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van Rijen, M.M.L.

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Chapter 3.1

Increase in a Dutch hospital of meticillin-resistant *Staphylococcus aureus* related to animal farming

MML van Rijen¹, PH van Keulen¹, JAJW Kluytmans^{1,2}

¹Laboratory for Microbiology and Infection Control, Amphia Hospital, Breda,
The Netherlands

²Department of Medical Microbiology and Infection Control, VU Medical Centre,
Amsterdam, The Netherlands

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Abstract

In The Netherlands a new reservoir of MRSA has recently been identified in pigs and veal calves upon which the 'Dutch Working Party on Infection Prevention' modified the national MRSA guidelines. In June 2006 a new group at risk of MRSA carriage was included, consisting of patients that reported direct exposure to living pigs or veal calves. After the implementation of this modification in a training hospital located in an area with a relatively high density of pig farming, a threefold increase in the annual incidence of MRSA was found. Upon screening, thirty-two percent of the individuals in the new risk group was shown to carry MRSA. In conclusion, a new reservoir of MRSA in pigs and calves has been established which is associated with an extremely high carriage rate among people who are exposed to these animals.

Introduction

Meticillin-resistant *Staphylococcus aureus* (MRSA) has become an increasingly important pathogen in hospitals and recently also in the community.¹ MRSA incidence in hospitals are still low in Scandinavian countries and The Netherlands ($\leq 1\%$), while in other European countries these rates are up to 50%.² The low rates are maintained by an active policy called 'Search and Destroy'.

In The Netherlands a new clone of MRSA has emerged. The first isolate was found in 2003 and since then it has been reported with increased frequency. This clone is characterized by being non-typeable (NT) with Pulsed Field Gel-Electrophoresis (PFGE) using SmaI, which is the typing method used at the National Reference Centre.^{3,4} All NT-MRSA belong to one single clonal complex, characterised by Multi-Locus Sequence Type 398. NT-MRSA has been related to pig-farming by Voss et al who described a pig farmer's child who was colonised by MRSA prior to cardiac surgery.³ Further investigations revealed that both the father and the mother of the girl carried MRSA. MRSA was also isolated from one of the pigs on the farm. Twenty-six regional farmers were also screened and six (23%) of them were shown to be colonised with MRSA. Subsequently, a survey among pigs at slaughterhouses was performed by De Neeling et al who found that 39% of the pigs carried NT-MRSA.⁵ Based on these results it was concluded that a reservoir of MRSA in pigs had been established that could spread to humans. An epidemiological survey found a strong relation between NT-MRSA and pigs, as well as to veal calves.⁶ The clinical consequences are potentially severe as was shown by Ekkelenkamp et al who described a case of endocarditis caused by NT-MRSA.⁷ Therefore, the 'Dutch Working Party on Infection Prevention (WIP)' modified the guidelines for the control of MRSA in June 2006. People who are directly exposed to living pigs or veal calves were considered to be at increased risk of MRSA carriage and should be screened and isolated upon admission to hospitals.⁸ By the end of 2006 nearly 25% of all MRSA found in the Netherlands were NT-MRSA.

The objective of this survey was to determine the epidemiology of NT-MRSA in a hospital located in an area with a relatively high density of pig farming and the MRSA carriage rate in patients with pig/calf exposure.

Methods

A prospective surveillance was performed from 2002 through 2006 in the Amphia Hospital, a training hospital with 1370 beds, which is located in the south-western part of The Netherlands. The catchment population of the hospital consists of approximately 440,000 inhabitants and 7000 pig farms. Both patients and health care workers who

carried MRSA, were identified by means of the files of the infection control department and from the laboratory information system. Individuals who were found to be colonised for the first time were included. Newly identified MRSA were classified based on PFGE type and proposed source. PFGE typing results were obtained from the National Reference Centre (RIVM: National Institute for Public Health and the Environment). The proposed source was based on the patient's history. Statistical significance was calculated using the 2-tailed Fisher's Exact test.

Epidemic curve of MRSA

From 2002 through 2006, 95 cases of MRSA were found in the Amphia hospital, consisting of 73 newly identified cases and 22 secondary cases. Twenty-three (31.5%) of the newly identified cases had NT-MRSA (figure 1). The first NT-MRSA was found in 2004 in a child who was adopted from China. In 2005, the second NT-MRSA was encountered in a pig farmer who was admitted to the emergency room with an infected thumb after being bitten by a pig. In the first half of 2006, before active screening was introduced, a pig farmer and a veterinary surgeon with frequent pig exposure were found to be colonised with NT-MRSA. After the introduction of active screening in July 2006, 19 individuals with NT-MRSA were found in 6 months.

