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Updated Epidemiology and Clinical Syndromes Associated with Community-Acquired Methicillin-Resistant Staphylococcal aureus (CA-MRSA) Infections

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Introduction

Community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) infections have appeared with increasing frequency around the world and are considered to be a rapidly emerging public health problem. The Centers for Disease Control (CDC) defines CA-MRSA as a diagnosis made in the outpatient setting or by a culture growing MRSA within 48 hours of hospital admission, obtained from a patient with no medical history of MRSA infection or colonization; no medical history in the past year of 1) hospitalization 2) admission to a nursing home, skilled nursing facility, or hospice 3) dialysis or 4) surgery; and, no permanent indwelling catheters or medical devices that pass through the skin.[1]

The objectives of this paper are to describe the epidemiology of CA-MRSA, examine the clinical syndromes associated with CA-MRSA, describe risk factors for developing CA-MRSA, and provide data about the impact and outcomes associated with this disease.

A case presentation of a 20-year old female with MRSA bacteremia is described in Figure 1.

The impact and medical outcomes of this disease can be catastrophic. The CA-MRSA infection in this young woman resulted in bilateral below the knee amputations (BKAs), loss of most of her digits, and a 104-day stay in the respiratory care unit.

Epidemiology

The increase in penicillinase-producing *S. aureus* has been occurring since the 1950s and MRSA began to increase dramatically in the U.S. in the 1970s.[2] The percentage of MRSA-related hospital-onset infections

Figure 1

Case presentation

- 12/25: 20 year old female with no underlying illness except occasional use of a "puffer" for mild asthma, Admitted with one day history of SOB after URI. Exposed to nephew 1 week PTA with ILI
- Bilateral pneumonia, intubation, sepsis and hypotension, WBC 700
- 12/26: MRSA bacteremia, MRSA in sputum, on vancomycin
- 12/27: Cavitary pneumonia, persistant MRSA bacteremia, ARDS and high frequency ventilation
- Strain susceptible to Clindamycin, TMP/sulfa, Vancomycin, and other; has PVL gene, PFGE similar to US clones
- Influenza A antigen was positive and >16 fold increase in serology

in intensive care patients in the U.S. has risen from 30% to over 50% in the past five years.[3] In a stratified national sample of 670 hospitals, two-thirds of hospitals reported increasing MRSA rates, resistance rates were highest with MRSA (36%), and 24% reported MRSA outbreaks within the previous year.[4]

However, the increase in MRSA prevalence is not limited to the inpatient setting. Data from 33 hospitals in The Surveillance Network (TSN) Database—USA (Focus Technologies, Inc., Herndon, VA.) indicated an increase in prevalence of outpatient MRSA isolates from 17% in 1996 to 29% in 2000 along with an increase in inpatient MRSA isolates from 30% to 46% in 2000 (Figure 2).[5]

The increase in MRSA prevalence, and particularly CA-MRSA, is not just a U.S. phenomenon. In Western Australia, for example, reported cases of CA-MRSA

