *St. Louis Rams* football players and staff members. *S. aureus* recovered from wound, nasal, and environmental cultures was analyzed by means of pulsed-field gel electrophoresis (PFGE) and typing for resistance and toxin genes. MRSA from the team was compared with other community isolates and hospital isolates. **RESULTS:** During the 2003 football season, eight MRSA infections occurred among 5 of the 58 Rams players (9 percent); all of the infections developed at turf-abrasion sites. MRSA infection was significantly associated with the lineman or linebacker position and a higher body-mass index. No MRSA was found in nasal or environmental samples; however, methicillin-susceptible *S. aureus* was recovered from whirlpools and taping gel and from 35 of the 84 nasal swabs from players and staff members (42 percent). MRSA from a competing football team and from other community clusters and sporadic cases had PFGE patterns that were indistinguishable from those of the Rams’ MRSA; all carried the gene for Panton-Valentine leukocidin and the gene complex for staphylococcal-cassette-chromosome mec type IVa resistance (clone USA300-0114). **CONCLUSIONS:** We describe a highly conserved, community-associated MRSA clone that caused abscesses among professional football players and that was indistinguishable from isolates from various other regions of the United States.
<table>
<thead>
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<th>Rank</th>
<th>Player</th>
<th>Salary (US$)</th>
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<tr>
<td>1</td>
<td>Orlando Pace</td>
<td>$18,000,000</td>
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<td>Isaac Bruce</td>
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<td>Jeff Wilkins</td>
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<td>La'Roi Glover</td>
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<td>Dexter Coakley</td>
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<td>6</td>
<td>Marshall Faulk</td>
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<td>7</td>
<td>Leonard Little</td>
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<td>Daren Bennett</td>
<td>$2,751,050</td>
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<td>Stephen Davis</td>
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<td>11</td>
<td>Steven Jackson</td>
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<td>Randy McMichael</td>
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<td>15</td>
<td>Jason Field</td>
<td>$1,769,510</td>
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<td>Kan Bartel</td>
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<td>Sus Frerotte</td>
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<td>Lenny Walls</td>
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<td>Will Witherspoon</td>
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<tr>
<td>21</td>
<td>Alex Barron</td>
<td>$1,230,000</td>
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</table>
MRSA: typing

- Staphylococcal Cassette Chromosome \textit{mec} (SCC\textit{mec})
  - 5 identified SCC\textit{mec} types I, II, III, IV, V, (VI)

- Typing:
  - PFGE
  - Spa-typing
  - MLST

- NT-MRSA
MRSA: typing

- Staphylococcal Cassette Chromosome mec (SCCmec)
  - 5 identified SCCmec types I, II, III, IV, V, (VI)

- Typing:
  - PFGE
  - Spa-typing
  - MLST

- NT-MRSA
MRSA in hospitals: a problem?
% of blood isolates of *S. aureus* resistant to methicillin

- Greece: 45%
- UK: 40%
- Malta: 30%
- Ireland: 25%
- Israel: 20%
- Italy: 15%
- Portugal: 10%
- Croatia: 5%
- Romania: 4%
- Bulgaria: 3%
- France: 2%
- Belgium: 1%
- Spain: 1%
- Poland: 0%
- Germany: 0%
- Luxembourg: 0%
- Slovenia: 0%
- Austria: 0%
- Hungary: 0%
- Slovakia: 0%
- Czech Republic: 0%
- Denmark: 0%
- Estonia: 0%
- Finland: 0%
- Netherlands: 0%
- Sweden: 0%
- Iceland: 0%

Proportion of blood isolates of *S. aureus* resistant to methicillin in Europe, 2002
Proportion of blood isolates of *S. aureus* resistant to methicillin in Europe, 2002

MRSA in Europe

Proportion of blood isolates of *S. aureus* resistant to methicillin in Europe, 2002

% of blood isolates of *S. aureus* in US hospitals: 60% MRSA

- Iceland
- Sweden
- Netherlands
- Finland
- Estonia
- Denmark
- Czech Republic
- Slovakia
- Hungary
- Austria
- Slovenia
- Luxembourg
- Germany
- Poland
- Spain
- Belgium
- France
- Bulgaria
- Romania
- Croatia
- Portugal
- Italy
- Israel
- Malta
- UK
- Greece
MRSA in health care settings

- MRSA infections are more difficult to treat
  - less effective antibiotics available
  - no new drugs on the horizon
  - without an effective control strategy > 50-60%
  - high morbidity and mortality
  - increases costs (more expensive drugs, longer duration of hospitalization, more diagnostics)
MRSA and animals (slide 2003....)