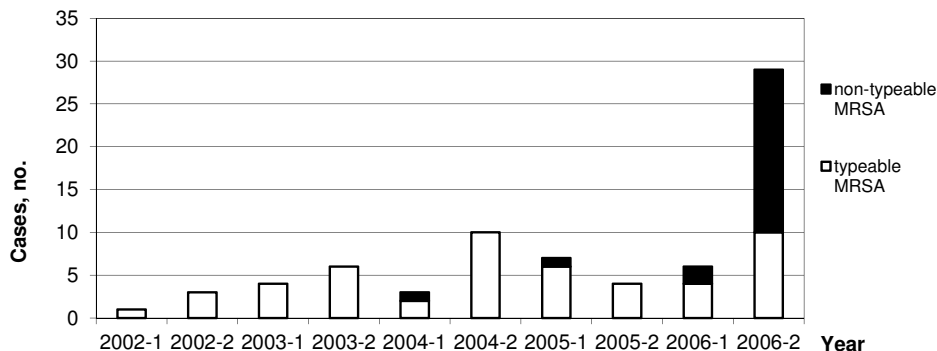


Figure 1. Increase of non-typeable MRSA in the Amphia hospital.

Number of typeable and non-typeable MRSA from 2002 through 2006, shown per six months. In July 2006 active screening of patients reporting pig/calf exposure was introduced.

Sources of MRSA

The proposed sources of MRSA in patients with typeable strains ($n=50$) were as follows: 46% related to a foreign country, 14% related to another Dutch healthcare institute, 2% related to exposure to pigs/calves and in 38% the source could not be identified. For NT-MRSA ($n=23$) these figures were 4%, 0%, 87% and 9%, respectively. There was a strong and significant relation of NT-MRSA to exposure to pigs/calves (OR 326.7, 95%

CI 37.9-2514.0), whereas typeable MRSA was related to a foreign country (OR 18.7, 95% CI 2.9-115.8).

Invasive infections

Twenty-one out of 50 patients with a typeable MRSA suffered from an infection caused by MRSA, i.e. wound infections, skin infections, urinary tract infections and pneumonia. Three out of 23 patients with a NT-MRSA had an active infection, i.e. one thumb infection, one pneumonia and one case of osteomyelitis. The risk of developing an infection was significantly higher in patients with a typeable MRSA (OR 4.83, 95% CI 1.34-17.09).

Nosocomial transmission

To determine the difference in likelihood of secondary transmission between typeable and NT-MRSA, a comparison was made by selecting patients who were approached without transmission-based precautions. Sixteen patients with a typeable MRSA stayed in the hospital without precautions for a total of 138 days. Twenty-two out of 2139 persons exposed to these sixteen patients were shown to be colonised with the index strain. For NT-MRSA, during 37 exposure days in 8 patients, 0 of the 408 exposed patients and health care workers were colonised. The difference between typeable MRSA and NT-MRSA was statistically significant ($p=0.037$). Only recently, in 2007, one health care worker was colonised with NT-MRSA, acquired from a patient not treated in isolation.

MRSA carriage rate in patients reporting pig/calf exposure

In the second half of 2006, a total of 57 patients who reported exposure to pigs or veal calves were screened. Eighteen (32%), of them carried MRSA, i.e. 36% (14/39) of the patients that were exposed to pigs and 22% (4/18) of the patients with exposure to calves ($p>0.05$). This group consisted of eleven pig farmers, one pig farmer's wife, one artificial inseminator, one student from the Agricultural University, three calf farmers and one calf farmer's daughter.

