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Extended Abstract

# The Influence of Livestock on Human Infections with LA-MRSA

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**Abstract:**

Infections caused by the methicillin resistant Staphylococcus aureus (MRSA) are traditionally nosocomial, but recent reports have indicated an increased frequency of community acquired infections. Livestock associated MRSA (LA-MRSA) is usually present in livestock, especially in pigs. Although LA-MRSA strains usually don't cause the disease in animals, they might function potential source for human infections. In Slovenia, the number of people colonized with LA-MRSA is increasing. Both human and animal samples additionally to environmental samples were collected from 16 farms in Slovenia, where a minimum of one case of LA-MRSA was previously confirmed per family. All the obtained isolates were tested for his or her antimicrobial susceptibility with the microdilution method for the minimal inhibitory concentration (MIC). In addition, they were confirmed by the multiplex PCR for 16S rRNA, nuc, mecA, mecC and PVL genes. Spa arrange was also performed, using the Ridom StaphType software. All the humanc of LA-MRSA were immune to Cefoxitin, Tetracycline and Penicillin, a number of them also to Ciprofloxacin and Clindamycin. In animals, similar susceptibility patterns were found, but none of the animal isolates were immune to Ciprofloxacin. The human confine mostly belonged to spa types t011 and t034, but t1451, t10765 and t1344 were also present. The evidence of LA-MRSA in animals was confirmed for five farms and every one of these isolates belonged to the spa type t011. It are often assumed that pigs are a possible source of human infection, but it also can be concluded that LA-MRSA strains are already spreading within the human population. Namely, LA-MRSA was isolated from humans at farms, where both the animal samples and dust samples collected from the stables were negative.

**Introduction:** In the past decade, livestock-associated methicillin-resistant Staphylococcus aureus (LA-MRSA) strains especially of the clonal complex (CC) 398 have emerged in many parts of the planet especially in areas with a high density of pig farming. In those regions, farmworkers and other individuals with professional contact to livestock are very frequently colonized with LA-MRSA. These persons are the presumably source for LA-MRSA transmission to household members and other parts of the human population. Altogether, colonization and/or infection of those individuals cause the introduction of LA-MRSA into hospitals and other healthcare facilities. Since LA-MRSA CC398 are found to be specifically adapted to their animal hosts in terms of the equipment with virulence factors, their pathogenicity to human patients may be a matter of debate with first reports about clinical cases. Meanwhile, case reports, case series and few studies have demonstrated the potential of LA-MRSA to cause all kinds of infections attributed to S. aureus in general including fatal courses. Human infections observed comprise e.g. bacteremia, pneumonia, osteomyelitis, endocarditis and lots of manifestations of skin and soft tissue infections. However, inpatients suffering from MRSA CC398 generally show different demographic (e.g. younger, shorter length of hospital stay) and clinical characteristics (e.g. less severe complications) which can explain or a minimum of contribute to a lower disease burden of LA-MRSA compared to other MRSA clonal lineages.

**Methods:** Efficient horizontal gene transfer requires: (i) resistance genes to be located on mobile genetic elements; (ii) close contact between the partners, which is usually provided in the polymicrobial environments on the skin and on the mucosal surfaces; and (iii) a selective pressure, such as imposed by the use of antimicrobial agents. Studies on the mobility and the localization of resistance genes in LA-MRSA CC398 isolates showed that many resistance genes were located on mobile genetic elements such as plasmids or transposons. As a colonizer of the skin and the mucosal surfaces of the anterior nares, LA-MRSA CC398 is in close contact with various other bacteria present in the respective hosts. As LA-MRSA CC398 isolates have been encountered not only in different hosts (e.g. humans, pigs, cattle, horses, poultry, dogs, and rats), but also in various geographical regions (e.g. Europe, North America, and Asia), such isolates may be subject to variable selective pressures based on preferences in the application of antimicrobial agents in humans and different animal species in different countries and parts of the world. Moreover, LA-MRSA CC398 may also be subject to selective pressures by antimicrobial agents that are not primarily used to control staphylococcal infections, and—under such a selective pressure—may develop or acquire corresponding resistance genes. It is

important to understand that, although the application of an antimicrobial agent is aimed at combating the target pathogens, the commensal or temporarily colonizing microflora is also put under selective pressure by the antimicrobial agent. In this regard, all phenicol-resistant LA-MRSA CC398 isolates seen so far in pigs and cattle carry fexA or cfr but none of the chloramphenicol acetyl transferase genes, catpC221, catpC223, catpC194, which are widespread in staphylococci. This may be because florfenicol is commonly used in pigs and cattle to control respiratory tract infections, and the chloramphenicol acety ltransferases encoded by the aforementioned cat genes do not confer florfenicol resistance.

**Results:** The authors declare no conflict of interest. The work of K. Kadlec, A. T. Feßler, T. Hauschild and S. Schwarz on antimicrobial resistance in LA-MRSA CC398 is financially supported by the German Federal Ministry of Education and Research (BMBF) through the German Aerospace Centre (DLR), grant number 01K11014D (MedVet-Staph).

**Conclusion:** Recent studies analyzing 80 genomes of LA-MRSA CC398 isolates from all over the world have suggested that LA-MRSA CC398 started as an MSSA CC398 in humans, which changed hosts and acquired new resistance properties (such as methicillin resistance and tetracycline resistance) in the new host [97]. The analysis of further resistance genes and their location in LA-MRSA CC398 provides insights into the gene acquisition capacities of these isolates, their role as recipients and donors of resistance genes, and possible partners for resistance gene exchange processes beyond the genus Staphylococcus. In addition, the knowledge about co-localization, organization in clusters and physical linkage of antimicrobial resistance genes furthers our understanding of the co-selection and persistence of resistance genes even in the absence of a direct selective pressure.