Human methicillin-resistant *Staphylococcus aureus* (MRSA) colonization: a major public health concern?

[Editorial Comment]

Edna Ribeiro

H&TRC – Health & Technology Research Center, Escola Superior de Tecnologia da Saúde de Lisboa, Instituto Politécnico de Lisboa. Lisboa, Portugal. edna.ribeiro@estesl.ipl.pt

The World Health Organization (WHO) describes antimicrobial resistance in human pathogens as a global health challenge[1]. For the past decades, with the global escalation in the development of antibiotic-resistant microorganisms[2] both social and scientific concerns have emerged regarding the intensive prescription of antibiotics and its widespread use in agriculture and livestock[3]. These antibiotic-resistant microorganisms can be found as components of bioaerosols which may occur as solid or liquid particles in the air. In numerous workplaces, particularly in the context of animal production and health care, continued exposure to bioaerosols can represent a significant health hazard for workers and for the spread of potentially pathogenic microorganisms in the community[4]. Several studies, performed in the past years, have provided scientific data on occupational exposure to bioaerosols in order to better understand potential relationships between exposure and health effects[5].

In a Portuguese context, occupational health concern has been increasing and efforts have been made to standardize exposure assessment procedures in occupational settings. Among the acknowledged health risks to which workers are exposed, airborne microorganisms such as *Staphylococcus aureus,* namely methicillin-resistant *S. aureus* (MRSA), are a major concern.

S. aureus is a commensal gram-positive bacterium that can colonize humans, particularly in the nasopharynx and are also a cause of staphylococcal food poisoning (SFP), resultant from ingestion of staphylococcal enterotoxins present in contaminated food. SFP has diverse associated symptoms such as violent emesis, nausea, diarrhea and prostration and is one of the most prevalent and sub diagnosticated foodborne intoxications in the world, with fatality rates ranging from 0.03% in the general population to 4.4% in children and the elderly[6].

Some *S. aureus* strains are resistant to multiple antibiotics, which difficult the treatment of infections caused by this pathogen. MRSA is one of the most important human pathogens, being a major cause of infections worldwide[7] associated with extremely high mortality rates for invasive blood-stream and pneumonic infections[8]. MRSA infections are currently characterized as Community-Associated MRSA infections (CA-MRSA) associated with healthy individuals, Health Care-associated MRSA infections (HA-MRSA) typically associated with invasive procedures or devices and Livestock-Associated MRSA infections (LA-MRSA) with divergent molecular profiles. Human MRSA carriers have increased risk for subsequent occurrence of clinical disease (up to 10-fold) and become a bacterial reservoir with associated high risk to transfer the infection to others or contaminate foods and food surfaces during handling[9].

Moreover, besides humans, animals such as pigs are also important reservoirs of MRSA[10] which constitutes a professional hazard, particularly for individuals that spend several hours *per day* in direct contact with MRSA-positive animals. Occupational studies performed in these occupational settings have demonstrated that human colonization of MRSA is higher in intensive antibiotic-using piggeries in comparison to antibiotic-free farms, which sustains the claim that antibiotic use is a driver force for the increased prevalence of workers colonization[11]. Additionally, the presence of resistant bacteria in piggery environments and related areas linked with antibiotics and the associated contamination comprises a reservoir of resistance genes for animals and humans in contact with the contaminated environment[12].

For the past years, we have performed MRSA occupational biomonitoring studies in different settings regarding workers colonization ranging from high-risk occupational settings (e.g. health care facilities and pig-farms), high-risk public health settings (e.g. bakeries), as well as in community individuals and environmental surfaces contamination, which are discussed in this comment.

In the context of high-risk public health settings, we performed an occupational biomonitoring case study from a Portuguese bakery[13]. Our data revealed a 40% prevalence of *S. aureus* asymptomatic carriers in food handlers, which is higher than levels detected in the community (31%)[14] and a high prevalence of MRSA (10% in bakery workers in comparison to 2%-3% in the community)[14]. These results are particularly worrying considering that CA-MRSA has been associated with toxic shock syndrome cases[15]. Relevantly, we also reported that one of the asymptomatic carriers of MSSA was a worker who assumed to have regular and persistent cough occurrences, which clearly increases the probability of spreading this microorganism trough bioaerosols. It is also important to notice that, in the nasopharynx sample form a bakery worker, we have also isolated a strain of *Proteus spp*., a gram-negative bacteria found in human intestine and feces, commonly responsible for urinary and septic infections,

often nosocomial, which can suggest poor hygiene although colonization has been found in pig-exposed individuals[16].

