

# Community Acquired Methicillin Resistant *Staphylococcus aureus*: A Wisconsin Perspective

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## ABSTRACT

Community-acquired methicillin-resistant *Staphylococcus aureus* have swept across the United States, causing severe morbidity and mortality (see Table 1). This manuscript provides some illustrative cases seen in Wisconsin.

## INTRODUCTION

Isolation of methicillin resistant *Staphylococcus aureus* (MRSA) strains has progressively increased over the past 2 decades in hospitals.<sup>1,2</sup> MRSA was carried from the hospitals by patients into nursing homes and hemodialysis centers, and these have been called hospital associated (HA)-MRSA.<sup>1</sup> In the past, patients admitted from the community could be assumed to be free of MRSA. However, this situation began to change in 1998 when Dr Daum's group reported that children were entering the University of Chicago emergency department with community acquired (CA)-MRSA.<sup>3</sup> Over the next 7 years, CA-MRSA was reported by other investigators over very widely dispersed geographical areas, including South Dakota, Alaska, Minnesota, Texas, Oklahoma, California, Western Europe, and Japan.<sup>2,4-26</sup>

There was some clustering of CA-MRSA in the United States, with reports of skin abscesses in prisoners,<sup>6,22</sup> IV drug users in San Francisco,<sup>26</sup> and in Native Americans, perhaps associated with community centers and steam bath houses.<sup>4,5,25</sup> The first cluster of cases of CA-MRSA in Wisconsin was in Native Americans living in the Marshfield Clinic area.<sup>25</sup> Most of these initial Wisconsin cases had skin and soft tissue abscesses.

Not only had CA-MRSA moved into the community, but also a disturbing new report from France revealed that these organisms could produce a highly lethal form of pneumonia in young people (mean age=14 years old).<sup>9</sup> Further reports indicated that the CA-MRSA was causing serious skin and soft tissue infections.<sup>18</sup> These strains were carrying the Patton-Valentine Leukotoxin (PVL),<sup>18</sup> which is moved by bacterial phages between strains of *S. aureus*.<sup>4,22,27,28</sup> PVL had been associated with skin abscesses in the past,<sup>18</sup> but strains of *S. aureus* that caused cases of hemorrhagic pneumonia following respiratory tract infections (e.g., influenza) carried PVL.<sup>9</sup> PVL is a lytic toxin, and its presence in *S. aureus*, whether in MRSA or MSSA, is associated with more severe disease.<sup>29</sup>

Despite the proximity of Madison to Chicago and Marshfield, Madison remained free of these organisms until November 2003, when 11 patients came to my attention over a period of 2 weeks. Six of these cases are detailed below and are discussed in relationship to syndromes being reported in other parts of the United States. Also, information concerning other new CA-MRSA syndromes is provided.

## ILLUSTRATIVE CASES OF CA-MRSA

### Case #1

A previously healthy 54-year-old man thought he might have been bitten by a spider on the dorsum of the wrist while hiking in the Rocky Mountains. He felt well except for a red, swollen, tender lesion that progressed over a 60-hour period despite treatment with cephalexin 500 mg orally 3 times daily. He was afebrile and the rest of his physical exam was normal. Fifteen milliliters of pus was drained, and cephalexin continued. When cultures revealed MRSA, his therapy was changed to trimethoprim-sulfamethoxazole (SXT), 1 double strength tablet twice daily plus rifampin 600 mg daily, for 2 weeks. This MRSA was susceptible to clindamycin, erythromycin, rifampin, tetracycline, and

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SXT. He was also decolonized with mupirocin to the nose and Hibiclen washes for 2 weeks. He recovered uneventfully. A search for exposures revealed that his teenage daughter, a gymnast, had hidradenitis suppurativa (infection of the axillary sweat glands). His organism was positive for PVL by PCR testing.

### Comments on Case #1

This case captures a number of important points about CA-MRSA. First, most people entering the medical care system with what is perceived to be a spider bite in fact have CA-MRSA. The characteristics of CA-MRSA lesions are marked swelling (initially) and often pruritic that later develop a necrotic center and surrounding erythema that is 4-5 times larger than typical *S. aureus* skin abscesses.<sup>30</sup> In contrast, embolic lesions start as a small, hemorrhagic, sometimes tender, lesion that then may develop a suppurative center with modest surrounding erythema (see Table 2).

