CA-MRSA Abscess Care and Treatment Guidelines *in Urgent Care Practice*

Urgent message: In the absence of controlled outpatient trials, the author proposes urgent-care specific guidelines for treatment of community-acquired MRSA, informed by clinical experience and local and regional case reports.

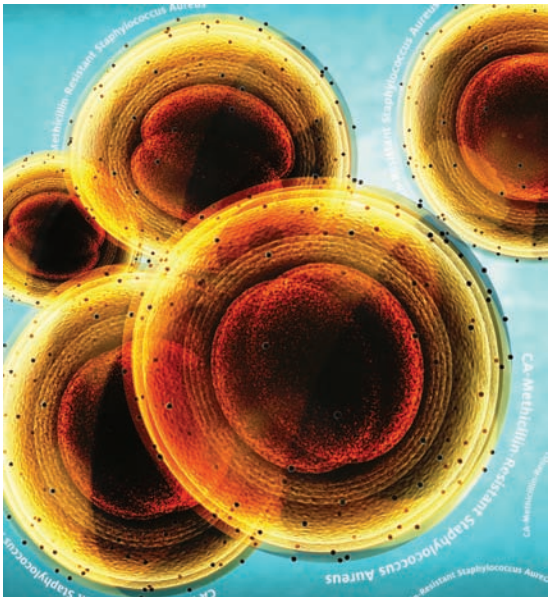
Michael Dickey, MD

PURPOSE

The goal of any treatment is to maximize the chance of a positive outcome for a patient. The purpose of a treatment *guideline* is to maximize the chance of positive outcomes in groups of patients that present with a similar disease states.

While there remain "many ways to skin a cat," the theory behind the use of treatment guidelines in the primary care specialties and subspecialties—including urgent care—is not necessarily complete uniformity of treatment, but to assure that treatment is consistent with available evidence from the medical literature.

The best treatment plan utilizes those treatment options that appear to show higher cure rates and shorter treatment intervals.



BACKGROUND

Ideally, we would have multiple large, controlled, community-based outpatient trials comparing various treatment options and combinations of treatments for community-acquired methicillin-resistant *Staphylococcus aureus* (CA-MRSA).

In the imperfect world of clinical medical practice, however, we do not always have perfect evidence to rely on.

The reality is that, to date, there is little controlled research on the treatment of CA-MRSA, probably owing much to the recent genesis of this problem, but also due to the difficulty of controlled trials on such a genetically diverse disease agent as CA-MRSA. Some of the most useful clinical information available at present comes from case reports.

This proposed treatment guideline is also influenced by the author's observations during treatment of approximately 1,200 cases of skin and soft tissue infections (SSTIs), of which approximately 85% were CA-MRSA, during a five-year interval (2002-2007).

A review of available literature reveals diversity of opinion on the treatment of CA-MRSA SSTIs, particularly when it comes to appropriate use of antibiotics. The diversity is so great that it leaves the impression that many regions of the country may well be dealing with less virulent strains of CA-MRSA or are just now beginning to see the problem. A literature review confirms that there is significant diversity of CA-MRSA phenotypes, and widely different prevalence rates of CA-MRSA depending on region of the U.S.[1-3]

Some have even advocated against the routine use of antibiotics to treat most cases of CA-MRSA SSTIs, arguing that incision and drainage is usually adequate therapy.[4,5] Others have been more cautious and note that even when abscesses are treated with antibiotics showing in-vitro resistance, they usually get better.[6]

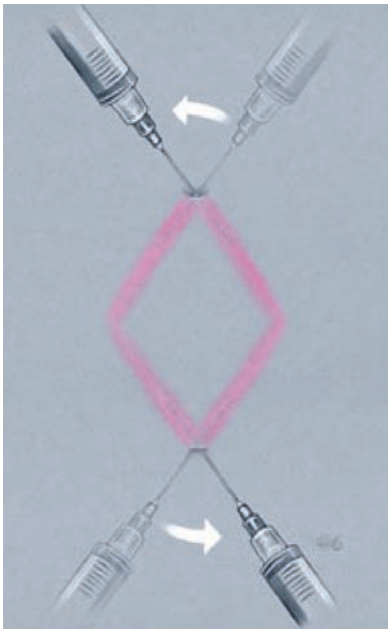


Figure 1. Field infiltration.