Figure 2

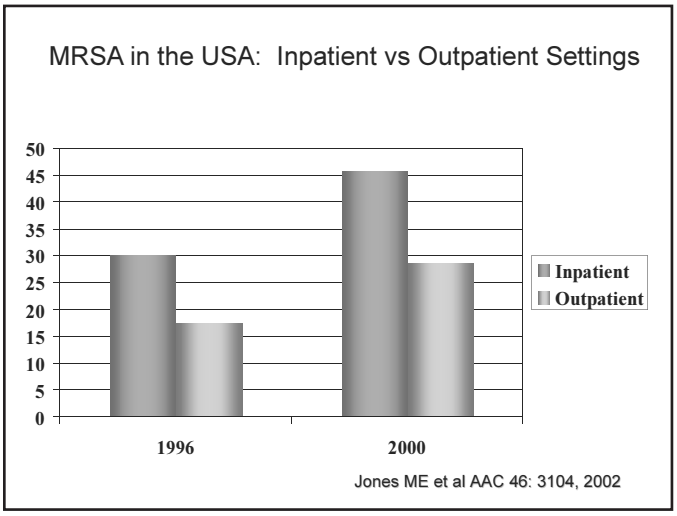
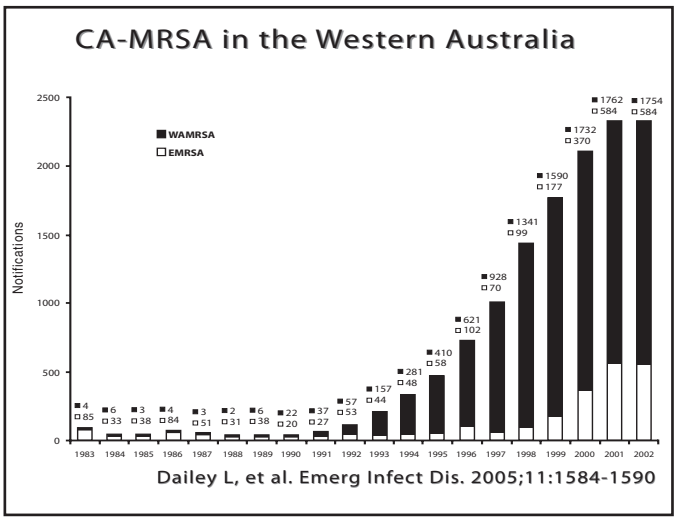


Figure 3



increased dramatically from 1998 to 2002 (Figure 3).[6] Children represent one of the primary groups that have been affected by CA-MRSA. Surveillance of community-acquired *S. aureus* infections at Texas Children's Hospital revealed that CA-MRSA isolates increased from 72% in 2001 to 76% in 2004 (p=0.008), which was larger than the increase noted in methicillin-susceptible *S. aureus* (MSSA) isolates. More patients with MRSA versus MSSA infections were admitted to the hospital (62% versus 53%, respectively; P=0.0001).[7]

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CDC surveillance of CA-MRSA in three regions (Baltimore, Atlanta, and 12 hospitals in Minnesota) from 2001-2002 determined that CA-MRSA represented between 8% and 20% of all isolates.[8] There was a wide range in the incidence of the disease by geographic location; the incidence was greater in Atlanta (25.7 cases per 100,000) than in Baltimore (18.0 per 100,000). Children two years of age or younger were at greater risk of acquiring CA-MRSA than children older than two years of age (RR 1.51; 95% CI, 1.19-1.92). Multi-drug resistance was common with MRSA strains (73%). MRSA was the primary reason for hospitalization in the majority of patients (Atlanta-74%, Baltimore-57%, Minesota-83%); 6% of cases were invasive (40/100,000 in Baltimore vs. 19/100,000 in Atlanta). The vast majority of cases (77%) involved skin and soft tissue infections.

Healthcare-associated and CA-MRSA have different demographic, clinical, and microbiologic profiles.[9] Out of 1100 MRSA infections identified at 12 Minnesota hospitals in 2000, 12% of cases were community-acquired and 85% were health-care associated. Community-associated MRSA infections occurred more frequently in younger people (median age, 23 years) compared with healthcare-associated MRSA infections (median patient age, 68 years). The proportion of nonwhite patients with CA-MRSA was 32% compared with 11% with HA-MRSA infections, a statistically significant difference. The vast majority of CA-MRSA infections involved skin and soft tissue (75%) compared with hospital-acquired infections (37%), which generally involved the urinary tract, bloodstream, or lower respiratory tract (52%). The CA-MRSA isolate was generally more virulent. The majority of CA-MRSA isolates were positive for Panton-Valentine leukocidin along with enterotoxins a, c, and k compared with ≤ 4% of healthcare-associated MRSA.

