What’s the Real Deal with MRSA in Pigs, Pork & People?

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University of Minnesota
Outline

- *Staphylococcus aureus* and MRSA
- MRSA in human medicine
  - Changing patterns
- MRSA in animals
  - ‘Livestock associated’ MRSA
- What we do and don’t know
- Implications
Staphylococcus aureus

- Staphylococcus genus – 33 species, most harmless
- *S. aureus*
  - Normal inhabitant of warm-blooded animals
  - Opportunistic pathogen
- Most common bacteria in infections of people
  - Bloodstream, lower respiratory tract, and skin/soft tissues
  - Can cause serious invasive disease and death
Context

- 30% of healthy people carry *S. aureus*
  - 20% permanent
  - 60% transient
  - 20% never

- *S. aureus* readily acquires resistance to antibiotics
  - MRSA are resistant to methicillin and all related antibiotics
  - Methicillin is a penicillin analog no longer used to treat *S. aureus*
  - MRSA are often also resistant to other unrelated antibiotics
  - Both MRSA and ‘MSSA’ can cause fatal disease
Antimicrobial resistance in *S. aureus*

- **Hospital acquired MRSA**
  - Vancomycin, linezolid, quinupristin-dalfopristin, tigecycline, daptomycin
- **Community acquired MRSA**

**Timeline**
- **1940s**: Penicillin
- **1960s**: Methicillin
- **1990s**: Penicillin resistant *S. aureus*, Methicillin resistant *S. aureus*, Still little resistance

Flowchart:
- S. aureus → Penicillin resistant *S. aureus* → Methicillin resistant *S. aureus* → Still little resistance
Not all *S. aureus* (or MRSA) are equal!

- Many methods used to ‘type’ strains of *S. aureus*
  - More ‘clonal’ than many other bacterial species
- Particular clones dominate in epidemiological niches
  - Hospital acquired
  - Community acquired
  - Livestock associated (ST398)
- 34 known ‘virulence determinants’ occur variably among *S. aureus* isolates
Proportion of *S. aureus* clinical isolates that are MRSA varies greatly among countries

USA
- 50% of clinical isolates are MRSA
- 1.5% of healthy population carry MRSA

Holland
- 1% of clinical isolates are MRSA
- 0.03% of healthy population carry MRSA
Conventional wisdom – MRSA

- Major nosocomial (hospital acquired) infection
  - Problem of chronically ill patients in institutions
- Resistance linked to antimicrobial use in hospitals
- Not a concern for broader, ‘healthy’ community
- Animal reservoirs not important
  - Nor antimicrobial use in animals
‘Quantum Change’ in MRSA epidemiology

- Global emergence of Community Acquired MRSA
  - Different clones than hospital acquired (HA-MRSA)
  - More superficial infections (but some fatalities)
  - Multiple resistance less common than HA-CAMRSA
- Emergence/increased recognition of MRSA in animals
  - Companion and zoo animals
  - Livestock
Staphylococci in animals

- Ubiquitous
- Multiple species including *S. aureus*
- Typically not major pathogens
  - Sporadic infections of soft tissues
  - Wound infections, abscesses etc
- *S. aureus* disease
  - Bovine mastitis
  - Rabbits
- Pigs
  - ‘Greasy pig’ - *S. hyicus*
## MRSA in animals (adapted from Leonard 2007)

<table>
<thead>
<tr>
<th>Years</th>
<th>Cattle</th>
<th>Cat</th>
<th>Dog</th>
<th>Horse</th>
<th>Chicken</th>
<th>Sheep</th>
<th>Rabbit</th>
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MRSA in animals

- Strains in pets generally human epidemic strains
- Strains from other species usually not human epidemic strains (Leonard 2007)
  - Cattle, horse, pig
- Strong evidence of transmission between humans and other species
- High prevalence in veterinarians and animal handlers
# MRSA in veterinary groups