Discussion

This study showed an increase of MRSA in the Amphia hospital that was caused entirely by the emergence of a new clone, NT-MRSA. This clone was almost completely related to exposure to pigs and calves. The MRSA carriage rate in this new risk group was 32%, which is higher than in any other population that has been described to date. For example, in 2000, in The Netherlands the MRSA carriage rate of patients on admission to the hospital was 0.03%.⁹ The most important risk group for MRSA carriage used

to be patients that were transferred from foreign hospitals. Kaiser *et al.* reported a carriage rate of 4.7% in this group, which is approximately 150 times higher than the carriage rate of the general population.¹⁰ Patients who reported exposure to pigs and calves carry a risk that is approximately 1000 times higher than the general population in The Netherlands. Patients who reported exposure to pigs carried a higher risk than patients who reported exposure to calves but this was not statistically significant (RR 1.6, 95% CI 0.7-4.3). The rate of patients with invasive infections and of secondary cases was lower for NT-MRSA which may indicate a lower virulence and transmissibility of this veterinary strain for humans, although Witte *et al.* reported an outbreak of VAP with ST398 in Germany.¹¹ The methodology of our study is not suitable for drawing final conclusions on these issues, so more research is required.

The conclusion is that a new reservoir of MRSA associated with an unpredicted high carriage rate has been established outside the hospital. After introducing the new MRSA risk category in the Amphia Hospital, which is located in a region with a relatively high density of pig farms, the number of MRSA positive patients instantly increased more than 300%. This challenges the Search and Destroy strategy. Part of this strategy is the screening of patients at risk of MRSA and isolating them until they are proven to be free of MRSA. If MRSA is present, isolation is continued until discharge from the hospital. The unexpected and sudden increase resulted in a shortage of isolation facilities. An additional problem is the treatment of carriers, also part of the Search and Destroy strategy. As pig and cattle farmers colonised with MRSA return to the source of MRSA after discharge, this raises questions about treatment of carriage. Our findings indicate that currently this strain does not spread easily between humans, but more research on this aspect is needed. Although the increase in absolute numbers of MRSA carriers is obvious, the true impact for hospitals will depend on the virulence and transmissibility of this new clone.

At present it is clear that people who work with pigs or calves are at risk of developing an infection with NT-MRSA which should be taken into consideration by physicians treating these patients.

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References

1. Kluytmans-VandenBergh MFQ, Kluytmans JAJW. Community-acquired methicillin-resistant *Staphylococcus aureus*: current perspectives. *Clin Microbiol Infect* 2006; 12(Suppl.1):9-15.
2. Tiemersma EW, Bronzwaer SL, Lyytikäinen O, et al. Methicillin-resistant *Staphylococcus aureus* in Europe 1999-2002. *Emerg Infect Dis* 2004; 10(9):1627-34.
3. Voss A, Loeffen F, Bakker J, et al. Methicillin-resistant *Staphylococcus aureus* in pig farming. *Emerg Infect Dis* 2005; 11(12):1965-66.
4. Bens CC, Voss A, Klaassen CH. Presence of a novel DNA methylation enzyme in methicillin-resistant *Staphylococcus aureus* isolates associated with pig farming leads to uninterpretable results in standard pulsed-field gel electrophoresis analysis. *J Clin Microbiol* 2006; 44(5):1875-6.
5. De Neeling AJ, Van den Broek MJ, Spalburg EC, et al. High prevalence of methicillin-resistant *Staphylococcus aureus* in pigs. *Vet Microbiol* 2007; 122(3-4):366-72.
6. van Loo I, Huijsdens X, Tiemersma E, et al. Emergence of methicillin-resistant *Staphylococcus aureus* of animal origin in humans. *Emerg Infect Dis* 2007; 13:1834-9.
7. Ekkelenkamp MB, Sekkat M, Carpaïj N, et al. Endocarditis due to methicillin-resistant *Staphylococcus aureus* originating from pigs. *Ned Tijdschr Geneesk* 2006; 150(44):2442-7.
8. Vandenbroucke-Grauls CM, Beaujean DJ. Methicillin-resistant *Staphylococcus aureus* in pig breeders and cattle breeders. *Ned Tijdschr Geneesk* 2006; 150(31):1710-2.
9. Wertheim HF, Vos MC, Boelens HA, et al. Low prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA) at hospital admission in the Netherlands: the value of search and destroy and restrictive antibiotic use. *J Hosp Infect* 2004; 56(4):321-5.
10. Kaiser AM, Schultsz C, Kruithof GJ, et al. Carriage of resistant microorganisms in repatriates from foreign hospitals to The Netherlands. *Clin Microbiol Infect* 2004; 10(11):972-9.
11. Witte W, Strommenger B, Stanek C, et al. Methicillin-resistant *Staphylococcus aureus* ST398 in humans and animals, Central Europe. *Emerg Infect Dis* 2007; 13(2):255-8.