

Why We Should Be Concerned about Methicillin-Resistant *Staphylococcus aureus* (MRSA)¹

Austin B. Mogen and Kelly C. Rice²

What is MRSA?

According to the Centers for Disease Control and Prevention (CDC), methicillin-resistant *Staphylococcus aureus* (MRSA) is among the most common causes of bacterial infections in the United States and is responsible for approximately 80,000 infections per year, with an incidence of 25 per 100,000 population (CDC 2012; Dantes et al. 2013). Approximately 19,000 hospitalized American patients die of MRSA infections each year. This statistic is close to the number of AIDS, tuberculosis, and viral hepatitis deaths combined (Boucher and Corey 2008). Diseases caused by both MRSA and methicillin-susceptible *S. aureus* (MSSA) include skin and soft tissue infection (abscess, boils), bacteremia, heart valve infection (endocarditis), pneumonia, bone/bone marrow infection (osteomyelitis), brain abscess, and central nervous system infection (meningitis) (Archer 1998). Treatment and complete resolution of MRSA infections can be extremely challenging, since many MRSA strains are multidrug-resistant.

Resistance to penicillin, a cell-wall active β -lactam antibiotic, was first detected in *S. aureus* clinical isolates in the 1940s (Rammelkamp and Maxon 1942). This resistance problem became widespread in healthcare settings and the community-at-large by the 1950s (Roundtree and Freeman 1956). As a countermeasure to this emerging threat, a second-generation β -lactam antibiotic, methicillin, was developed and introduced into clinical usage in 1959.

However, it took less than two years for the first methicillin-resistant *S. aureus* (MRSA) strains to emerge in patients (Jevons, Coe, and Parker 1963; Jevons 1961). Unfortunately, the genetic mechanism that confers methicillin resistance to *S. aureus* also enables this bacterium to resist the action of all β -lactam antibiotics (Gordon and Lowy 2008). Currently, many MRSA strains carry genes that confer resistance to nearly all types of antibiotics used in the clinical setting. The antibiotic vancomycin is considered the “last line of defense” against MRSA infection; however, reduced susceptibility to vancomycin in clinical *S. aureus* isolates has also been observed in a few cases (Gardete and Tomasz 2014; Howden et al. 2010).

What is the difference between hospital-acquired, community-acquired, and livestock-associated MRSA?

Historically, MRSA infections were primarily limited to hospitals and other healthcare environments. These “hospital-acquired” MRSA (HA-MRSA) strains can readily spread from patient to patient, posing a significant risk to patients who have recently undergone surgery and/or are immunocompromised. In addition to these hospital-acquired infections, community-acquired MRSA (CA-MRSA) strains have also emerged over the last 30 years. Although

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2. Austin B. Mogen, graduate student; and Kelly C. Rice, assistant professor, Department of Microbiology and Cell Science; UF/IFAS Extension, Gainesville, FL 32611.

CA-MRSA strains are generally susceptible to a wider range of antibiotics compared to HA-MRSA, they tend to be highly virulent and transmissible, causing devastating disease in otherwise healthy individuals (Thurlow, Joshi, and Richardson 2012). These MRSA infections are defined as “community-acquired” because they are diagnosed in people who have not had any contact with a hospital or healthcare setting prior to infection. CA-MRSA infections have been reported in many high school and college athletes across the US (Rihn, Michaels, and Harner 2005).