Illustration used courtesy of Gohar Salam, MD, FACS.

The increased virulence of CA-MRSA strains appears linked to factors such as a shorter doubling times and the Panton-Valentine leukocidin (PVL) toxin, rarely identified in healthcare-associated MRSA (HA-MRSA) isolates.[7,8] This increased virulence of CA-MRSA sets it apart clinically from methicillin-sensitive *S aureus* and the primarily opportunistic HA-MRSA.

These distinguishing clinical features are:

- rapid or explosive growth
- large cellulitis area
- associated fever
- increased malaise, myalgia, and/or arthralgias
- toxic appearance or lethargy.

However, the clinical presentation of a CA-MRSA infection is often indistinguishable from other causes of SSTI.[7]

While it is important for providers in endemic areas to be aware that the vast majority of the SSTIs that we see today are MRSA, we also must be cautious to remember that SSTIs can still be caused by other organisms, as well.

Other organisms responsible for SSTIs include the relatively common Group A *Streptococcus* (GAS) (including more severe necrotizing fascitis), as well as *Haemophilus influenza*, *Aeromonas hydrophilia* (fresh water-exposed wounds), *Pasteurella multocida* (from animal bites), Group B, C, G *Streptococcus*, and, rarely, pneumococci and *Escherichia coli*.

In addition, patients who are immunocompromised with granulocytopenia (e.g., transplant recipients and chemotherapy patients) may develop cellulitis due to gram-negative bacilli such as *Citrobacter*, *Enterobacter, Pseudomonas*, *Proteus*, and *Serratia*. Thus, providers should continue to culture wounds for confirmation of pathogen identification whenever possible.[4]

PRIMARY TREATMENT PRINCIPLES FOR SSTIs AT RISK FOR CA-MRSA

In essence, there are three primary principles for treatment of SSTIs at risk for CA-MRSA:

1. Thorough and complete wound debridement and maintenance of debrided state
2. Aggressive multi-drug antibiotic treatment
3. Treatment of underlying comorbid factors, e.g., diabetes and edema states affecting venous return

We will break down each of these principles further.

Wound Debridement

Anesthesia

Good wound debridement begins (and ends) with adequate anesthesia. In general, this is a matter of a good field infiltration (**Figure 1)**. A good infiltration over a large abscess can take several minutes to obtain. The use of multiple drugs (e.g., bupivacaine, lidocaine, and epinephrine) often makes for more complete and durable anesthesia.

If adequate anesthesia cannot be obtained in the outpatient setting, the patient should be immediately referred for operating room surgical debridement under regional or general anesthesia.

For pediatric cases or very apprehensive patients, a mixture of lidocaine and prilocaine or an occlusive dressing of viscous lidocaine for 30 minutes to one hour prior to field infiltration may be beneficial.

Also, topical viscous lidocaine used to moisten packing and placed inside abscess cavities prior to subsequent wound care appears to be a useful adjunct for reducing discomfort and allowing for adequate wound irrigation and/or cleaning.

Incision and Drainage

Adequate exposure of the abscess cavity is likely the

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Please see adjacent page for brief summary of Prescribing Information.

Reference: 1. Task Force on Postovulatory Methods of Fertility Regulation. Randomised controlled trial of levonorgestrel versus the Yuzpe regimen of combined oral contraceptives for emergency contraception. *Lancet*. 1998;352:428-433.

