

MRSA: professionals in swine industry at risk?

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Outline of the presentation

- Introduction on MRSA
- MRSA in (farm) animals
- Transmission from farm animals to humans
- Conclusions



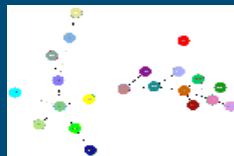
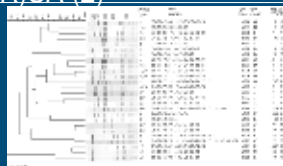
Introduction on MRSA

From SA to MRSA

- When?
 - 1961 - introduction methicillin
 - within 3 months first MRSA detected
- How?
 - staphylococcal cassette chromosome (SCC_{mec})
 - *mecA* gene
 - protein binding protein variant (PBP2a)
→ resistant to all β -lactam antibiotics

Molecular typing of (MR)SA (2)

- Commonly used methods – often in combination
 - Pulsed Field Gel Electrophoresis (PFGE)
 - Multi Locus Sequence Typing (MLST)
 - CC = Clonal Complex
 - SCC_{mec} typing
 - Staphylococcal protein A (*spa*) typing



Public health – hospital acquired

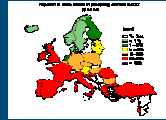
- healthcare associated risk factors
- clinical features
 - predominantly invasive infections
 - outbreaks
- often multi-resistant
- mostly SCC_{mec} type I, II and III



Prevalence HA-MRSA

- increasing proportions of MRSA of invasive SA isolates worldwide

- USA: 35.9% → 64.4% (1992 – 2003)
- UK: 2% → 40% (1990 – 2000)
- Denmark: 0.3% → 1.7% (1999-2006)
- Netherlands: 0.3% → 0.9% (1999-2006)

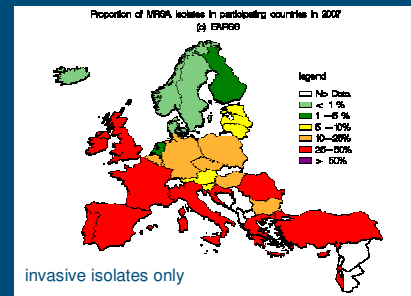


- high (>25%) - and low (< 3%) prevalence countries

- 'search-and-destroy' policy

- known (ex-) carriers
- patients transferred from hospitals abroad

European Antimicrobial Resistance Surveillance System



Changing epidemiology

- community acquired MRSA

- no standard definition yet

- prevalences hard to determine
- CA also in hospitals and vice versa



- different from HA-MRSA in

- genetic background
- clinical features
- epidemiology
- antibacterial resistance



MRSA in animals

MRSA in animals

- 1972 – first publication in mastitic cows
- since then multiple reports on MRSA in different animal species (predominantly companion animals and horses)
- 2005 – first publication on MRSA in pigs
- companion animals versus farm animals

- individual / group
- antimicrobial use
- contact with humans
- transmission
- type of strains



MRSA in pigs – first signs

- initial findings in CWZ Nijmegen (NL)
 - case A – July 04 – 6 mth. old daughter of a pig farmer
 - case B – Feb 05 – an adult pig farmer
 - case C – Feb 05 – son of a pig veterinarian

- in all cases

- positive family members
- unsuccessful repeated decolonization
- strains not typeable by PFGE

MRSA in pigs – first publication

Methicillin-resistant *Staphylococcus aureus* in Pig Farming

Andreas Voss et al.

Emerging Infectious Diseases • www.cdc.gov/eid • Vol. 11, No. 12, December 2005

- follow up
 - pigs on farm from case A → 1 positive
 - 26 pig farmers on regional meeting → 6 positive (23%)
- pig farmers >760 × higher frequency of MRSA colonization than the general Dutch population (0.03%)

Survey on pig slaughterhouses (NL)

- 9 pig slaughterhouses
 - each 6 batches of 10 pigs (n=540)
 - 39% of the pigs positive
 - 81% of the batches (≈ farms??) positive
 - all slaughterhouses positive
- all ST398 and non typable by PFGE

De Neeling et al., Vet Microbiol, 2007

Preliminary results of ongoing studies on pig farms

- Farm data (100 breeding and farrowing (to finish) farms):
 - 65% of farms positive
- Strong association between results of pool samples (pigs) and environmental samples
 - OR=48.6, P<0.0001; κ=0.70, 95%CI 0.56-0.84
- Piglets, weaners and finishers more often positive than sows and gilts (based on pool results)
- Strong suggestion that transmission of MRSA between farms by the purchase of positive pigs is an important route (OR=7.2; P=0.08)

Broens et al., in preparation

Survey on pigs in several other countries

- Denmark (2007), Canada (2007), Germany (2008), USA (2008), Belgium (2008), Sweden (2008)
 - Different protocols - data hard to compare
- Prevalences at farm level:
 - 18 – 68%
- Prevalences at individual pig level:
 - 11 – 70%
- Most countries also included humans in their surveys

Risk factor analysis on veal farms

- preliminary results

Animal and farm data:

- 90/102 (88%) veal farms positive
- 458/2151 (28%) calves positive



Graveland et al., poster at ASM conference, Copenhagen, June 2008

ST398 MRSA in poultry?

- pilot study in Dutch slaughter house
 - positive samples in 2 batches

not published
- Belgian survey on *S. aureus* isolates originated from poultry
 - 10/171 isolates positive

Nemati et al., Antimicrob Agents Chemother, 2008



ST398 MRSA in equine?