Regarding high-risk occupational settings, we highlight the assessment of MRSA colonization in workers (*n*=26) and animals (*n*=72) from five pig farms in Portugal[17]. *S. aureus* colonization was identified in workers from all studied productions with associated extremely high prevalence, reaching 80% and 100%, and relevantly most of the identified strains were MRSA. Additionally, MRSA colonization in animals was also extremely high with a reported prevalence of 34% and 66% in pigs from maternities and piglets, respectively. We reported alarming high colonization levels of S. *aureus* and particularly of resistant strains (MRSA), both in workers and in animals, which are exceedingly higher than levels previously, reported in the community for *S.aureus* (31%) and for MRSA (2%-3%)[14] and in other Portuguese swine productions[18].

Another high-risk occupational setting analyzed by our research group is healthcare facilities. The dissemination of MRSA in the hospital environment occurs mainly through hands to hand contact between healthcare workers and patients. One of the most exposed workers is the Clinical Analysis and Public Health technicians due to the close contact with infected/colonized patients, through the collection of biological samples. Recently we have reported, in a hospital in Lisbon, a prevalence of 43% MRSA colonization of workers (*n*=30) nasal flora which is higher than any other described by the literature consulted in healthcare professionals in Portugal which clearly demonstrated that Clinical Analysis and Public Health technicians have, in fact, higher risk of MRSA colonization[19]. Our results sustain the claim that prolonged exposure to bioaerosols, particularly at workplaces, can represent a health hazard and potentially result in infectious disease[4] either for workers and for the spread of these microorganisms in the community.

Another pertinent point of debate is the identification of MRSA environmental contamination in healthcare facilities. We have isolated an MRSA strain from a primary health care center surface swab sample, which represented a frequency lower than 1% (1/185; 0.54%). In the same study, from the 25 samples recovered from the community (healthy controls), one sample was confirmed to be an MRSA (1/25; 4%). Both MRSA isolated were characterized by trough molecular biology methods. The results obtained revealed that booth isolates (one from an occupationally exposed individual in health care facilities and the other from an individual from the community with no exposure to HA-MRSA strains) were pediatric clones, which are well-known hospital clones previously described in Portuguese clinical settings and therefore classified as HA-MRSA[20]. Thus, our results undoubtedly indicate a transposition of HA-MRSA strains to the community.

Overall, the reported data clearly advocate the urge to monitor bacterial strains, including MRSA, associated with animal carriers, occupationally exposed individuals and potential sources of environmental contamination and relevantly efforts must be made to determine and regulate the antibiotic selection pressure that is driving their emergence and proper and valuable bioburden risk assessments in the context of food handlers must be implemented, which can endorse major implications in public health.

