Skin and Soft Tissue Infections Caused by Community-Acquired Methicillin-Resistant *Staphylococcus aureus*

Christopher Graber, MD, MPH

Skin and soft tissue infections (SSTI) are a source of significant illness and accounted for over 2 million visits to emergency room departments in the United States in 2004. While most infections are minor and do not require hospitalization, some can be life-threatening—particularly for people living with HIV.

The majority of outpatient SSTI are caused by gram-positive bacteria, typically *Streptococcus* and *Staphylococcus* species. In the past, SSTI caused by these organisms were reliably treated with beta-lactam antibiotics (penicillins and cephalosporins). Resistance to these antibiotics was uncommon and was typically only seen in infections caused by *Staphylococcus aureus* that had acquired a gene conferring resistance to all beta-lactams, including the drug methicillin. These resistant infections typically only occurred in hospitalized or recently-hospitalized individuals.

Since the late 1990s, however, there has been a startling rise in the incidence of SSTI caused by methicillin-resistant *Staphylococcus aureus* (MRSA) in individuals with no prior exposure in hospitals. These infections were termed "community-acquired MRSA" (CA-MRSA) infections. The vast majority of CA-MRSA infections in the United States are caused by one particular bacterial clone that is remarkable for its transmissibility, persistence, and virulence.

SSTI caused by CA-MRSA have disproportionately affected the HIV positive population, and the reason for this phenomenon remains unclear. This article provides an overview of CA-MRSA SSTI in HIV positive people, providing a brief history of the microbiology of skin and soft tissue infections and outlining the epidemiology of CA-MRSA SSTI in the HIV positive patient, the types of SSTI that can be caused by CA-MRSA, and available treatment and prevention options.

The Microbiology and Treatment of Skin and Soft Tissue Infections

With the advent of penicillin in the early 1940s, streptococci and staphylococci were initially universally sensitive to penicillin and its related synthetic versions. While most streptococci have remained sensitive to penicillins since that time, staphylococci—particularly *Staphylococcus aureus,* the most virulent of all staphylococci species—have become increasingly resistant to penicillin and its derivatives. This phenomenon began in the mid-1940s, when certain strains of

S. aureus found in hospital settings (where penicillin was widely used) developed an enzyme called penicillinase that broke down penicillin, rendering it ineffective against the bacterial strains. This property had spread to most *S. aureus* strains in the community by the 1970s.

Penicillin-resistant *S. aureus* was checked with the advent of the penicillinase-resistant penicillin drugs methicillin, nafcillin, and oxacillin, as well as the cephalosporin compounds cefazolin (Ancef) and cephalexin (Keflex). However, in a manner similar to their development of penicillinase, *S. aureus* strains exposed to selection pressure from antibiotics used in hospital settings evolved resistance to all penicillins and cephalosporins. By the mid-1990's, these MRSA strains accounted for greater than 25% of all in-hospital *S. aureus* infections.

In contrast to the slow, gradual movement of penicillinase-producing *S. aureus* strains from the hospital to the community over the course of multiple decades, MRSA has exploded into the community setting since the late 1990s. While initial cases of CA-MRSA appeared to result from the introduction of the in-hospital strain into the community by people with frequent contact with the health care system and inpatient care, subsequent reports emerged of severe and fatal MRSA infections in children in Chicago and in rural Minnesota and North Dakota with no prior hospital exposures, indicating the presence of new virulent strains distinctly different from previously observed MRSA.