Second, CA-MRSA strains are more susceptible to antibiotics than HA-MRSA strains.<sup>3,31</sup>

Third, the source of the infection in this patient came from his daughter and the mat used by the gymnasts and wrestlers. Contact sports, crowding, shaving of hair, and failure to clean small abrasions are all possible means of transmission.<sup>4,5,7,11,15,22,25,26,32</sup> Some of the members of the wrestling team had skin abscesses, suggesting that CA-MRSA is able to remain viable and infectious on the mat as one team practiced in the morning and the other team at night. Similarly, the patient placed his wrist on the back of a couch and his daughter would sit with her arm over the couch, thereby explaining the somewhat unusual location of his skin abscess.

Fourth, the choices of antibiotics to treat his infection are also instructive. Cephalexin is slowly absorbed and rapidly excreted, giving low blood and tissues levels. The pharmacokinetics are such that the time above the minimal inhibitory concentration would be <25% of dosing interval for treating skin infections caused by methicillin susceptible *S. aureus*.<sup>33</sup> Were cephalexin to come onto the market today, it probably would only be recommended for urinary tract infections. In addition, *S. aureus* produce DNase, which breaks down DNA and releases thymidine. It is well known that thymidine greatly reduces the activity of both trimethoprim and sulfamethoxazole, thus SXT should be used with caution when pus is present. In all likelihood, this patient improved because the pus was drained, allowing these drugs to be active because there was no large release of thymidine from pus. In addition, the presence of rifampin will greatly increase the efficacy of the SXT. Of interest, SXT can be effective prophylac-

**Table 1.** Syndromes caused by CA-MRSA

Syndrome	References
Deep skin abscess with marked surrounding erythema occurring with or without new nasal colonization	3,7,14,30
Invasion into deep veins with pulmonary emboli	11,12
Necrotizing pneumonia	9
Post-partum infections	17,27,48
Pleural empyema in children	12
Waterhouse-Friderichsen Syndrome	41
Periorbital cellulitis (extending from ethmoid sinusitis) causing blindness	42,43
Prosthetic joint infections	44

**Table 2.** Furuncle vs. Septic Emboli

Furuncle	Septic Emboli
Begins as a red papule that slowly evolves	Begins acutely as a small hemorrhage
Itching initially, then becomes tender	Tender
Over hairy parts of body	Palms, soles, digits
Necrotic center develops over time around a hair follicle	Forms a pustule inside of a hemorrhagic center

tically against CA-MRSA as was shown in IV drug users who were HIV positive.<sup>19</sup>

Fifth, the patient was afebrile despite drainable pus. While patients with the more severe forms of infections associated with strains carrying the PVL genes are febrile, we have found that many of the patients with PVL infections are afebrile early in the course of their infections. This may relate to the lysis and death of leukocytes (neutrophils, macrophages, and monocytes) thereby decreasing the ability to release cytokines involved in stimulating a pyrogenic response.<sup>34</sup>

### Case #2

A 21-year-old woman who was 2 months pregnant came to the emergency department with a 4-day history of pain in her right shoulder. She was previously healthy and had no history of diabetes or skin infections. She had muscle tenderness over the right lower scapula and was diagnosed as having a muscle strain from carrying her 2-year-old son. She was afebrile and had no shortness of breath or chest pain. A day later, she returned with fever, hypotension, and severe myalgias, especially in her right leg and right back. A presumptive diagnosis of toxic shock syndrome was made, and she was urgently transferred to the University Hospital. Upon admission, she was found to be febrile to 101.4°F, pulse=148, blood pressure=100/55. She was perfusing



**Figure 1.** The photograph is of the left lateral thigh from case #3. The large amount of erythema and spontaneous drainage of pus are typical of CA-MRSA lesions.