<table>
<thead>
<tr>
<th>Study population</th>
<th>Country</th>
<th>Prev.</th>
<th>Reference</th>
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</thead>
<tbody>
<tr>
<td>Small animal (SA) Vets.</td>
<td>USA</td>
<td>4.4%</td>
<td>Hanselman et al. (2006)</td>
</tr>
<tr>
<td>Vets./students-livestock contact</td>
<td>Holland</td>
<td>4.6%</td>
<td>Wulf et al. (2006)</td>
</tr>
<tr>
<td>AASV 2008 attendees (US Vets)</td>
<td>USA</td>
<td>5.6%</td>
<td>Davies (unpublished)</td>
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<tr>
<td>Equine Vets.</td>
<td>USA</td>
<td>10.1%</td>
<td>Anderson et al. (2007)</td>
</tr>
<tr>
<td>Vet. Technicians</td>
<td>USA</td>
<td>12.0%</td>
<td>Hanselman et al. (2006)</td>
</tr>
<tr>
<td>Equine farm personnel</td>
<td>Canada</td>
<td>12.0%</td>
<td>Weese et al. (2005a)</td>
</tr>
<tr>
<td>IPVS attendees</td>
<td>Multiple</td>
<td>12.5%</td>
<td>Wulf et al (2007)</td>
</tr>
<tr>
<td>Horse owners and Vets</td>
<td>USA/Canada</td>
<td>13.0%</td>
<td>Weese et al. (2005b)</td>
</tr>
<tr>
<td>Equine vet. hopital personnel</td>
<td>Canada</td>
<td>14.0%</td>
<td>Weese et al. (2005a)</td>
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<tr>
<td>Large animal Vets.</td>
<td>USA</td>
<td>15.6%</td>
<td>Hanselman et al. (2006)</td>
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<tr>
<td>Small animal vet. clinic staff</td>
<td>UK</td>
<td>18.0%</td>
<td>Loeffler et al. (2005)</td>
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<tr>
<td>People: veal calf contact</td>
<td>Holland</td>
<td>32.0%</td>
<td>Graveland et al (2008)</td>
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<tr>
<td>Hospitalized people: pig/calf contact</td>
<td>Holland</td>
<td>32.0%</td>
<td>van Rijen et al (2008)</td>
</tr>
</tbody>
</table>

Adapted from Weese and van Duijkeren 2009
Holland – an issue emerges!

- Very low MRSA prevalence
  - ‘Search and destroy’ policy
  - Common preoperative screening
  - All isolates typed with sma1 PFGE
- 2005: 3 ‘cases’ not typable (NT) on sma1 PFGE
  - All epidemiologically linked to pig farming
- Prompted a study of MRSA prevalence in pigs
MRSA in market hogs  
(de Neeling et al., 2006)

- National survey of market hogs in Holland
  - 39% positive (nasal swabs)
- All isolates a ‘single clonal group’
  - Nontypable (NT) by standard PFGE method
  - ST398
  - 3 closely related spa types
- Isolates also resistant to tetracycline
  - use of tetracyclines may be selecting for MRSA
Colonization of farm workers (Voss et al 2005)

- ST398 also isolated from pig farmers
  - Risk of MRSA carriage 760x > than general population
- Dutch health authorities now categorize people exposed to pigs (and calves) as high risk for MRSA
  - Intensive screening before hospital admission if people have ‘livestock’ contact
NT-MRSA at one hospital in Holland

Screening of all patients with livestock contact

Case = positive culture regardless of disease status
Non typable MRSA are clustered in livestock dense regions in Holland
(Wulf et al., 2007)
MRSA in pigs in Ontario (Khanna et al, 2007)

- Convenience sample of 20 Ontario herds
  - 25% (71/285) of pigs positive
  - 70% median prevalence in positive herds
  - 20% (5 of 25) farmers positive

- Predominant (75%) spa type similar to ST398 Dutch isolates
  - Spa type 539 (egenomics; Ridom t034))
  - Common human epidemic strains also found on 3 farms
# Reports of MRSA in swine