Epidemiologic studies in several communities throughout the United States have since identified increasing incidence of disease caused by a particular CA-MRSA clone termed "USA300." USA300 was initially described in reports of cases from fairly discrete populations, such as prisoners, military recruits, athletic teams (including high school wrestling teams and a professional football team), and HIV-positive men who have sex with men (MSM). However, it has been increasingly recognized over the past three years that USA300 is now responsible for infections among all populations in the United States and has become an important cause of hospital-acquired infection, as well. In particular, a recent study published in the *New England Journal of Medicine* determined that, in August 2004, among eight different emergency departments scattered around the United States, MRSA was responsible for 59% of all SSTI in which a bacterial culture was available. Of the cases caused by MRSA, 97% were caused by the USA300 clone. While USA300 has classically been described as a cause of SSTI, it can also cause several other infections, such as pneumonia, endocarditis (infection of the heart valves, often seen in injection drug users), urinary tract infections, osteomyelitis (infection of the bone), and orthopedic hardware infections.

While it is ultimately unclear exactly what is responsible for the propensity of USA300 to spread throughout the United States in such a short time period and to cause, in general, more severe SSTI than other clones, genetic analysis of USA300 has revealed the presence of two genes—the Arginine Catabolic Mobile Element (*ACME*), a gene heretofore unrecognized in *S. aureus,* and the gene for Panton-Valentine leukocidin (*PVL*)—that may play roles in colonization and virulence.

S. aureus typically preferentially colonizes the anterior nasal mucosa (the tissue lining the inside of the nose), where it will often reside without causing disease. The relationship between colonization of the anterior nasal mucosa and the development of subsequent skin disease is not well understood, but SSTI caused by *S. aureus* are typically caused by the individual's colonizing strain. It is thought that *ACME,* a gene that USA300 likely acquired from *Staphylococcus epidermidis* (a typically non-virulent colonizer of human skin), may promote survival on skin surfaces, suggesting that USA300 may more readily colonize human skin than other *S. aureus* strains.

The role of *PVL* remains unclear. It was initially described as being toxic to human white blood cells and to promote abscess formation, but recent studies have contradicted this idea. USA300 has also been described as a cause of severe, necrotizing pneumonia, and it is also thought that *PVL* has a role in the ability of the organism to invade lung tissue. Again, however, the exact causal mechanism remains unclear.

The Epidemiology of MRSA SSTI in the HIV Positive Population

Studies have demonstrated that people living with HIV generally have a higher proportion of colonization and disease caused by CA-MRSA. One of the first studies to focus on risk factors for CA-MRSA SSTI among HIV positive MSM was performed at the Los Angeles County Department of Health Services outpatient clinic in 2002. Thirty-five individuals presenting with MRSA SSTI were compared with 76 control HIV positive MSM individuals matched by treating physician and week of presentation. HIV positive MSM with MRSA SSTI were more likely to have had close contact with a person with a skin infection; to have routinely used public saunas or hot tubs; to have used methamphetamine, nitrates, or sildenafil (Viagra); and to have had high-risk sexual behavior in the three months prior to presentation. Use of the antibiotic trimethoprim-sulfamethoxazole (TMP-SMX, Bactrim, Septra) as prophylaxis for opportunistic infections appeared to be protective in this small study. No significant relationship was found between CD4 cell count or HIV viral load and MRSA SSTI.

The link between high-risk sexual activity and the acquisition of MRSA SSTI remains relatively unexplored. While MRSA has not been explicitly documented to spread sexually among MSM, heterosexual transmission of

USA300 has recently been demonstrated. The early association made between USA300 SSTI and contact sports suggested an enhanced role for skin-to-skin transmission of USA300, which may explain this relationship between CA-MRSA SSTI and risky sexual behavior among HIV positive MSM. It may, in fact, be worthwhile to conceptualize CA-MRSA as a sexually transmitted disease, at least in a broader sense of skin-to-skin transmission.

Another study examining the incidence of and risk factors for MRSA infection among HIV positive people was performed at the Owen Clinic at the University of California, San Diego. Ninety-four infections were identified in the clinic cohort of 3455 HIV positive individuals between January 2000 and December 2003. Paralleling the rise of USA300 across the United States over this time frame, the investigators noted a dramatic rise in the number of infections toward the end of the study period, with over 60 of the infections occuring in the last year of the study. In their analysis, acquisition of MRSA infection was associated with acquisition of HIV via sex or intravenous drug use, low CD4 cell count, high HIV viral load, and lack of TMP-SMX prophylaxis for opportunistic infection.