- MRSA in dogs, cats, rabbits, horse, chickens, cattle, pigs: sporadic cases
- MRSI in dogs with pyodermia from Spanje
- Methicillin resistant CoNS in sheep UK and horses from Japan
2004: 3 human cases NT-MRSA pig related (NL)

- Daughter of a pig farmer (+ pigs)
- Son of pig veterinarian
- Pig farmer (+ pigs)
- Studygroup pig farmers (23% +)

- Not identified as risk group!
- Till 2002 no “pig-MRSA” (NT-MRSA)
- Many pig farmers, many people in contact with pigs, nurses living on farms……..
Pigs: preliminary screening

- 9 slaughterhouses with 6 herds each (10 swabs per herd):
  - 209/540 pig +
  - 44/54 herds +

- All isolates tetracyclin resistant

- All isolates TMPS sensitive

- No clinical signs in pigs

De Neeling et al., Vet. Microbiol. 2007

- Cross-sectional study: 40% pigs (RIVM/GD/WUR)
## MRSA in different kinds of pig farms

- Screening of 31 pig farms (farrowing, rearing and finishing)
- 7/31 farms MRSA positive (23 %)
- 1 farm MRSA negative, farmer MRSA positive
  - Treatment with tetracycline
  - 8/10 pigs MRSA positive
- All MLST 398, NT-MRSA
- Use of antibiotics risk factor

Van Duijkeren et al., Vet Micobiol. 2007

- More about risk factors: study Els Broens RIVM/GD/WUR
Clinical disease in pigs?

- One case with exsudative dermatitis

Methicillin-Resistant *Staphylococcus aureus* in Pigs with Exudative Epidermitis

Engeline van Duijkeren,* Marc D. Jansen,† S. Carolien Flemming,* Han de Neeling,‡ Jaap A. Wagenaar,* Anky H.W. Schoormans,* Arie van Nes,* and Ad C. Fluit‡

EID 2007
Humans and NT-MRSA

- Many asymptomatic carriers (farmers etc)
- Few clinical cases are described
- Source: case control study => pig and cattle farmers
- Problem: risk for introduction into hospitals
- Spread within hospitals does not (yet) occur often (but what if.....)
- MRSA in food
- Risk for humans – specific groups – community
What is the origin of MRSA in pigs?

- emerging and not only by improved detection
- coagulase negative Staphylococci contain resistance cassette - transfer of genetic material?
- non MRSA ST398 was already in pigs!
- NT-MRSA clonal but not the same: one recombination and subsequently development of this clone into diverse lines?
- Not restricted to the Netherlands
MRSA Transmission between Cows and Humans

Éva Juhász-Kaszanyitzky,* Szilárd Jánosi,*
Pál Somogyi,* Ádám Dán,*
Linda van der Graaf-van Bloois,†‡
Engeline van Duijkeren,‡
and Jaap A. Wagenaar†‡

We isolated methicillin-resistant *Staphylococcus aureus* (MRSA) from cows with subclinical mastitis and human patients with MRSA-positive skin lesions. The MRSA strains isolated from the cows were identical to those isolated from humans. The results suggest that MRSA can be transmitted from cows to humans through direct contact or the environment.
Isolation of MRSA/MRSI from companion animals

Year | Number MRSI
--- | ---
2005 | 5
2006 | 15
2007 | 80
Isolation of MRSI from companion animals

Transmission of methicillin-resistant *Staphylococcus intermedius* between humans and animals.

Dutch MRSA programme (Min Agriculture)

1. MRSA Prevalence and risk factors
   - In pigs
   - In veal calves
   - In poultry
   - In cattle
   - In farmers
   - In slaughterhouse workers

2. MRSA transmission in production chains

3. MRSA in raw meats

4. MRSA and Disease

Programme management
Communication and education
Data management & internet wg environment
Harmonization & optimalization MRSA detection
Genotyping MRSA isolates
Resistance testing MRSA isolates
Genetic characterization MRSA

UNIVERSITEIT UTRECHT
OIE
CENTRAL VETERINARY INSTITUTE WAGENINGEN
1. MRSA Prevalence and risk factors
   - In pigs
   - In veal calves
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   - In cattle
   - In farmers
   - In slaughterhouse workers

Dutch MRSA programme (Min Agriculture)

- RIVM
- Faculty of Veterinary Medicine
- Animal Health Service (GD)
- Central Veterinary Institute
- Erasmus University
- University Medical Center Utrecht
- Food Safety Authority (VWA)
- VU-Medical Center
- Amphia hospital Breda
Wat did we learn?

- To differentiate HA-MRSA, CA-MRSA and NT-MRSA
- Different typing methods available for MRSA
- NT-MRSA is emerging in production animals
- NT-MRSA is clonal
- MRSI may be emerging in companion animals
Thanks to:

- Engeline van Duijkeren
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- Dick Heederik
- Isabella Oosting
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- Arie van Nes
- Ad Fluit
- Marc Jansen
- Marjan Wassenberg
- Annet Troelstra
- Jan Kluymans
- Mireille Wulf
- Arjen van de Giessen
- Han de Neeling
- Xander Huijsden
- Peter van der Wolf
- Els Broens
- Enne de Boer