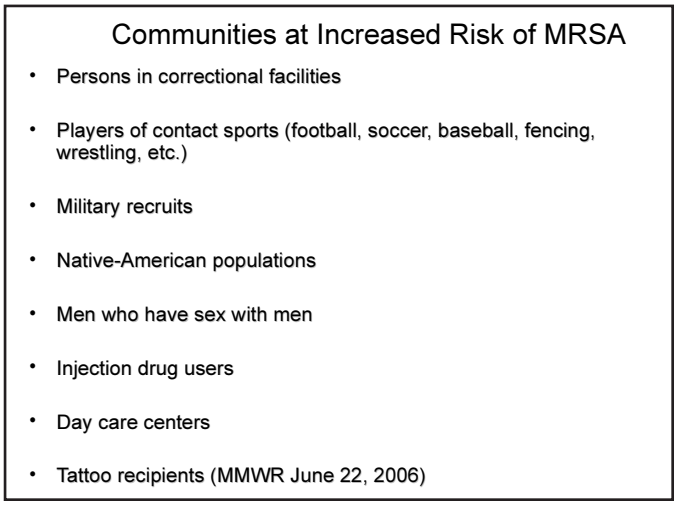
Fusion of CA-MRSA into the healthcare setting was also reported at Emory University in Atlanta, Georgia over a 7.5-month period in 2004.[10] Out of 132 patients with bloodstream infections (incidence, 6.8/1000 admissions), 116 isolates were available for genotyping. The demographics of these 116 cases were as follows: mean age 47 years, 62% male, 82% African American, and 22% human immunodeficiency virus (HIV) seropositive. Among these cases, 92% had contact with a health care facility within the previous year and 42% met the criteria for a nosocomial infection. The USA300 genotype–the type commonly associated with CA-MRSA infection–accounted for 34% of the 116 isolates; 29% had the USA100 genotype, which is most commonly seen with health care

associated cases. Most concerning was that 28% of healthcare associated blood stream infections and 20% of nosocomial blood stream infections were identified as the MRSA USA300 genotype. Multivariate analyses suggested that the conditions associated with having an infection due to the MRSA USA300 genotype were injection drug use (OR 3.7, 95% CI 1.1–12.3) and skin and soft tissue infection (OR 4.3, 95% CI 1–16.8). Long-term care (OR 0.1, 95% CI 0.01–0.82) and treatment with antibiotics in the previous year (OR 0.10, 95% CI 0.02–0.49) were considered to be protective against acquiring the CA-MRSA USA300 genotype. The CA-MRSA USA300 genotype appears to be emerging as a significant cause of health care-associated and nosocomial blood stream infections.

Risk Factors

When CA-MRSA was first recognized, individuals with CA-MRSA infection generally had risk factors predisposing them to the disease. Populations at increased risk of acquiring MRSA included individuals at close quarters such as inmates at correctional facilities, athletes who play contact sports, and military recruits. A high incidence of CA-MRSA has also been reported in Native Americans, men who have sex with men, injection drug users, daycare centers, and recipients of tattoos from unlicensed tattooists (Figure 4).[11]

Figure 4



The independent risk factors for MRSA were determined from 320 adult patients with *S. aureus* skin and soft tissue infections in 11 university-affiliated emergency departments in 2004.[12] The overall prevalence of MRSA was 59%. The SCC*mec* type IV and Panton-Valentine leukocidin (PVL) toxins were detected in 98% of MRSA isolates. The MRSA isolates had varying susceptibility rates to rifampin and trimethoprim-sulfamethoxazole (100%), clindamycin (95%), tetracycline (92%), fluoroquinolones (60%), and erythromycin (6%). The potential risk factors were identified through multivariate logistic regression analyses included non-Hispanic black race (OR 1.9; 95% CI, 1.1–3.4), use of any antibiotics in the past month (OR 2.4; 95% CI 1.3–4.3), reported spider bite (OR 3; 95% CI 1.6–5.7), underlying medical illness (OR 0.3; 95% CI 0.2–0.6), history of MRSA infection (OR 3.4; 95% CI, 1.1-10), and close contact with a person with a similar infection (OR 3.8; 1.6–9.3).