One other aspect of the epidemiology of CA-MRSA SSTI in the HIV positive population concerns multidrug resistance. The hallmark of CA–MRSA—and USA300 in particular—in comparison with the traditional MRSA acquired in the health care setting, has been its susceptibility to multiple non-beta-lactam antibiotics, such as trimethoprim-sulfamethoxazole, clindamycin (Cleocin), and doxycycline. However, multidrug resistance in USA300 has begun to emerge over the last four years, and much of it has been mediated by a cluster of genes on a plasmid carried by the organism that encodes resistance to clindamycin, macrolides (erythromycin and its derivatives azithromycin [Zithromax] and clarithromycin [Biaxin]), and mupirocin (Bactroban), an antibiotic ointment often used for eradication of *S. aureus* colonization and for treatment of impetigo. Our laboratory at San Francisco General Hospital (SFGH) has noticed an association with USA300 carrying this drug-resistance plasmid and HIV positive MSM presenting with SSTI. More research is planned to determine why this relationship exists.

Types of SSTI that can be Caused by MRSA

MRSA can cause a wide variety of SSTI. They are summarized very well in the treatment guidelines for SSTI put forth by the Infectious Diseases Society of America and are as follows:

IMPETIGO

Impetigo is an infection of the superficial layers of the skin that is characterized by its discrete, well-defined borders. Lesions are typically seen on the exposed parts of the body, most often the face and extremities, and may be single or multiple. Often, these lesions develop into blisters (bullous impetigo). Systemic symptoms (such as fever) are rare.

Impetigo is most commonly seen in young children and is most commonly caused by streptococci. However, CA-MRSA has been recognized as an increasingly more common cause of impetigo, particularly in populations where CA-MRSA is more frequently seen, such as among people living with HIV.

CUTANEOUS ABSCESSES

Cutaneous abscesses are collections of pus that arise within the deeper structures of the skin. They typically present as painful red nodules that are exquisitely tender to the touch. They arise when bacteria are introduced into the deeper layers of the skin, such as with skin popping or intravenous drug use. However, abscesses may also arise without any preceding event known to the patient. Abscesses may contain more than one species of bacteria, but when *S. aureus* is present, it is often the only pathogen isolated. Abscesses caused by MRSA have been said to resemble spider bites.

FOLLICULITIS, FURUNCLES, AND CARBUNCLES

Folliculitis is an infection of the hair follicle that is confined to the superficial layers of the skin. While they are frequently caused by *S. aureus,* and CA-MRSA in particular, other organisms, including fungi, are common causes as well. It also may be difficult to distinguish folliculitis caused by CA-MRSA from eosinophilic folliculitis, a non-infectious rash commonly seen in HIV positive individuals with CD4 counts lower than 300 cells/mm^3 that can frequently flare with the initiation of antiretroviral therapy.

Furuncles, also known as “boils,” are infections of hair follicles in which purulence (presence of pus) extends down the hair follicle shaft into the deeper layers of the skin, forming a small abscess. Furuncles are most commonly caused by *S. aureus.* They can occur anywhere on the skin where hair is present.

When the infection from one furuncle extends to involve several adjacent hair follicles, it is termed a carbuncle. Carbuncles are often seen on the back of the neck and are frequently seen in people with diabetes mellitus.

Folliculitis, furuncles, and carbuncles are very common presentations of CA-MRSA; several of the well-described outbreaks of CA-MRSA infection have involved these infections. CA-MRSA is also remarkable for its ability to cause repeated attacks of these infections.