More recently, livestock-associated MRSA (LA-MRSA) strains have also become a point of epidemiological interest. LA-MRSA strains belonging to the sequence type 398 (ST398) group are prevalent in Europe (Witte et al. 2007; Wulf and Voss 2008; Wulf et al. 2012), and have also emerged in North America as colonizers of livestock and humans (Mendes et al. 2011; Smith et al. 2009; Bhat et al. 2009) as well as sources of human infections (Schijffelen et al. 2010; Golding et al. 2012; Mediavilla et al. 2012; Uhlemann et al. 2013). Previous comparison of LA-MRSA ST398, CA-MRSA, and HA-MRSA genome sequences revealed that these LA-MRSA strains represent a homogeneous lineage distinct from the HA-MRSA and CA-MRSA strains, lacking several human-associated virulence and adhesion factors present in most CA-MRSA and HA-MRSA (Hallin et al. 2011). However, another analysis of both MSSA and MRSA ST398 genome sequences suggests that MRSA ST398 originated in humans as MSSA, jumped to livestock where it acquired methicillin resistance, and adapted to humans once more through the acquisition of various human-specific immune evasion factors (Price et al. 2012). Epidemiological and comparative genomic studies have been conducted to assess transmissibility, antibiotic resistance, and virulence of LA-MRSA because of its potential to cause disease in humans and contribute to the spread of antibiotic resistance (Christiansen et al. 2014; Ballhausen et al. 2014).

What makes MRSA such a formidable pathogen?

S. aureus (Figure 1) is an extremely successful bacterial pathogen of both humans and mammalian livestock. This bacterium is a common colonizer of the human nose and skin. It is possible that up to 30% of humans are asymptomatic nasal carriers of *S. aureus*. These carriers are at a higher risk of succumbing to *S. aureus* infection and are presumed to be important contributors to the spread of *S. aureus* among the population (Gorwitz et al. 2008; Kluytmans, van Belkum, and Verbrugh 1997). If *S. aureus* enters the human

body through cuts or micro-abrasions of the skin, it has the potential to infect most tissue and organ systems. This bacterium expresses a variety of proteins on its cell surface which facilitate attachment to many different types of host proteins and cells. It possesses an arsenal of secreted toxins and tissue-degrading enzymes that contribute to immune system evasion, host cell damage, tissue destruction, and the ability to spread to various body sites (Gordon and Lowy 2008). Additionally, *S. aureus* has an extremely versatile metabolism which regulates the production of several virulence factors and allows it to grow in a variety of infection sites (Somerville and Proctor 2009). It is also capable of persisting in the body by hiding inside of host cells (Loffler et al. 2014; Tuchscher et al. 2010; Tuchscher et al. 2011) and growing on certain body site surfaces (i.e., implanted medical devices, heart valves, chronic wounds) as a multicellular biofilm (Otto 2013). Its intracellular and biofilm capabilities allow *S. aureus* to resist antibiotic treatment and effectively hide from the host immune system.

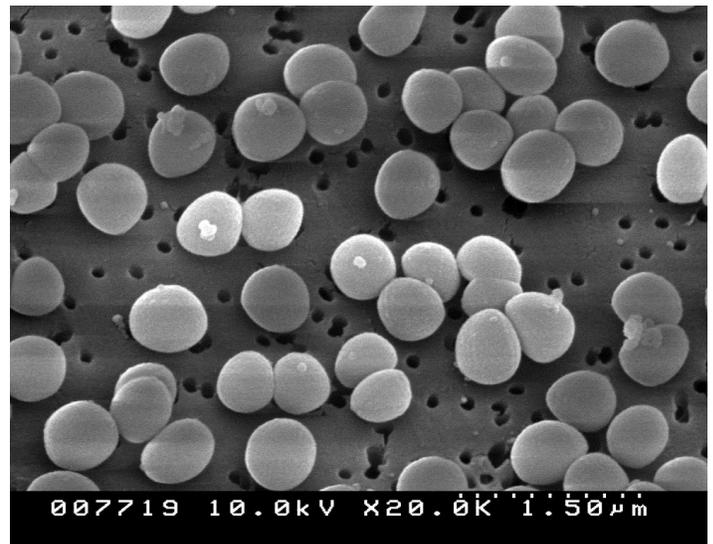


Figure 1. Scanning electron microscope image of *S. aureus* cells (20,000X magnification, unpublished data).
Credits: K. C. Rice, UF/IFAS

What are the symptoms and risk factors of MRSA infection?