The first reports of CA-MRSA in patients who did not have risk factors occurred in children at the University of Chicago Children's Hospital.[13] Investigators reported that the prevalence of CA-MRSA in children without risk factors increased from 10 per 100,000 admissions in 1988-90 to 259 per 100,000 admissions in 1993-1995 (P<0.001).[13] Most cases were cellulitis, abscesses, or skin infections that were susceptible to trimethoprim-sulfamethoxazole and clindamycin. The majority of isolates obtained from children with an identified risk were not susceptible to at least two drugs compared with 24% of isolates obtained from children without an identified risk (P=0.02).

Subsequent to this initial report in children, there have been CA-MRSA outbreaks involving inmates, football teams, wrestling teams, fencing teams, men who have sex with men, intravenous drug abusers, post partum women, and many other patient groups. In the 2003 football season, the St Louis Rams had an outbreak of MRSA abscesses. The transmission and characteristics of the MRSA isolates were evaluated in a retrospective cohort study of 84 players and staff.[14] Eight of the 58 players acquired MRSA infections, which developed at turf-abrasion sites. The development of a MRSA infection was significantly associated with the linebacker position and higher body mass index. Forty-two percent of players and staff had nasal colonization for MSSA but not MRSA. All isolates carried the PVL gene and had staphylococcal cassette chromosome *mec* (SCC*mec*) type IVa resistance, characteristic of the CA-MRSA pathogen.

An increasing number of patients without traditional risk factors are acquiring CA-MRSA. Hospital transmission of CA-MRSA, particularly the USA300 genotype, is also being reported more frequently. At Columbia University Medical Center in New York, eight postpartum women developed MRSA skin and soft tissue infections 23 days (mean) post-delivery.[15] The infections consisted of four cases of mastitis (three of these cases progressed to breast abscess), a post-operative wound infection, cellulitis, and pustulosis. Pulsed field gel electrophoresis showed that the pathogens were from a prototype CA-

MRSA strain MW2 (a mid-Western U.S. strain). All of these strains carried the SCC*mec* type IV cassette and produced PVL along with enterotoxins C and H. The route of transmission was never found. All cultures of the environment, healthcare workers, and newborns were negative. In the case control study, group B streptococcal vaginal carriage was considered to be a risk factor for a MRSA infection.

Clinical Syndromes

The natural history of CA-MRSA colonization and infection was evaluated in 812 U.S. Army soldiers over a three-year period in a prospective observational study.[16] Three percent had nasal colonization with CA-MRSA. Of these soldiers, 38% developed soft tissue infections compared with 3% of 229 soldiers who were colonized with MSSA. In another outbreak of 235 CA-MRSA infections in military recruits, the predominant site of infection was in the lower extremity (44%) compared with upper extremity (29%), face/neck (4%), and other areas (24%).[17] Out of 874 healthcare workers who were in close contact with the recruits, 24 (2.7%) with direct patient contact carried MRSA intranasally. All MRSA isolates were susceptible to clindamycin and trimethoprim/sulfamethoxazole.

Necrotizing pneumonia is a more serious manifestation of infection due to CA-MRSA which may occur without apparent predisposition or following another respiratory illness. Four cases of CA-MRSA necrotizing pneumonia have recently been evaluated at Johns Hopkins Hospital. All of these cases were post-influenza syndromes; the isolates were positive for the PVL toxin and the SCC*mec* type IV genotype.

One of the most concerning infections is necrotizing fasciitis, a life-threatening infection. In a retrospective review of 843 patients with wound cultures that grew MRSA, 14 patients (median age, 46 years) were diagnosed with necrotizing fasciitis, necrotizing myositis, or both.[18] Monomicrobial MRSA wound cultures were present in 86% of patients; four out of ten patients had MRSA positive blood cultures. All patients had serious complications that required medical and surgical therapy including a prolonged stay in the ICU and reconstructive surgery. All MRSA isolates carried the PVL leukocidin gene, contained the classic SCC*mec* type IV gene, and were susceptible to trimethoprim/sulfamethoxazole, clindamycin, and rifampin.