CELLULITIS AND ERYSIPELAS

Cellulitis and erysipelas are terms for diffuse, spreading skin infections without underlying purulence or necrosis (tissue death). The terms are often used interchangeably but, classi-

cally, erysipelas is defined by the fact that the lesion is raised above the level of the surrounding skin and that there is a clear line of demarcation between involved and uninvolved tissue. Cellulitis, on the other hand, is not so clearly demarcated and tends to involve the deeper skin tissues and subcutaneous fat. The microbiology is typically different as well. Streptococci are by far the most common cause of erysipelas, although *S. aureus* may also be involved in the more severe, blistering form of the disease. Cellulitis, on the other hand, can be caused by a wide variety of pathogens, though streptococci are still the most common etiology if no underlying abscess is present.

Both erysipelas and cellulitis are characterized by rapidly spreading areas of warmth, redness, and edema (swelling). Both may also be associated with lymphangitis (inflammation of the lymph vessels manifest by "streaking" erythema, or redness, extending from the lesion) and swelling of regional lymph nodes. Often, the skin can take on a brawny, wooden texture. Superficial blisters may develop, as well. Systemic symptoms, such as fever, rapid heart rate, and low blood pressure, can often accompany erysipelas or cellulitis and are signs of serious illness that requires prompt evaluation and treatment with systemic antibiotics. In less than 5% of all cases, the infecting organism can be isolated from the bloodstream.

Conditions that predispose to the development of erysipelas or cellulitis typically make the skin more fragile or impair the local immune response; these include obesity, prior cutaneous damage, venous insufficiency, or lymphatic obstruction from any cause, such as from prior surgeries on the affected limb. Damaged, disrupted skin is a frequent portal of bacterial entry. Cellulitis is often confused with other skin disorders, such as allergic, eczematous, or contact dermatitis, gout, and herpes zoster (shingles).

NECROTIZING FASCIITIS

Necrotizing fasciitis is a rare infection of the deep subcutaneous tissues that can spread beneath the skin very rapidly from the initial site of infection. The initial lesion is often minor, such as an abrasion, an injection site, or a small abscess. Approximately 20% of patients have no visible skin lesion.

In its initial stages, the presentation is very similar to cellulitis. However, severe systemic symptoms (high fever, low blood pressure, disorientation and/or lethargy) typically develop rapidly, and the site of infection may show skin discoloration or gangrene. Other factors that may distinguish necrotizing fasciitis from cellulitis include severe, constant pain, severe blistering, gas in the soft tissues that can be palpated or seen on X-ray imaging, and edema that extends beyond the redness of the affected area and also extends much deeper into subcutaneous tissues. Most patients who present with necrotizing fasciitis have an underlying predisposing factor, such as diabetes or arterial or venous insufficiency. Immediate medical and surgical attention is warranted for the management of this aggressive and often fatal infection.

There are two main types of necrotizing fasciitis: one that is caused by a single bacteria (monomicrobial) and one caused by multiple bacteria at the same time (polymicrobial). In the monomicrobial form, streptococci and *S. aureus,* including CA-MRSA, are the most common causes. The polymicrobial form typically involves anaerobic organisms that arise from the normal bacteria found in the large intestine and is often seen in patients who had surgical procedures involving the bowel, sacral ulcers, or trauma to the abdomen.

PYOMYOSITIS

Pyomyositis is the presence of pus within muscle. It is characterized by pain localized within a single muscle group, muscle spasm, and fever. *S. aureus,* including CA-MRSA, is a common cause. Often, it may not be possible to delineate a specific abscess, but the area will often have a firm, wooden feel. Surgery and intravenous antibiotics are typically required in the management of these infections.

People presenting with pyomyositis will often have a predisposing cause, such as injection drug use, but these infections can arise spontaneously, as well.