her extremities poorly and had marked tenderness of the right thigh and right shoulder, and swelling of her right knee. Workup revealed a thrombosis of the right axillary vein, multiple septic emboli to the lungs, an abscess within the right thigh, and septic arthritis of the right knee. Her white blood count was 5.0 k with marked left shift. MRSA grew from lung lavage fluid, and right knee and right thigh abscess. However, all blood cultures were negative. The MRSA strain showed the same susceptibility pattern as in the first case. She was treated with linezolid, clindamycin, and rifampin. Her course was stormy with the development of pancreatitis from the rifampin, spontaneous abortion, and acute respiratory distress syndrome (thought secondary to toxic shock syndrome), but she eventually recovered.

#### Comments on Case #2

First, a search for epidemiological clues as to where this patient acquired this organism was unrevealing. She had none of the typical risk factors for CA-MRSA as noted above, although pregnancy might be a risk factor for CA-MRSA.

Second, the patient's initial presentation led the physicians away from the diagnosis of infection. There was no break in the skin, again suggesting that this organism is more invasive than most strains of *S. aureus*. She was afebrile and non-toxic at initial presentation. Thus, one must have a heightened awareness for CA-MRSA because presentation can show minimal initial signs of serious infectious diseases and our 'usual' drugs will not be active against MRSA.

Third, the propensity of CA-MRSA to invade deep veins has been reported recently by other investigators.<sup>11,12</sup> Previously healthy teenagers who received

minor skin injuries developed superficial skin infections that eventually penetrated into the deep veins of the leg.<sup>11,12</sup> The ability of CA-MRSA to traverse tissue planes and invade deeply across fascial planes provides another a warning that this may be CA-MRSA.

Fourth, mothers carrying CA-MRSA pose a threat to newborns, as there is a long history of serious *S. aureus* outbreaks in nurseries, which are made even more severe in the presence of CA-MRSA. Active surveillance and aggressive infection control measures, including contact isolation, cohorting, and decolonization can eradicate MRSA from neonatal ICUs.<sup>16</sup>

Fifth, the choice of antibiotics was based on several lines of reasoning. Linezolid was used because it has superiority in pulmonary infections over vancomycin in head to head clinical trials for its use.<sup>35-40</sup> Daptomycin is inactivated by surfactant<sup>40</sup> and not indicated for MRSA pneumonia. Rifampin was added for synergic killing of *S. aureus*, although clinical trials for this use are lacking. Clindamycin was given with the hope of decreasing toxin production. Clindamycin also has activity against the majority of CA-MRSA, but in 1 large series, 4.5% were resistant.<sup>48</sup>

#### Case #3

A 29-year-old man came to the University of Wisconsin Hospital emergency department with a "spider bite" on his fifth finger as well as skin abscesses on his right lateral thigh, and kissing lesions on his medial thighs. He worked as a carpenter, had a history of a bicuspid aortic valve, and had dental work 10 days before admission (3 doses of 1 gm amoxicillin every 8 hours as prophylaxis). He had no history of boils or diabetes mellitus. On exam, he was afebrile and appeared non-toxic. The lesion on his finger was draining creamy yellow pus, had erythema extending from his middle to the base of his finger, a 1 cm draining ulcer/abscess on the left lateral thigh with 12 cm of surrounding erythema (Figure 1), and 2 developing abscesses on the mid-thighs that were tender, raised, and red, but with no break in the skin. There was concern about endocarditis, but he had no typical embolic lesions, and his heart murmur had not changed. His blood cultures were negative and transesophageal echocardiogram showed no vegetations. The pus cultured from his finger and thigh wounds grew CA-MRSA with susceptibilities as for the first case. This strain carried the gene for PVL. His only laboratory abnormality was a white blood count of 13.1k. He was hospitalized and initially treated with vancomycin and rifampin for 6 days, but he went home on clindamycin plus rifampin. The abscess on his left thigh was opened and drained. He was also decolonized with mu-

pirocin to the nose for 7 days twice a day plus Hibiclens baths for 7 days.