Plan B® (Levonorgestrel) Tablets, 0.75 mg

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Rx only for women age 17 and younger

For women age 17 and younger, Plan B® is a prescription-only emergency contraceptive. Plan B® is intended to prevent pregnancy after known or suspected contraceptive failure or unprotected intercourse. Emergency contraceptive pills (like all oral contraceptives) do not protect against infection with HIV (the virus that causes AIDS) and other sexually transmitted diseases.

CONTRAINDICATIONS

Progestin-only contraceptive pills (POPs) are used as a routine method of birth control over longer periods of time, and are contraindicated in some conditions. It is not known whether these same conditions apply to the Plan B® regimen consisting of the emergency use of two progestin pills. POPs however, are not recommended for use in the following conditions:

- Known or suspected pregnancy
- Hypersensitivity to any component of the product

WARNINGS

Plan B® is not recommended for routine use as a contraceptive.
Plan B® is not effective in terminating an existing pregnancy.

Effects on Menses

Menstrual bleeding patterns are often irregular among women using progestin-only oral contraceptives and in clinical studies of levonorgestrel for postcoital and emergency contraceptive use. Some women may experience spotting a few days after taking Plan B®. At the time of expected menses, approximately 75% of women using Plan B® had vaginal bleeding similar to their normal menses, 12-13% bled more than usual, and 12% bled less than usual. The majority of women (87%) had their next menstrual period at the expected time or within ± 7 days, while 13% had a delay of more than 7 days beyond the anticipated onset of menses. If there is a delay in the onset of menses beyond 1 week, the possibility of pregnancy should be considered.

Ectopic Pregnancy

Ectopic pregnancies account for approximately 2% of reported pregnancies (19.7 per 1,000 reported pregnancies). Up to 10% of pregnancies reported in clinical studies of routine use of progestin-only contraceptives are ectopic. A history of ectopic pregnancy need not be considered a contraindication to use of this emergency contraceptive method. Health providers, however, should be alert to the possibility of an ectopic pregnancy in women who become pregnant or complain of lower abdominal pain after taking Plan B®.

PRECAUTIONS

Pregnancy

Many studies have found no effects on fetal development associated with long-term use of contraceptive doses of oral progestins (POPs). The few studies of infant growth and development that have been conducted with POPs have not demonstrated significant adverse effects.

STD/HIV

Plan B®, like progestin-only contraceptives, does not protect against HIV infection (AIDS) and other sexually transmitted diseases.

Physical Examination and Follow-up

A physical examination is not required prior to prescribing Plan B®. A follow-up physical or pelvic examination, however, is recommended if there is any doubt concerning the general health or pregnancy status of any woman after taking Plan B®.

Carbohydrate Metabolism

The effects of Plan B® on carbohydrate metabolism are unknown. Some users of progestin-only oral contraceptives (POPs) may experience slight deterioration in glucose tolerance, with increases in plasma insulin; however, women with diabetes mellitus who use POPs do not generally experience changes in their insulin requirements. Nonetheless, diabetic women should be monitored while taking Plan B®.

Drug Interactions

Theoretically, the effectiveness of low-dose progestin-only pills is reduced by hepatic enzyme-inducing drugs such as the anticonvulsants phenytoin, carbamazepine, and barbiturates, and the antituberculosis drug rifampin. No significant interaction has been found with broad-spectrum antibiotics. It is not known whether the efficacy of Plan B® would be affected by these or any other medications.

Nursing Mothers

Small amounts of progestin pass into the breast milk in women taking progestin-only pills for long-term contraception resulting in steroid levels in infant plasma of 1-6% of the levels of maternal plasma. However, no adverse effects due to progestin-only pills have been found on breastfeeding performance, either in the quality or quantity of the milk, or on the health, growth or development of the infant.

Pediatric Use

Safety and efficacy of progestin-only pills have been established in women of reproductive age for long-term contraception. Safety and efficacy are expected to be the same for postpubertal adolescents under the age of 16 and for users 16 years and older. Use of Plan B® emergency contraception before menarche is not indicated.