SURGICAL SITE INFECTIONS

Infections of surgical wounds are the most common adverse events in patients who are hospitalized and have undergone surgery, accounting for 38% of all hospital-acquired infections in surgical patients. They are classified according to how deep the infection is: superficial incisional infection, deep incisional infection, and organ/space infection. Superficial incisional infections do not extend below the subcutaneous space and are notable for purulent drainage from the incision, pain, tenderness, swelling, and redness. They typically occur within 30 days of the initial surgery. A deep incisional infection extends into the underlying fascia and muscle. It presents in a similar fashion as the superficial incisional infection and also typically arises within 30 days of initial surgery. However, if a prosthesis was inserted, deep incisional infections can occur up to a year after initial surgery. An organ/space infection involves any part of the body other than the incision site itself. Any deep incisional infection that does not resolve as expected raises the possibility that, in fact, the incisional infection may just be a superficial manifestation of a deeper organ/space infection.

Diagnosis and treatment of surgical site infections are highly individualized. Diagnosis of surgical site infections may be delayed in those who are morbidly obese or in those who had deep, multilayer incisions. Oftentimes, there may be redness and

other inflammatory changes around or near a surgical incision that just reflect wound healing or allergic sensitivity to tape or other dressing and do not indicate true infection. Intravenous antibiotics that are given immediately before the time of surgery reduce the incidence of surgical site infections, but prolonged courses of antibiotics following surgery do not prevent surgical site infections and only serve to promote antibiotic resistance and other side effects associated with antibiotic use.

A wide variety of bacteria can cause surgical site infections, and the type of bacteria involved typically depends on the type of surgery (particularly whether the operation involved the gastrointestinal or genital tracts), when the infection occurred relative to the time of surgery, and how long the patient has been in the hospital. When *S. aureus* (including CA-MRSA) is the cause of a surgical site infection, the preceding surgery typically did not involve the gastrointestinal or genital tract, and the infection typically does not manifest until two to five days after the operation. Data from SFGH and other institutions suggest that patients who are colonized with the USA300 *S. aureus* clone as outpatients are more likely to have infections caused by USA300 while hospitalized, blurring USA300's distinction as "community acquired."

Treatment of MRSA SSTI in the HIV Positive Patient

The treatment of SSTI in the HIV-positive person depends on a number of factors: the type of SSTI (as described above), the extent and severity of the infection, the immune status of the individual, the likelihood that the lesion is caused by MRSA, and the person's prior antibiotic exposure.

ANTIBIOTICS ACTIVE AGAINST MRSA

One of the most reliably active oral antibiotics against CA-MRSA, and USA300 in particular (>98% susceptible), is TMP-SMX, even though it is not approved by the Federal Drug Administration for the treatment of SSTI. Its advantages in treatment of HIV positive people include familiarity with its use (as it is also used for prophylaxis and treatment of *Pneumocystis* pneumonia) and affordability. Disadvantages include intolerance due to gastrointestinal upset (particularly with higher doses) and an inability of individuals to take the medicine if they have a sulfa allergy or G6PD deficiency. Another disadvantage is that it has poor activity against streptococci, so if the etiology of the SSTI is more likely to be streptococcal (such as impetigo, erysipelas, or cellulitis without underlying abscess), another antibiotic may be more appropriate. TMP-SMX also does not penetrate well into the anterior nares (nostrils) for eradication of nasal colonization. For serious infections in which MRSA is suspected, the dose given should approximate 8 to 12 mg of TMP-SMX per kilogram per day, divided two to three times daily—a larger dose than for what is used for *Pneumocystis* prophylaxis or for the treatment of urinary tract infection. For the average 70-kg (154-pound) person, two double-strength tablets twice a day is appropriate.

An antibiotic with excellent activity against both streptococci and MRSA is clindamycin, though the susceptibility of MRSA to clindamycin is lower than that to TMP-SMX (85%–90% susceptibility in CA-MRSA; much lower in traditional hospital-acquired MRSA). Clindamycin is recommended if the etiology of the SSTI (i.e., streptococcal vs staphylococcal) is in question. Clindamycin also penetrates well into the anterior nares and has been effective in eradicating nasal colonization of *S. aureus* in low doses.