#### *Comments on Case #3*

First, the lesions produced by CA-MRSA do not resemble emboli, thus endocarditis was unlikely even though he had had dental work and a bicuspid aortic valve, placing him at risk for endocarditis. The very wide area of surrounding erythema and the abscess-like, rather than embolic, lesions suggest PVL-containing *S. aureus* infection<sup>30</sup> (see Table 2 for differentiation of furuncle from an embolus).

Second, the patient was not placed in isolation when he entered the emergency department, despite having pus draining from his wounds. He should have been automatically placed in isolation as soon as the ward clerk heard the words “spider bite.”

Third, the patient had received antibiotics, which is a risk factor for acquiring CA-MRSA.<sup>7</sup>

Fourth, most of his treatment was with clindamycin plus rifampin. This combination was chosen because the patient had no health insurance. While there is little data on CA-MRSA treatment with clindamycin, the economics of the situation were such that this was what the patient desired.

Fifth, although the patient had multiple abscesses, he was afebrile. This may be due to the PVL toxin lysing phagocytes and reducing cytokine/endogenous pyrogens production.

Sixth, because of the virulence of CA-MRSA and his bicuspid valve, we elected to decolonize him, which was successful (decolonization protocol is discussed below).

#### *Cases #4-6*

While sitting in a Lay Z Boy chair, a 48-year-old man developed pain in the right buttock while watching the Packers football game. Because of pain, he left in the middle of the game to go to the emergency department. He was in good health and taking no medications. Examination revealed a tender red lesion about the size of a ping pong ball in the right gluteal fold. The skin was unbroken and there was no adenopathy. He was afebrile and white blood count was normal. After several consultations, the decision was made that there was a developing abscess, but it was too early to attempt drainage. He returned for outpatient surgery the next afternoon. In the meantime, his daughter and wife had sat in the Lay Z Boy chair while he was absent from the home for 7 hours. When the drainage fluid revealed MRSA, I was consulted. By now, 72 hours had passed, and he was improving. His dicloxacillin was stopped, and he was

treated with linezolid orally. However, both his wife and daughter now had red, painful lesions on their right buttocks. They were also treated with linezolid and resolved their evolving abscesses without the need for surgery.

#### *Comments on Cases #4-6*

The source of the CA-MRSA in the father was unknown; however, the timing strongly suggested that the infections in the wife and daughter arose from sitting in the same chair. No one had sat in the chair without clothes and no one had any open lesions when sitting in the chair. Again this suggests that CA-MRSA can penetrate normal skin and that the infectious disease-producing inoculum is likely to be quite small. Unfortunately, we lack epidemiology where investigators would perform environmental sampling and define the duration of persistence nor are there animal studies that define the infectious inoculum. We do, however, know that some CA-MRSA strains can form a biofilm on environmental surfaces, which should greatly enhance their persistence.<sup>5</sup>

### SUMMARY

Spectrum of *S. aureus* diseases has broadened. Recently, CA-MRSA has rapidly spread into many areas of Wisconsin. Practitioners should be aware of the cardinal clinical and laboratory features. The new syndromes and hypervirulence relate to the presence of PVL in the CA-MRSA strains.<sup>45</sup> Very severe syndromes can arise out of relatively minor wounds and can progress without the usual warning signs such as toxicity and fever. However, when the lungs are involved, the CA-MRSA can progress at an alarming rate, such as with the hemorrhagic pneumonia and Waterhaus-Friderischen syndrome. Patients who claim to have spider bites should be placed in immediate isolation and not be allowed to sit on the furniture in waiting rooms. This practice should also be extended to anyone coming into an office with the complaint of a skin abscess. Finally, we must consider CA-MRSA when selecting antibiotics for necrotizing fasciitis, any severe cellulitis, and septic emboli. With the continued and rapid spread of CA-MRSA,<sup>46</sup> antibiotics with activity against MRSA should be included in treatment regimens whenever these syndromes are encountered. In addition, intravenous immune globulin (IVIG) neutralizes PVL toxin<sup>47</sup> and has been used by physicians for severe cases, but controlled, randomized studies are not available.