Fertility Following Discontinuation

The limited available data indicate a rapid return of normal ovulation and fertility following discontinuation of progestin-only pills for emergency contraception and long-term contraception.

ADVERSE REACTIONS

The most common adverse events in the clinical trial for women receiving Plan B® included nausea (23%), abdominal pain (18%), fatigue (17%), headache (17%), and menstrual changes. The table below shows those adverse events that occurred in ≥ 5% of Plan B® users.

Table 3: Adverse Events in ≥ 5% of Women, by % Frequency

Most Common Adverse Events	Plan B® Levonorgestrel N=977 (%)
Nausea	23.1
Abdominal Pain	17.6
Fatigue	16.9
Headache	16.8
Heavier Menstrual Bleeding	13.8
Lighter Menstrual Bleeding	12.5
Dizziness	11.2
Breast Tenderness	10.7
Other complaints	9.7
Vomiting	5.6
Diarrhea	5.0

Plan B® demonstrated a superior safety profile over the Yuzpe regimen for the following adverse events:

- Nausea: Occurred in 23% of women taking Plan B® (compared to 50% with Yuzpe)
- Vomiting: Occurred in 6% of women taking Plan B® (compared to 19% with Yuzpe)

DRUG ABUSE AND DEPENDENCE

There is no information about dependence associated with the use of Plan B®.

OVERDOSAGE

There are no data on overdosage of Plan B®, although the common adverse event of nausea and its associated vomiting may be anticipated.

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most critical aspect of good drainage and continued care of an abscess.

One of the greatest obstacles to clearing an infection is reformation of abscess and/or tunneling of the infection through subcutaneous tissue or into deeper structures. The primary wound incision must be large enough to allow adequate wound care and inspection to prevent formation of additional abscesses.

The primary incision length over an abscess should in most cases approach one half the diameter of the abscess (e.g., a 2 cm abscess should have a 1 cm incision).

In the author's experience, the vast majority of abscesses can be treated adequately through incisions measuring 1 cm to 3 cm. No incision into an abscess should be smaller than 8 mm to 10 mm. Incisions any smaller than this do not allow for adequate wound care and drainage. Deep abscesses need a proportionately larger incision in order to maintain adequate drainage.

Abscesses that are beneath 3 cm to 4 cm of subcutaneous tissue do best with incisions that approach their full diameter. Wounds should be thoroughly probed with a hemostat or similar instrument with an effort to coalesce the abscess into a single well confluent cavity.

The wound cavity should then be irrigated copiously with sterile saline or water. Either a drain or packing must be placed for the initial 24 hours following drainage. Plain packing, normal saline wet to dry, iodoform gauze or Penrose drain are all suitable. Strong consideration should be given to using a drain instead of packing in fistulous tracks.

Often, a more expedited sterilization of a wound can be obtained by making a second incision into the distal end of a subcutaneous track and running the drain out of both ends of the tract.

These wounds should be treated twice daily with normal saline wet-to-dry dressing changes or cleanings twice daily with saline or hydrogen peroxide and cotton swabs in order to maintain adequate wound debridement.

Wound packing *should not* be left in a wound for an extended period of time. Packing left as long as 48 hours in the wound appears to foster formation of second abscesses.

This does not apply to drains, however; usually, drains should be left until drainage is minimal and the cellulitis component of the infection is significantly improved. The area around the drain should be cleared of debris with saline or peroxide at least once daily to maintain adequate drain function as long as the drain is in place.

With certainty, inadequate drainage of the CA-MRSA SSTI(s) appears to be a significant cause for treatment resistance and treatment failure. However, as large SSTIs with a significant cellulitis component are the rule and these areas of cellulitis routinely produce satellite abscesses, it seems unlikely that drainage of the abscess alone is an appropriate empiric treatment of any but the smallest and most superficial lesions.