Clindamycin is inexpensive and generally well tolerated, though occasionally its eradication of a significant proportion of the normal bacteria in the large intestine can cause diarrhea. It may also in rare cases promote a particular infection of the large intestine called *Clostridium difficile* ("C-diff") colitis. Another disadvantage of clindamycin in the HIV positive population is the issue of increasing resistance, as mentioned above. Resistance is most likely to be encountered in individuals who have recurrent MRSA SSTI and have received multiple courses of clindamycin.

Doxycycline (and its relatives tetracycline and minocycline) are typically active against MRSA (80%–95% susceptibility in CA-MRSA). Doxycycline, tetracycline, and minocycline are inexpensive and well tolerated, though skin phototoxicity (accelerated sunburning with exposure to sunlight) is common. However, there is limited clinical experience in the treatment of MRSA infections with this class of drugs; they should not be relied upon alone for serious infections. These medications are contraindicated in pregnant women due to defects in bone and enamel development.

Linezolid (Zyvox) is highly active against MRSA (near-100% susceptibility in CA-MRSA) and has performed well in studies of complicated SSTI. It is generally well tolerated, though bone marrow toxicity, manifest by anemia and/or thrombocytopenia (low platelet count), is a common side effect and often limits extended or repeated use. It is also extremely expensive, as a 10-day course costs over $1300.

Rifampin is highly active against MRSA (90%–100% susceptibility in CA-MRSA) but must be used in combination with other drugs in order to avoid potential resistance. It is particularly useful in the treatment of infections involving orthopedic hardware and also in eradication of nasal colonization. A major disadvantage of its use in HIV positive individuals is its metabolism by the cytochrome p450 system in the liver, the same route of metabolism as efavirenz (Sustiva) and most protease inhibitors (PIs). Rifampin induces the metabolism of efavirenz and PIs, resulting in decreased levels of these drugs in the

body. Rifabutin, a relative of rifampin, also has anti-MRSA activity and has less of an effect on the metabolism of efavirenz and PIs, so it can be substituted for rifampin in individuals on these antiretrovirals. Consultation with a pharmacist or health care provider knowledgeable about antiretroviral drug interactions is recommended to determine the proper dosing of rifampin/rifabutin along with antiretroviral therapy.

Oral antibiotics that are *ineffective* against MRSA include beta-lactams and cephalosporins, such as amoxicillin (with or without clavulanate), dicloxacillin, and cephalexin (Keflex). Macrolides (erythromycin, azithromycin, clarithromycin) are also largely ineffective against MRSA. Fluoroquinolones (ofloxacin, ciprofloxacin, levofloxacin, moxifloxacin) have unreliable activity against MRSA (30% to 60% of CA-MRSA is quinolone-susceptible), and resistance can develop rapidly.

If intravenous therapy is required or deemed necessary, vancomycin is typically the first-line intravenous drug used against MRSA. It is typically given twice a day, but blood levels should be drawn to determine if more or less frequent dosing is required. Resistance to vancomycin in MRSA is extremely rare, though there is concern that, during long courses of treatment in a particular individual, sub-strains of MRSA that have reduced susceptibility to vancomycin may persist and lead to recurrent disease when the antibiotic treatment is discontinued. Very recently, a research team at SFGH reported the first strain of USA300 to display reduced susceptibility to vancomycin in an individual who had recurrent, deep-seated MRSA infections. Other new intravenous drugs that are active against MRSA include daptomycin and tigecycline, both of which have been approved by the Federal Drug Administration for the treatment of complicated SSTI.