- MRSA in equine reported before - no ST398

- Dutch equine hospital

- recurrent infections with ST398
not published

- Belgian survey

- 110 horses nasal swab at clinic admission
- 11% ST398 positive

Van den Eede et al., Vet Microbiol, 2008



ST 398 MRSA on meat products



- 1293 unheated products derived from retail
- 22 different *spa*-types
- 116 (84%) ST398

Assumed to be of minor importance for public health

www.vwa.nl



meat type	no. analyzed	no. (%) positive
beef	218	21 (9.6)
veal	119	20 (16.8)
lamb	161	9 (5.6)
pig	192	20 (10.4)
chicken	143	39 (27.3)
import	150	2 (1.3)
turkey	83	26 (31.3)
other	95	4 (4.2)
fowl		
game	132	4 (3.0)
total	1293	145 (11.2)



Transmission from farm animals to humans

Case-control study in humans - 1

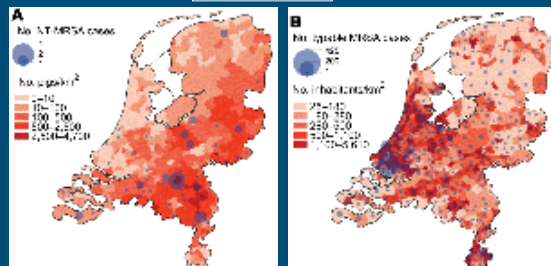
- cases (NT-MRSA; n=35); controls (T-MRSA; n=76)

- first NT-MRSA found in Feb 03
- cases significantly more often in contact with pigs and veal
- NT-MRSA is of animal origin
- 32/35 cases belonged to MLST type 398
- no ST398 among controls

van Loo et al., Emerg Inf Dis, 2007

Case-control study in humans - 2

cases Jan 03 – Jun 05 controls



van Loo et al., Emerg Inf Dis, 2007

Dutch Workingparty on Infection Prevention (WIP)

- MRSA guidelines for hospitals

- 4 categories
 1. proven carriers
 2. high risk patients
 3. moderate risk patients
 4. no risk patients

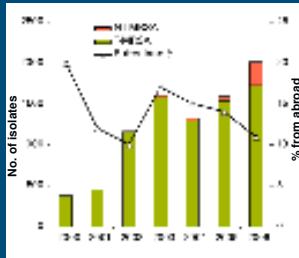
screened and isolated at admission

- 2005: 1st adjustment – pigfarmers and their householdmembers in group 2

- 2007: 2nd adjustment - people in contact with alive pigs and/or veal calves in group 2

MRSA Surveillance at RIVM

- a new epidemic or increased awareness??

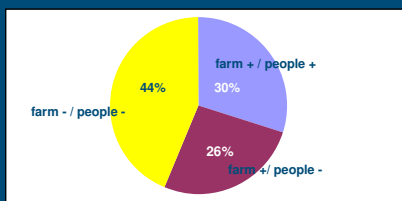


www.rivm.nl

Surveys among professionals in swine industry

- IPVS 2006: 12.5% participants (n=272) from 9 countries carried MRSA
 - 91% ST398
 - risk factor = frequency of pig contact
Wulf et al., Clin Microbiol Infect, 2007
- Danish veterinary conferences: 1.6% participants (n=702) MRSA positive
 - 36% CC398
 - Veterinarians more at risk (3.9%) than unexposed people (0.7%)
 - Contact with small animals, cattle or horses, but not pigs were risk factors
Moodley et al., Scand J Work Environ Health, 2008

Risk factor analysis on pig farms



No positive people on negative farms!!

van den Broek et al., Epid Inf, 2008

Risk factor analysis on 50 pig farms

- | Total no. of people (n=232) | People on positive farms (n=139) |
|-----------------------------|----------------------------------|
| ● 14 % positive | ● 24% positive |
| ● 29% if intensive contact | ● 49% if intensive contact |

Most important risk factor for humans:
intensive contact: OR=39.9 (P<0.0001)

van den Broek et al., Epid Inf, 2008

Professionals in other agricultural sectors?

Veal as a source:

- 32% veal calf farmers
- 8% household members
- Intensity of contact associated with MRSA prevalence (no exact figures)
- Graveland et al., poster at ASM conference, Copenhagen, June 2008



Poultry as a source:

- Dutch case patient from hospital abroad
 - 5/9 household members
 - 1/16 poultry houses
 - all identical strains

Leenders et al., Infectieziektenbulletin, 2007



Clinical cases in humans MRSA ST398

- Dutch case report on endocarditis in female patient without risk factors
Ekkelenkamp et al., Ned Tijdschr Geneesk, 2006
- Young mother with mastitis
Huijsdens et al., Ann Clin Microb Antimicrob, 2006
- Belgian case report on soft tissue infection originating from a pig bite
Declercq et al., Infection, 2007
- Two Danish cases of human MRSA infection
Ruhlmann et al., Ugeskr Laeger, 2008



First hospital outbreak of MRSA ST398

- 5 patients and 5 healthcare workers positive
- One healthcare worker lived on the grounds of a pig farm but neither she nor her partner came directly into contact with pigs themselves
- Permission to sample the pigs on this farm was not granted

Wulf et al., Eurosurveillance, 13(9), 2008

Is MRSA ST398 different from other MRSAs?

- The number of infections and secondary cases seems lower in ST398 than in typable MRSAs
van Rijen et al., Clin Inf Dis, 2008
- Veterinary sample collectors showed transient MRSA carriage only during the day of the farm visit
van den Broek et al., Epid Inf, 2008



Conclusions

Conclusions

- New emerging strain in farm animals
- Extensive spread among animals worldwide
- Animal-to-human transmission occurs
- Especially people with intensive contact at risk
- Clinical infections and outbreaks occur
- Virulence and human-to-human transmission of ST398 seem lower than from other MRSAs
- More research is needed on transmission dynamics, risk and preventive factors

Thanks for your attention