### REFERENCES

1. Chambers HF. Community-associated MRSA—resistance and virulence converge. *N Engl J Med*. 2005;352(14):1485-1487.

2. Fridkin SK, Hageman JC, Morrison M, et al. Active Bacterial Core Surveillance Program of the Emerging Infections Program Network. Methicillin-resistant *Staphylococcus aureus* disease in three communities. *N Engl J Med*. 2005;352(14):1436-1444.
3. Herold BC, Immergluck LC, Maranan MC, et al. Community-acquired methicillin-resistant *Staphylococcus aureus* in children with no identified predisposing risk. *JAMA*. 1998;279(8):593-598.
4. Baggett HC, Hennessy TW, Leman R, et al. An outbreak of community-onset methicillin-resistant *Staphylococcus aureus* skin infections in southwestern Alaska. *Infect Control Hosp Epidemiol*. 2003;24(6):397-402.
5. Baggett HC, Hennessy TW, Rudolph K, et al. Community-onset methicillin-resistant *Staphylococcus aureus* associated with antibiotic use and the cytotoxin Pantone-Valentine leukocidin during a furunculosis outbreak in rural Alaska. *J Infect Dis*. 2004;189(9):1565-1573.
6. Baillargeon J, Kelley MF, Leach CT, Baillargeon G, Pollock BH. Methicillin-resistant *Staphylococcus aureus* infection in the Texas prison system. *Clin Infect Dis*. 2004;8(9):92-95.
7. Ellis MW, Hospenthal DR, Dooley DP, Gray PJ, Murray CK. Natural history of community-acquired methicillin-resistant *Staphylococcus aureus* colonization and infection in soldiers. *Clin Infect Dis*. 2004;39(7):971-879.
8. Frazee BW, Salz TO, Lambert L, Perdreau-Remington F. Fatal community-associated methicillin-resistant *Staphylococcus aureus* pneumonia in an immunocompetent young adult. *Ann Emerg Med*. 2005;46(5):401-404.
9. Gillet Y, Issartel B, Vanhems P, et al. Association between *Staphylococcus aureus* strains carrying gene for Pantone-Valentine leukocidin and highly lethal necrotizing pneumonia in young immunocompetent patients. *Lancet*. 2002;359(9308):753-759.
10. Goergens ED, McEvoy A, Watson M, Barrett IR. Acute osteomyelitis and septic arthritis in children. *J Paediatr Child Health*. 2005;41(1-2):59-62.
11. Gonzalez BE, Martinez-Aguilar G, Hulten KG, et al. Severe staphylococcal sepsis in adolescents in the era of community-acquired methicillin-resistant *Staphylococcus aureus*. *Pediatrics*. 2005;115(3):642-648.
12. Gonzalez BE, Hulten KG, Dishop MK, et al. Pulmonary manifestations in children with invasive community-acquired *Staphylococcus aureus* infection. *Clin Infect Dis*. 2005;41(5):583-590.
13. Huang YC, Su LH, Lin TY. Nasal carriage of methicillin-resistant *Staphylococcus aureus* in contacts of an adolescent with community-acquired disseminated disease. *Pediatr Infect Dis J*. 2004;23(10):919-922.
14. Issartel B, Tristan A, Lechevallier S, et al. Frequent carriage of Pantone-Valentine leukocidin genes by *Staphylococcus aureus* isolates from surgically drained abscesses. *J Clin Microbiol*. 2005;43(7):3203-3207.
15. Kazakova SV, Hageman JC, Matava M, et al. A clone of methicillin-resistant *Staphylococcus aureus* among professional football players. *N Engl J Med*. 2005;352(5):468-475.
16. Khoury J, Jones M, Grim A, Dunne WM Jr, Fraser V. Eradication of methicillin-resistant *Staphylococcus aureus* from a neonatal intensive care unit by active surveillance and aggressive infection control measures. *Infect Control Hosp Epidemiol*. 2005;26(7):616-621.
17. Laibl VR, Sheffield JS, Roberts S, McIntire DD, Trevino S, Wendel GD Jr. Clinical presentation of community-acquired methicillin-resistant *Staphylococcus aureus* in pregnancy. *Obstet Gynecol*. 2005;106(3):461-465.