Impact, Outcomes, and Susceptibility

The impact of CA-MRSA infections is high, with 4% to 10% of cases leading to admissions to the intensive care unit.[8] Prevention of CA-MRSA outbreaks may reduce potentially serious complications associated with the disease. Targeting preventive and educational efforts at groups in the community that are at higher risk of CA-MRSA infections, such as athletic teams, is an important step toward preventing infection.

Practical management of the spread of MRSA in athletics will need to include infection prevention strategies.[19] Common hygiene deficiencies in contact sport situations that have been noted by investigators include the following: 1) Trainers did not have regular access to hand hygiene; 2) Towels were shared; approximately three players per towel; 3) Players did not shower before using communal whirlpools (where MSSA was isolated); and 4) Team members received on average 2.6 antibiotic courses per year (10 times the rate of age and gender adjusted general population).

A hallmark feature of CA-MRSA infections, perhaps owing to the organism's small genome, is its antibiotic susceptibility pattern compared with healthcare-associated MRSA. Susceptibility of CA-MRSA to multiple drugs has been noted in several studies.[12,13,17,18,20] In a prospective study at King Fahad Hospital in Saudi Arabia, the prevalence of CA-MRSA increased from 5% in 1998 to 33% in 2000.[20] Unlike healthcare-associated MRSA, which was 100% susceptible to vancomycin/teichoplanin and only 59% susceptible to clindamycin in this study, CA-MRSA was 100% susceptible to gentamicin, ciprofloxacin, vancomycin/teichoplanin, and rifampin; and 95% of isolates were susceptible to clindamycin and trimethoprim/sulfamethoxazole.

In summary, MRSA acquisition in the community is increasingly reported worldwide. These infections are most commonly associated with skin and soft tissue infections. Necrotizing pneumonia and fasciitis are serious manifestations of infection with CA-MRSA. Risk factors for acquisition of CA-MRSA or USA300 are different from those associated with the traditional healthcare associated strains. There are growing numbers of infected individuals who have no risk factors for CA-MRSA infection. Finally, the USA300 strain is now associated with healthcare associated infections and outbreaks in healthcare settings.

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A minimum assessment score of 80% is required.

1) Based on the emerging literature, which groups appear to be at increased risk of developing community acquired MRSA infections?

a. Wrestlers and football players
b. Prisoners
c. IV drug abusers
d. Men who have sex with men
e. All of the above

Answer: _____

2) Which of the following statements best describes the clinical presentation of community-acquired MRSA (CA-MRSA) infections when compared with traditional MRSA infections?

a. Skin and soft tissue infections and pneumonia are rare presentations.
b. Primary bloodstream infections and urinary tract infections are rare presentations.
c. Skin and soft tissue infections and pneumonia are responsible for ¾ of CA-MRSA infections.

Answer: _____

3) The following describe the phenotypic or genotypic characteristics of the CA-MRSA in the US:

a. It does not contain the *mec*A gene
b. It does not produce Panton Valentine leukocidin
c. It is usually called the USA 300 on PFGE
d. It contains the SCC II

Answer: _____

4) Community-acquired MRSA (CA-MRSA) strains are commonly susceptible which of the following antibiotics?

a. vancomycin, TMP/sulfa, rifampin, clindamycin, linezolid, minocycline
b. vancomycin, cefazolin, clindamycin, doxycycline
c. vancomycin, TMP/sulfa, cefazolin, ceftriaxone

Answer: _____

5) Outbreaks of community acquired MRSA among athletes are associated with all of the following "risks" except:

a. Turf burns
b. Crowding
c. Sharing of equipment, clothing and other items
d. Colds

Answer: _____

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Infectious disease physicians, hospital epidemiologists, clinical microbiologists, pharmacists, public health authorities, practicing physicians, and other healthcare professionals interested in the treatment of serious infections due to CA-MRSA.

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Participant will be able to discuss newly recognized risk factors associated with CA-MRSA infections.

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