TREATMENT ACCORDING TO TYPE OF SSTI

For impetigo with a limited number of lesions, topical mupirocin (Bactroban) is the treatment of choice, though resistance to mupirocin in MRSA is on the rise in the HIV positive population. Impetigo with multiple lesions may require a short course of an oral antibiotic, such as clindamycin or doxycycline. Folliculitis and small furuncles will typically respond to the application of warm compresses, which appears to promote drainage. Antibiotics may not be necessary for these SSTI, particularly if the lesions are limited in number and extent and the infected person is not particularly immunocompromised. If, however, there is extensive surrounding redness or systemic signs such as fever, antibiotics should be considered. If cellulitis without underlying abscess is present, adequate coverage of streptococci is necessary, so clindamycin is favored over TMP-SMX. If cellulitis is extensive and associated with severe systemic symptoms, prompt medical evaluation is required to rule out necrotizing fasciitis. Surgical wound infections are best evaluated by the surgeon who performed the preceding surgery, and treatment is highly individualized.

The most effective treatment of abscesses, large furuncles, and carbuncles is surgical excision and drainage, which, depending on the extent of the lesion, are typically performed on an outpatient basis. It is important that drainage be done in a controlled, sterile setting—it should not be performed at home. Manual squeezing of an abscess may only push bacteria into deeper layers of skin and soft tissue, causing worsening of the infection. Surgical probing of the abscess cavity at the time of drainage to break up collections of pus may speed healing. After drainage, simply covering the wound with a dry dressing, with or without gauze packing, is typically sufficient. Antibiotics are not necessary if complete drainage is achieved, but they can be considered for those who present with multiple lesions, extensive surrounding erythema, or systemic symptoms such as fever, or in patients who are more severely immunocompromised.

The treatment of individuals who have recurrent abscesses or furunculosis due to CA-MRSA is not well established. Classically, efforts to reduce recurrent disease have focused on eradication of nasal colonization. One strategy has been to apply mupirocin to the anterior nares for the first five days of each month. Another is a single small (150-mg) dose of clindamycin given daily for three months. However, there may be several problems with eradication of nasal colonization as a strategy to reduce disease recurrence. First of all, while eradication of nasal colonization may lead to an immediate reduction in subsequent staphylococcal disease, individuals often just become re-colonized when treatment is stopped. Secondly, the emergence of resistance to mupirocin and clindamycin that we have seen in HIV positive individuals in San Francisco may severely limit options for nasal decolonization in this population. Lastly, the identification of the *ACME* gene in the USA300 clone suggests that colonization of the skin and other areas instead of the anterior nares may be one of the driving forces in the emergence of CA-MRSA. Combining nasal decolonization with body cleansing with chlorhexidine has been suggested and may be of benefit.

While not yet formally evaluated in a clinical trial, prophylaxis with TMP-SMX may be of benefit to those with recurrent staphylococcal abscesses or furunculosis. Another approach to treat recurrent disease, which has not been formally evaluated, is to combine TMP-SMX with rifampin or rifabutin for a two-week course, as rifampin and rifabutin penetrate well into the anterior nares. Again, consultation with a pharmacist or health care provider knowledgeable

about antiretroviral drug interactions is advised if this approach is to be considered.

Prevention of MRSA Infection

As with many aspects of staphylococcal disease, strategies for prevention have not been well evaluated. Inadequate personal hygiene has been demonstrated to promote CA-MRSA SSTI, so measures such as regular bathing, frequent hand-washing, and keeping fingernails trimmed may be beneficial. Alcohol-based hand sanitizers are active against MRSA, and their use is highly encouraged in all health care environments. Routine examination of the skin is important to identify small cuts and abrasions that could serve as points of bacterial entry. Any person who has an active SSTI should keep draining wounds covered and thoroughly wash or dispose of all material that comes into contact with the wound.

Studies of the emergence of CA-MRSA among athletic teams have demonstrated that fomites (inanimate objects such as towels, bars of soap, and whirlpools) may harbor MRSA and facilitate transmission of the organism. Avoiding public hot tubs and saunas may reduce the risk of SSTI and may be recommended for people with recurrent SSTI. Avoidance of close contact (including sexual contact) with those with active SSTI is also likely to be beneficial. Pets, including dogs and cats, have also been demonstrated to have MRSA infections and to facilitate MRSA transmission, so examination of them for the development of skin disease and veterinary treatment when indicated may also reduce transmission.