The Centers for Disease Control and Prevention continues to recommend the routine culture of *all* abscesses, even in areas with epidemic outbreaks of CA-MRSA. The CDC's Summary of Experts Meeting on MRSA in March of 2006 rationalized this by stating that "obtaining cultures of purulent skin and soft tissue infections is still important to monitor trends in susceptibility of *S aureus* to non beta-lactam agents."[4]

Antibiotic Treatment

The area of greatest disagreement in the treatment of SSTI is the use of antibiotics. Possible causes for such divergent opinions include geographic variations in frequency of CA-MRSA isolation, susceptibility patterns, and variations in virulence, as well as deep-seated disagreements on the use of certain classes of antibiotics in infections that are viewed by some as less serious or non life-threatening. It is possible that recent national press coverage of this disease may have an impact on those biases.

While some sources have recently advocated a "trial of incision and drainage" for CA-MRSA abscesses "smaller than 5 cm,"[9] this approach does not appear to take into account the geographic variability of the prevalence of MRSA (20% to 90%), the increased virulence of CA-MRSA in certain endemic areas, and unpredictable patient follow-up in urgent care and emergency medicine settings.

Often, in these endemic areas, many (if not most) patients present with a rapidly progressive cellulitis and/or explosive growth in abscess size. The common observation of significant growth of the area of cellulitis 24 to 48 hours after appropriate incision and drainage argues strongly for routine use of antibiotics.

The author speculates that those who argue against the routine use of antibiotics are from regions that are still seeing virulence more akin to HA-MRSA infections or less virulent strains of CA-MRSA.

The principles of CA-MRSA antibiotic treatment being proposed here include:

- frequent use of antibiotic combinations from the onset of treatment
- aggressive dosing of certain antibiotics (e.g., TMP-SMX)

Table 1. Antibiotic Therapy for CA-MRSA SSTIs

Trimethoprim-sulfamethoxazole	• Combination therapy with rifampin appears superior • Not active against GAS; consider adding B-lactam or clindamycin • Don't use in last trimester and infants under 2 months • Consider "high-dose therapy" (2 DS tablets BID)
Clindamycin	• D-test important, significant inducible resistance • May inhibit PVL and other exotoxins • Combination therapy with Rifampin appears superior • Dose 450 mg TID or 300 QID
Linezolid	• Expensive • Myelosuppression • Single drug oral or IV therapy for more severe infections • Dose 600 mg BID
Vancomycin	• Drug of choice for severe infections • Preliminary analysis shows once-a-day IV regimens effective and safe • 30 mg/kg divided q 12 hours (peak: 30-40 mg/L; trough 5-10 mg/L) • 30 mg/kg q 24 hours (peak: n/a; trough <10 mg/L)[12] • Infusion rate: Over 1 hour in BID regimen, over 2 hour in q day regimen[12]
Doxycycline, minocycline	• Combination with rifampin appears superior • Limited activity against GAS (consider adding B-lactam or clindamycin) • Minocycline may be slightly superior to doxycycline • Tetracycline not as effective • Dose 100 mg BID
Moxifloxacin	• Single-drug therapy with coverage that includes GAS • Some concerns about eventual resistance • Inducible resistance appears unlikely • Unique structure sets apart from older quinolones (ciprofloxacin, levofloxacin) which are less effective and more likely to experience inducible resistance • Dose 400 mg q day
Rifampin	• Not for monotherapy • Appropriate to combine with TMP-SMX, clindamycin, vancomycin, doxycycline, and minocycline • Potential for drug-to-drug interactions
Resistant antibiotics	• Macrolides (erythromycin, clarithromycin, azithromycin, telithromycin) • All penicillins and cephalosporins (penicillin, amoxicillinoxacillin, nafacillin, ticarcillin disodium + clavulanate potassium, ampicillin + sulbactam, amoxicillin + clavulanate, cloxacillin, dicloxacillin, ceftriaxone, cephalexin)

- early consideration of "second-line drugs," including intravenous vancomycin
- avoidance of drugs likely to have resistance or that are prone to develop resistance during treatment (i.e. avoidance of B-lactams, macrolides and older quinolones, D disk testing for inducible clindamycin resistance).