18. Lina G, Piemont Y, Godail-Gamot F, Bes M, et al. Involvement of Pantone-Valentine leukocidin-producing *Staphylococcus aureus* in primary skin infections and pneumonia. *Clin Infect Dis*. 1999;29(5):1128-1132.
19. Mathews WC, Caperna JC, Barber RE, et al. Incidence of and risk factors for clinically significant methicillin-resistant *Staphylococcus aureus* infection in a cohort of HIV-infected adults. *J Acquir Immune Defic Syndr*. 2005;40(2):155-160.
20. Miller LG, Perdreau-Remington F, Rieg G, et al. Necrotizing fasciitis caused by community-associated methicillin-resistant *Staphylococcus aureus* in Los Angeles. *N Engl J Med*. 2005;352(14):1445-1453.
21. *Morbidity Mortality Weekly Report*. 1999;48:707-710.
22. Pan ES, Diep BA, Carleton HA, et al. Increasing prevalence of methicillin-resistant *Staphylococcus aureus* infection in California jails. *Clin Infect Dis*. 2003;37(10):1384-1388.
23. Schultz KD, Fan LL, Pinsky J, et al. The changing face of pleural empyemas in children: epidemiology and management. *Pediatrics*. 2004;113(6):1735-1740.
24. Siddiqui MA, Richards PJ, Ahmed EB. Falling downstairs does not mean a fracture: the first case report of an immunocompetent community acquired MRSA disc/psaos abscess. *Injury*. 2005;36(4):569-572.
25. Stemper ME, Shukla SK, Reed KD. Emergence and spread of community-associated methicillin-resistant *Staphylococcus aureus* in rural Wisconsin, 1989 to 1999. *J Clin Microbiol*. 2004;42(12):5673-5680.
26. Young DM, Harris HW, Charlebois ED, et al. An epidemic of methicillin-resistant *Staphylococcus aureus* soft tissue infections among medically underserved patients. *Arch Surg*. 2004;139(9):947-951.
27. McDonald JR, KS Kaye, K Blake, K Caughlan, JF John. Familial clusters of skin infections due to methicillin-resistant *Staphylococcus aureus*. ISSSI Abstract #CA-14, Oct 2004.
28. Zou D, Kaneko J, Narita S, Kamio Y. Prophage, phiPV83-pro, carrying Pantone-Valentine leukocidin genes, on the *Staphylococcus aureus* P83 chromosome: comparative analysis of the genome structures of phiPV83-pro, phi-PVL, phi11, and other phages. *Biosci Biotechnol Biochem*. 2000;64(12):2631-2643.
29. Etienne J. Maternity clinic outbreak of community acquired methicillin resistant *Staphylococcus aureus*. ISSSI, Plenary Sessions Oct 2004.
30. Yamasaki O, Kaneko J, Morizane S, et al. The association between *Staphylococcus aureus* strains carrying Pantone-Valentine leukocidin genes and the development of deep-seated follicular infection. *Clin Infect Dis*. 2005;40(3):381-385.
31. Siberry GK, Tekle T, Carroll K, Dick J. Failure of clindamycin treatment of methicillin-resistant *Staphylococcus aureus* expressing inducible clindamycin resistance in vitro. *Clin Infect Dis*. 2003;7(9):1257-1260.
32. Centers for Disease Control and Prevention. Community-associated methicillin-resistant *Staphylococcus aureus* infections in Pacific Islanders—Hawaii, 2001-2003. *MMWR Morb Mortal Wkly Rep*. 2004;53:767-770.
33. Madaras-Kelly K, Michas P, George M, May MP, Adejare A. A randomized crossover study investigating the influence of ranitidine or omeprazole on the pharmacokinetics of cephalexin monohydrate. *J Clin Pharmacol*. 2004;44(12):1391-1397.
34. Genestier AL, Michallet MC, Prevost G, et al. *Staphylococcus aureus* Pantone-Valentine leukocidin directly targets mitochondria and induces Bax-independent apoptosis of human neutrophils. *J Clin Invest*. 2005;115(11):3117-3127.
35. Kollef MH. Appropriate empirical antibacterial therapy for nosocomial infections: Getting it right the first time. *Drugs*. 2003;63(12):2157-2168.
36. Kollef MH, Rello J, Cammarata SK, Croos-Dabrera RV, Wunderink RG. Clinical cure and survival in gram-positive