In the setting of an outbreak, several strategies can be employed: daily bathing with chlorhexidine soap; thorough laundering of clothing, towels, and bedding materials; separate use of towels and washcloths; and eradication of nasal colonization. An excellent source of suggestions for control of the spread of CA-MRSA is available from the Los Angeles County Department of Health Services (***www.lapublichealth.org/acd/MRSA.htm***).

Conclusion

Within a very short period, CA-MRSA (and USA300 in particular) has become epidemic throughout the United States as a cause of many diseases, of which SSTI have been the most common. The rapid spread of CA-MRSA and USA300 may be related to genetic factors within the organism that promote its transmissibility, persistence, and virulence. While CA-MRSA has now been recognized to cause disease among a wide variety of individuals across socioeconomic and health-related strata, the HIV positive population has been particularly afflicted. The reasons for the disproportionate effect of CA-MRSA on the HIV-infected individual remain unclear but may be related to immunosuppression and the bacteria's propensity to spread via skin-to-skin contact. CA-MRSA causes a wide variety of SSTI, but folliculitis, abscesses, and furunculosis have proved to be particularly vexing to HIV positive individuals, particularly when these conditions are recurrent.

Fortunately, most CA-MRSA infections are not life-threatening, and several treatment options remain available. Treatment may involve surgical drainage, antibiotic therapy, or a combination of the two. There remain several antibiotics that are highly active against MRSA, such as TMP-SMX, clindamycin, doxycycline, linezolid, rifampin, mupirocin, and vancomycin. However, increasing antibiotic resistance in CA-MRSA, particularly increasing resistance to clindamycin and mupirocin among people with HIV, is concerning. Efforts to prevent the spread of CA-MRSA should revolve around close attention to personal hygiene and avoidance of skin-to-skin contact with people who have active SSTI.

Christopher Graber is a clinical fellow in infectious diseases who practices at the Positive Health Program (Ward 86), San Francisco General Hospital, University of California, San Francisco.

Selected Sources

Diep, B. and others. Complete genome sequence of USA300, an epidemic clone of community-acquired methicillin-resistant *Staphylococcus aureus. The Lancet* 367:731–9. 2006.

Graber, C. and others. Intermediate vancomycin susceptibility in a community-associated MRSA clone. *Emerging Infectious Diseases* 13(3); available at *www.cdc.gov/EID/content/13/3/491.htm.* March 2007.

Hidron, A. and others. Risk factors for colonization with methicillin-resistant *Staphylococcus aureus* (MRSA) in patients admitted to an urban hospital: Emergence of community-associated MRSA nasal carriage. *Clinical Infectious Diseases* 41(2):159–66. July 15, 2005.

Lee, N. and others. Risk factors for community-associated methicillin-resistant *Staphylococcus aureus* skin infections among HIV-positive men who have sex with men. *Clinical Infectious Diseases* 40(10):1529–34. May 15, 2005.

Mathews, W. and others. Incidence of and risk factors for clinically significant methicillin-resistant *Staphylococcus aureus* infection in a cohort of HIV-infected adults. *JAIDS* 40(2):155–60. October 1, 2005.

Moran, G. and others. Methicillin-resistant *S. aureus* infections among patients in the emergency department. *New England Journal of Medicine* 355(7):666–74. August 17, 2006.

Stevens, D. and others. Practice guidelines for the diagnosis and management of skin and soft-tissue infection. *Clinical Infectious Diseases* 41(10):1373–406. November 15, 2005.

Tenover, F. and others. Characterization of a strain of community-associated methicillin-resistant *Staphylococcus aureus* widely disseminated in the United States. *Journal of Clinical Microbiology* 44(1):108–18. January 2006.