<table>
<thead>
<tr>
<th>Population</th>
<th>Country</th>
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<th>Reference</th>
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</thead>
<tbody>
<tr>
<td>Research pig herd</td>
<td>Singapore</td>
<td>6%</td>
<td>Sergio et al. (2007)</td>
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<tr>
<td>Healthy pigs on farms</td>
<td>Holland</td>
<td>11%</td>
<td>van Duijkeren et al. (2008b)</td>
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<td>Healthy pigs on farms</td>
<td>Germany</td>
<td>13%</td>
<td>Meemken et al., 2008</td>
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<td>Healthy pigs on farms</td>
<td>Canada</td>
<td>25%</td>
<td>Khanna et al. (2007)</td>
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<tr>
<td>Pigs in slaughterhouses</td>
<td>USA</td>
<td>38%</td>
<td>Davies (unpublished)</td>
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<tr>
<td>Pigs in slaughterhouses</td>
<td>Holland</td>
<td>39%</td>
<td>de Neeling et al (2006)</td>
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<tr>
<td>Healthy pigs on farms</td>
<td>USA</td>
<td>70%</td>
<td>Smith et al. (2008)</td>
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</table>

Adapted from Weese and van Duijkeren2009
Livestock adapted clone (ST398)

- Originally ‘pig’ associated
  - Calf, dog, horse, poultry, meat (various)
  - 10% of horses in Belgium
- Rapid spread vs. rapid discovery
  - Expanding biological niche?
- Multiple reservoirs
  - Infections in people without ‘pig’ contact do not implicate pork
People occupationally exposed to livestock are more likely to be colonized with MRSA

- As yet no data indicating increased risk of infection

Interspecies transmission of ST398 MRSA

- Frequency – apparently high
- Quantity – unknown
- Duration – unknown
Concepts of interspecies transmission

- **Complete host adaptation**
  - Human flora
  - Swine flora
  - No interspecies transmission

- **No host adaptation**
  - Human flora
  - Swine flora
  - Equal propensity to colonize both species

- **Marked host adaptation**
  - Human flora
  - Swine flora
  - Rare interspecies transmission

- **Some host adaptation**
  - Human flora
  - Swine flora
  - Common interspecies transmission
## MRSA in food (meat)

<table>
<thead>
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<th>Food</th>
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<tr>
<td>Chicken</td>
<td>0.5%</td>
<td>Kitai (2005)</td>
</tr>
<tr>
<td>Chicken</td>
<td>0.2%</td>
<td>Kwon (2006)</td>
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<tr>
<td>Pork</td>
<td>3.1%</td>
<td>Van Loo (2007)</td>
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<tr>
<td>Milk, Cheese</td>
<td>0.9%</td>
<td>Normanno (2007)</td>
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<td>Milk</td>
<td>1.3%</td>
<td>Lee (2003)</td>
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<tr>
<td>Chicken</td>
<td>1.7%</td>
<td>Lee (2003)</td>
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Table 2
MRSA in meat

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<tr>
<th>Meat type</th>
<th>n</th>
<th>Number (%) positive</th>
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<td>Beef</td>
<td>395</td>
<td>42 (10.6)</td>
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<tr>
<td>Veal</td>
<td>257</td>
<td>39 (15.2)</td>
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<tr>
<td>Pork</td>
<td>309</td>
<td>33 (10.7)</td>
</tr>
<tr>
<td>Lamb/mutton</td>
<td>324</td>
<td>20 (6.2)</td>
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<tr>
<td>Chicken</td>
<td>520</td>
<td>83 (16.0)</td>
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<tr>
<td>– Total</td>
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<tr>
<td>– NL+ other EU countries</td>
<td>302</td>
<td>75 (24.8)</td>
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<tr>
<td>– Import (non-EU countries)</td>
<td>162</td>
<td>2 (1.2)</td>
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<tr>
<td>– Biological</td>
<td>56</td>
<td>6 (10.7)</td>
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<td>Turkey</td>
<td>116</td>
<td>41 (35.3)</td>
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<td>Fowl</td>
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<td>4 (3.4)</td>
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<td>Game</td>
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<td>Total</td>
<td>2217</td>
<td>264 (11.9)</td>
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### MRSA types in Dutch meat

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<tr>
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<th>ST398</th>
<th>Other</th>
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<tr>
<td>Beef</td>
<td>25</td>
<td>42</td>
<td>60%</td>
</tr>
<tr>
<td>Veal</td>
<td>37</td>
<td>39</td>
<td>95%</td>
</tr>
<tr>
<td>Pork</td>
<td>32</td>
<td>33</td>
<td>97%</td>
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<tr>
<td>Lamb</td>
<td>14</td>
<td>18</td>
<td>78%</td>
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<tr>
<td>Chicken</td>
<td>67</td>
<td>75</td>
<td>89%</td>
</tr>
<tr>
<td>Turkey</td>
<td>38</td>
<td>41</td>
<td>93%</td>
</tr>
</tbody>
</table>