Following is a brief overview of the currently available classes of antibiotics for treatment of CA-MRSA SSTIs **(Table 1)**.

Vancomycin has been used to treat serious MRSA infections for the last 15 to 20 years and remains the gold standard for treating MRSA. However, despite a high in vitro sensitivity, treatment failure rates in the 40% range with single-drug therapy of serious infections are reported.[10,11,12]

Combination therapy with rifampin improves response rates. Once-daily intravenous therapy, while not currently in widespread use, makes for more feasible outpatient therapy in the urgent care setting.[12] Further studies into the efficacy of once-daily vancomycin are warranted.

Clindamycin is FDA-approved for the treatment of serious infections due to *S aureus* and has been used successfully to treat CA-MRSA. However, inducible clindamycin resistance is an issue in erythromycin-resistant, clindamycin-sensitive *S aureus* isolates.[13] Inducible clindamycin resistance can be detected through a specialized laboratory test called the D-zone test.[14]

Clindamycin appears to exhibit a unique inhibition of the PVL toxin, which may be of significant benefit in the inhibition of further cellulitis and abscess spread.[15] Another very important benefit to adding clindamycin to any regimen for treatment of SSTI is the addition of good-to-excellent coverage for GAS. Neither SMP-TMP nor doxycycline has adequate coverage for GAS.

Clostridium difficile-associated diarrhea (CDAD) may occur more frequently with clindamycin compared with other antibiotics commonly used to treat CA-MRSA; however, it is still a relatively rare complication of treatment or CA-MRSA, even with the use of clindamycin.

Tetracycline (specifically, doxycycline) is also FDA-approved for the treatment of *S aureus* skin infections. The prevalence of tetracycline resistance in CA-MRSA remains low.[16]

Further, much of the reported resistance to tetracycline is due to the tetK gene, which only confers resistance to tetracycline specifically; it does not confer resist-

Table 2. Proposed Decision Tree for Empiric Antibiotic Therapy for CA-MRSA

Severity	Presentation	Treatment
Mild SSTI	**Fever:** None **Cellulitis:** Area <2 cm **Severe signs:** None **Significant comorbidity*:** None, if present treat as moderate SSTI	**Aspiration negative:** Monotherapy or combination antibiotic therapy; consider possibility of GAS **Aspiration positive or obvious abscess:** I & D abscess immediately; strongly consider combination antibiotic therapy **Assess response to therapy:** Daily until infection clearly improving; reassess antibiotic therapy if any additional spread of cellulitis or if not improved appearance within 36 hours
Moderate SSTI	**Fever:** None **Cellulitis area:** 2-4 cm **Severe signs:** None **Significant comorbidity*:** None, if present treat as severe SSTI	**Aspiration and I&D:** As above **Antibiotics therapy:** Frequently used combinations: 1) Trimethoprim-sulfamethoxazole DS 1-2 BID and clindamycin 450 mg TID or 2) Minocycline (or doxycycline) 100 mg BID and clindamycin 450 mg BID; may additionally use rifampin with either regimen **Assess response to therapy:** Daily until infection clearly resolving; reassess antibiotic therapy if any additional spread of cellulitis or if not improved appearance within 36 hours; consider vancomycin if cellulitis area increasing at 36 hours or any rapid deterioration
Severe SSTI	**Fever:** If present, consider severe SSTI **Cellulitis area:** >4 cm **Severe signs:** If lethargy, toxicity, or myalgia present, consider severe **Significant comorbidity*:** If present, treat as severe and potentially life- or limb-threatening.	**Aspiration and I&D:** As above, use drain in any fistulous tracts to maintain drainage; refer for inability to obtain adequate anesthesia (rarely required) **Antibiotics therapy:** Intravenous antibiotics indicated; if aspiration is negative, may consider IV ceftriaxone in addition to oral coverage specific for MRSA as above; if aspiration positive, strong consideration must be given to IV vancomycin, may be used in combination with rifampin or other oral antibiotics; in particular, the additional use of oral or IV clindamycin in serious infections is prudent.