References

1. World Health Organization. Antimicrobial resistance: key facts [homepage]. Geneva: WHO; 2018 Feb 15. Available from: https://www.who.int/news-room/fact-sheets/detail/antimicrobial-resistance
2. Morris AK, Masterton RG. Antibiotic resistance surveillance: action for international studies. J Antimicrob Chemother. 2002;49(1):7-10.
3. Smith DL, Harris AD, Johnson JA, Silbergeld EK, Morris Jr JG. Animal antibiotic use has an early but important impact on the emergence of antibiotic resistance in human commensal bacteria. Proc Natl Acad Sci U S A. 2002;99(9):6434-9.
4. Walser SM, Gerstner DG, Brenner B, Bünger J, Eikmann T, Janssen B, et al. Evaluation of exposure-response relationships for health effects of microbial bioaerosols: a systematic review. Int J Hyg Environ Health. 2015;218(7):577-89.
5. Ghosh B, Lal H, Srivastava A. Review of bioaerosols in indoor environment with special reference to sampling, analysis and control mechanisms. Environ Int. 2015;85:254-72.
6. Wattinger L, Stephan R, Layer F, Johler S. Comparison of Staphylococcus aureus isolates associated with food intoxication with isolates from human nasal carriers and human infections. Eur J Clin Microbiol Infect Dis. 2012;31(4):455-64.
7. Rolo J, Miragaia M, Turlej-Rogacka A, Empel J, Bouchami O, Faria NA, et al. High genetic diversity among community-associated staphylococcus aureus in europe: results from a multicenter study. PLoS One. 2012;7(4):e34768.
8. Klevens RM, Morrison MA, Nadle J, Petit S, Gershman K, Ray S, et al. Invasive methicillin-resistant Staphylococcus aureus infections in the United States. JAMA. 2007;298(15):1763-71.
9. Jordan D, Simon J, Fury S, Moss S, Giffard P, Maiwald M, et al. Carriage of methicillin-resistant Staphylococcus aureus by veterinarians in Australia. Aust Vet J. 2011;89(5):152-9.
10. Cuny C, Wieler L, Witte W. Livestock-associated MRSA: the impact on humans. Antibiotics. 2015;4(4):521-43.
11. Rinsky JL, Nadimpalli M, Wing S, Hall D, Baron D, Price LB, et al. Livestock-associated methicillin and multidrug resistant Staphylococcus aureus is present among industrial, not antibiotic-free livestock operation workers in North Carolina. PLoS One. 2013;8(7):e67641.
12. Barton MD. Impact of antibiotic use in the swine industry. Curr Opin Microbiol. 2014;19(1):9-15.
13. Ribeiro E, Clérigo A. Assessment of staphylococcus aureus colonization in bakery workers: a case study. In: Vertentes e Desafios da Segurança 2017 = Views and Determinants of Safety & Security, Leiria (Portugal), 26-28 de outubro de 2017.
14. Hatcher SM, Rhodes SM, Stewart JR, Silbergeld E, Pisanic N, Larsen J, et al. The prevalence of antibiotic-resistant

Staphylococcus aureus nasal carriage among industrial hog operation workers, community residents, and children living in their households: North Carolina, USA. Environ Health Perspect. 2017;125(4):560-9.

15. Sada R, Fukuda S, Ishimaru H. Toxic shock syndrome due to community-acquired methicillin-resistant Staphylococcus aureus infection: two case reports and a literature review in Japan. IDCases. 2017;8:77-80.
16. Fischer J, Hille K, Mellmann A, Schaumburg F, Kreienbrock L, Köck R. Low-level antimicrobial resistance of Enterobacteriaceae isolated from the nares of pig-exposed persons. Epidemiol Infect. 2016;144(4):686-90.
17. Ribeiro E, Pereira A, Vieira C, Paulos I, Marques M, Swart T, Monteiro A. Bacteria bioburden assessment and MRSA colonization of workers and animals from a Portuguese swine production: a case report. In: Arezes PM, Baptista JS, Barroso MP, Carneiro P, Cordeiro P, Costa N, et al. Occupational safety and hygiene VI. London: CRC Press; 2018. p. 351-4. ISBN 9781138542037
18. Conceição T, De Lencastre H, Aires-de-Sousa M. Frequent isolation of methicillin resistant Staphylococcus aureus (MRSA) ST398 among healthy pigs in Portugal. PLoS One. 2017;12(4):e0175340.
19. Negrinho A, Serrano D, Shone S, Ferreira B, Ribeiro E. Prevalência da colonização nasal por MRSA nos técnicos de Análises Clínicas e Saúde Pública num hospital de Lisboa. In: III Congresso Nacional de Ciências Médicas Laboratoriais, ESTeSL, 25 a 27 de outubro de 2019.
20. Faria NA, Miragaia M, de Lencastre H. Massive dissemination of methicillin resistant Staphylococcus aureus in bloodstream infections in a high MRSA prevalence country: establishment and diversification of EMRSA-15. Microb Drug Resist. 2013;19(6):483-90.

Artigo recebido em 27.12.2019 e aprovado em 13.01.2020.