*High prevalence of MRSA in low numbers*
S. aureus & MRSA in retail meat in Louisiana
Pu et al (2009)

- S. aureus strains
  - 45.6% of pork samples
  - 20% of beef samples
- MRSA
  - 5 pork samples
  - 1 beef sample
  - Common human strains – no ST398
S. aureus in retail pork
(funded by National Pork Board)

- Convenience sampling
- 15 states
- 89 retail pork samples
  - 54 chops (1” cube samples and whole chops)
  - 35 ground pork
- 80% of samples positive for S. aureus
  - 83 spa types among 183 isolates tested
**S. aureus** in retail pork
(89 samples from 15 states)

egenomics spa type 539 (Ridom t034) consistent with ST398
MRSA in meat/food – what are the implications?

- VWA Risk Assessment Bureau (Holland)
  - provisional conclusion: foodstuffs play a negligible role, if any, in the spread of MRSA.

- Weese and van Duijkeren (2009)
  - Evidence implicating food as the source of infection appears to be tenuous.
  - Clinical relevance of MRSA contamination of food, ... is currently unclear
MRSA in meat: what are the implications?

De Boer (2009)

- MRSA in raw meats not shown to contribute significantly to the dissemination of MRSA to humans.
- Numbers of MRSA found are so low that risk of colonization is probably very slight.
- *S. aureus* is not a good competitor compared to spoilage organisms of raw meat
  - conditions for growth of MRSA in raw meats are very poor.
Where does that leave us?

‘Known knowns’

- MRSA common in pigs and other animals
- Livestock clones colonize people
- Livestock clones can cause human disease
  - Some reported cases of infections with ST398
  - Few cases of severe infection (no deaths reported)
- Colonization with human epidemic strains increases risk of disease
  - Not known for livestock associated MRSA
Human health burden of ST398

- Endemic in pigs in Holland, Germany and Denmark since at least 2003/2004
  - Few clinical infections and no fatal cases
- Denmark 2007
  - Produced 24 million pigs
  - 6 cases of minor infections with ST398 (all pig exposure)
- No evidence of community outbreaks
- Evidence of reduced transmission risk among people
Livestock MRSA: an epidemic waiting to happen?

(Wulf and Voss, 2008)

- Not just a “Dutch” problem
- May become an important source of CA-MRSA
- Assumptions about the ability of ST398 to spread and cause infections should be postponed until further data are available
- Inter-human spread is possible, therefore probably just a matter of time until an outbreak
What is the real deal?

- Troubling for pork industry
  - Legitimate concerns for occupational health
  - Other public health risks appear miniscule
- Prudent preventive practices on farm
  - Handwashing and personal hygiene
  - Rapid treatment of skin injuries
  - Seek medical treatment if infections develop
Powerful ammunition for industry critics

- Coming plague
- Scaremongering of public health risks from foodborne exposure or community spread
  - NYT article on Camden, Indiana community outbreak of MRSA
  - Much acclaimed but completely undocumented
- Fingerpointing regarding intensive production and antimicrobial use
Reported MRSA cases in Denmark

AGP ban in finishing
AGP ban in nurseries
When uncertainty rules

- Opinion runs ahead of evidence
  - Speculation will be rife
  - Bias and misinformation can rule
- Maintain calm and reason
  - Do not react with extreme haste
- Look at the data
  - Ask questions
<table>
<thead>
<tr>
<th>Cause</th>
<th>Annual Accidental Deaths</th>
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<tbody>
<tr>
<td>Motor Vehicle</td>
<td>43,000</td>
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<td>Falls</td>
<td>15,000</td>
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<tr>
<td>Poisoning</td>
<td>9,000</td>
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<tr>
<td>Drowning</td>
<td>4,000</td>
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<td>Fire and burns</td>
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<td>Suffocation</td>
<td>3,300</td>
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<td>Firearms</td>
<td>1500</td>
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<td>Lightning strike</td>
<td>60</td>
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<tr>
<td>Dog bite</td>
<td>20</td>
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