- ventilator-associated pneumonia: retrospective analysis of two double-blind studies comparing linezolid with vancomycin. *Intensive Care Med.* 2004;30(3):388-394.
37. Sharpe JN, Shively EH, Polk HC Jr. Clinical and economic outcomes of oral linezolid versus intravenous vancomycin in the treatment of MRSA-complicated, lower-extremity skin and soft-tissue infections caused by methicillin-resistant *Staphylococcus aureus*. *Am J Surg.* 2005;189(4):425-428.
  38. Wunderink RG, Rello J, Cammarata SK, Croos-Dabrera RV, Kollef MH. Linezolid vs vancomycin: analysis of two double-blind studies of patients with methicillin-resistant *Staphylococcus aureus* nosocomial pneumonia. *Chest.* 2003;124(5):1789-1797.
  39. Wunderink RG, Cammarata SK, Oliphant TH, Kollef MH, Linezolid Nosocomial Pneumonia Study Group. Continuation of a randomized, double-blind, multicenter study of linezolid versus vancomycin in the treatment of patients with nosocomial pneumonia. *Clin Ther.* 2003;25(3):980-992.
  40. Silverman JA, Mortin LI, Vanpraagh AD, Li T, Alder J. Inhibition of daptomycin by pulmonary surfactant: in vitro modeling and clinical impact. *J Infect Dis.* 2005;191(12):2149-2152.
  41. Adem PV, Montgomery CP, Husain AN, et al. *Staphylococcus aureus* sepsis and the Waterhouse-Friderichsen syndrome in children. *N Engl J Med.* 2005;353(12):1245-1251.
  42. Reichert B, Birrell G, Bignardi G. Severe non-pneumonic necrotising infections in children caused by Panton-Valentine leukocidin producing *Staphylococcus aureus* strains. *J Infect.* 2005;50(5):438-442.
  43. Rutar T, Zwick OM, Cockerham KP, Horton JC. Bilateral blindness from orbital cellulitis caused by community-acquired methicillin-resistant *Staphylococcus aureus*. *Am J Ophthalmol.* 2005;140(4):740-742.
  44. Kourbatova EV, Halvosa JS, King MD, Ray SM, White N, Blumberg HM. Emergence of community-associated methicillin-resistant *Staphylococcus aureus* USA 300 clone as a cause of health care-associated infections among patients with prosthetic joint infections. *Am J Infect Control.* 2005;33(7):385-391.
  45. Etienne J. Panton-Valentine leukocidin: a marker of severity for *Staphylococcus aureus* infection? *Clin Infect Dis.* 2005;41(5):591-593.
  46. Boyle-Vavra S, Ereshefsky B, Wang CC, Daum RS. Successful multiresistant community-associated methicillin-resistant *Staphylococcus aureus* lineage from Taipei, Taiwan, that carries either the novel *Staphylococcal* chromosome cassette mec (SCCmec) type VT or SCCmec type IV. *J Clin Microbiol.* 2005;43(9):4719-4730.
  47. Gauduchon V, Cozon G, Vandenesch F, et al. Neutralization of *Staphylococcus aureus* Panton Valentine leukocidin by intravenous immunoglobulin in vitro. *J Infect Dis.* 2004;189(2):346-353.
  48. Kaplan SL, Hulten KG, Gonzalez BE, Hammerman WA, Lamberth L, Versalovic J, Mason EO Jr. Three-year surveillance of community-acquired *Staphylococcus aureus* infections in children. *Clin Infect Dis.* 2005;40(12):1785-1791.
  49. Saiman L, O'Keefe M, Graham PL 3rd, et al. Hospital transmission of community-acquired methicillin-resistant *Staphylococcus aureus* among postpartum women. *Clin Infect Dis.* 2003;37(10):1313-1319.

# Wisconsin Medical Journal

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