According to the CDC, initial symptoms of a MRSA skin infection resemble those of a spider bite: a red, swollen bump or infected area on the skin that may be painful or warm to the touch (CDC 2016). The affected area may also drain pus or liquid, and the infected person may have a fever. It is very important to seek medical treatment right away if these symptoms (especially fever) occur with your “spider bite”; without treatment, MRSA skin infections can quickly lead to serious and even life-threatening illness. If a MRSA skin infection is suspected, the area should be

covered with clean, dry bandages until a medical professional can be consulted.

The CDC and Florida Department of Health summarize the risk factors for MRSA infection and transmission as the “five Cs” (Florida Department of Health 2016):

1. Crowding (prisons, military barracks, homeless shelters)
2. Contact (frequent skin-to-skin) (athletic teams)
3. Compromised skin (cuts, scrapes)
4. Contaminated items and surfaces (locker rooms, gym facilities)
5. Lack of Cleanliness

How is MRSA infection prevented?

The CDC reports that risk of MRSA infection can be reduced by maintaining good hand and body hygiene, especially after exercising, participating in team sports, or visiting high-risk MRSA areas such as healthcare facilities (CDC 2016). It is also advisable to keep any cuts, scrapes, or open wounds clean and covered until they are healed. Sharing of personal items such as towels and razors should be avoided (Abdelzaher et al. 2010).

Is MRSA a concern for Florida human health and agriculture?

MRSA represents a concern for human and animal health in Florida and beyond the state’s borders. Several notable examples are summarized below:

- According to antimicrobial resistance surveillance data reported by the Florida State Department of Health, MRSA was detected in 43% to 57% of tested *S. aureus* isolates in 2013. In this report, it was also noted that north Florida county residents had the highest proportion of MRSA isolates, a trend that has been consistently observed since surveillance began in 2006. The incidence of MRSA-related illness and death in Florida is unknown, as the Florida Department of Health does not require health care providers to report individual MRSA infections (Florida Department of Health 2015).
- The University of Florida Gator football team experienced a MRSA outbreak among several of its players at the beginning of the 2005 college football season. These infections required intravenous (IV) antibiotic treatment

and resulted in the loss of several playing days (Archibald et al. 2008).

- Another high-profile outbreak of CA-MRSA in the state of Florida occurred in 2013, when three Tampa Bay Buccaneer football players contracted MRSA infections (CBS News and Associated Press 2013). One player who can no longer play football as a result of this infection has since filed a lawsuit against the NFL team, claiming that “unsanitary conditions” at the Bucs’ facility constituted negligence on the team’s part, and the Bucs “failed to disclose and actively concealed ongoing incidents of infection” (Stroud and Auman 2015).
- Both MSSA and MRSA were recently identified and isolated from water and sand samples collected from a recreational south Florida marine beach. 17 out of 22 of these MRSA isolates were identified as CA-MRSA. Although an association between beach exposure to *S. aureus* and reported illness was not found in this study, the data suggest that humans are a potential source of *S. aureus* in marine waters (Plano et al. 2013).
- Bovine mastitis is a bacterial infection of the mammary gland, which can present as either a subclinical (i.e., absence of symptoms) or clinical (i.e., visible local and/or systemic symptoms) disease (De Vlieghe et al. 2012). Mastitis is one of the most prevalent diseases afflicting dairy herds, and outbreaks of these infections impose a significant financial burden on dairy farmers, due to costs associated with antimicrobial treatment of infected animals, decreased milk production, and reduced fertility (Cha et al. 2011; DeGraves and Fetrow 1993). The herd-level prevalence of *S. aureus* infection on dairy farms was reported to be 43% in a recent US study, making this bacterium a dominant mastitis pathogen in the United States (USDA-APHIS 2007).
- Staphylococci (including *S. aureus*) are also a common cause of a variety of skin diseases in cows, sheep, and pigs (Foster 2012). Colonization of livestock with either MSSA or MRSA has the potential to adversely affect human health, as LA-MRSA has been an emerging source of *S. aureus* infections in humans in the US and abroad (Golding et al. 2012; Schijffelen et al. 2010). Determining the incidence of LA-MRSA among Florida livestock represents a future research interest for the authors of this EDIS publication.

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