*Diabetes, immunosuppressive therapy, chemotherapy, organ transplant, granulocytopenia, venous insufficiency.

ance to doxycycline or minocycline. Replacement of tetracycline with doxycycline or minocycline on susceptibility testing may be desirable in the future, particularly if the prevalence of tetracycline resistance increases.

In a recent case series, the long-acting tetracyclines (doxycycline and minocycline) performed well for the treatment of MRSA SSTIs caused by tetracycline-susceptible isolates.[16]

The tetracyclines are not recommended during pregnancy or for children under the age of 8. In addition, as group A *Streptococcus* infections are also an important cause of SSTIs, it is important to remember that significant resistance to tetracycline is common in group A *Streptococcus* isolates.

Trimethoprim-sulfamethoxazole (TMP-SMX) is not FDA-approved for the treatment of any form of staphylococcal infection. However, TMP-SMX is "rapidly bactericidal against MRSA in vitro compared with most other orally available antimicrobials."[17] There are also a number of case reports reporting successful use of TMP-SMX in the treatment of *S aureus* infections, including MRSA. One case report describes the use of "high dose" (oral TMP 20 mg/kg/day SMX 100mg/kg/day) for the treatment multi-drug resistant *S aureus* infected orthopedic implants. Treatment periods were six to nine months, with overall success rate of 66.7%.[18]

Nonetheless, in clinical practice drug treatment failure remains an issue for TMP-SMX. Combination with rifampin appears to improve responses to treatment.[19-21] Also, it is clinically important to remember that GAS is another common cause of SSTIs, and GAS is usually resistant to TMP-SMX.

Additional coverage, such as clindamycin, should be considered to cover any SSTI until cultures have shown that GAS is not responsible for the infection.[4]

In Central Texas, TMP-SMX is often given as a preferred choice to treat SSTI abscesses by lecturers giving presentations to emergency medicine, urgent care, and primary care physicians. Antibiograms would seem to support this recommendation.

However, in clinical practice, we have found an extraordinarily high failure rate with standard doses of TMP-SMX alone. The addition of rifampin +/- clindamycin appears to substantially improve success rates.

Granted, this is vague and only anecdotal information, but our experience would speak strongly against TMP-SMX monotherapy in any abscess with significant overlying cellulitis, near joints, in the perineal area, and near facial structures. Also of concern is that GAS infections are another important cause of SSTIs and

are resistant to TMP-SMX therapy.

TMP-SMX should not be used in children under 2 months of age or in women in the last trimester of pregnancy.

Quinolones: Conversely, the CDC notes that fluoroquinolones and macrolides "are not optimal choices for empiric treatment of community-associated SSTI(s) possibly caused by *S aureus*…because of a relatively high prevalence of resistance among *S aureus* isolates in the community or the potential for rapid development of resistance."[4]

This statement bears further analysis, however.

Because of frequent resistance, macrolides are clearly not an appropriate therapeutic choice for treating SSTIs due to MRSA. However, in reviewing the literature, it would seem that the CDC—with input from the "expert panel"—may be overstating the case against the use of certain fluoroquinolones.

Currently, in many regions of the United States, the rates of CA-MRSA resistance to quinolones remain low. There is concern that this rate appears to be increasing, however.

While it is also true that older quinolones, such as ciprofloxacin, are prone to inducible resistance—particularly with *S aureus*[22,23]—this does not appear to be the case with newer C8 modified quinolones such as moxifloxacin and garenoxacin, which has yet to be approved in the U.S.[24-26] Because the minimum inhibitory concentrations of the newer quinolones are lower than those of the older quinolones (ciprofloxacin and levofloxacin), there is less chance for inducible resistance to develop.

However, it should be remembered that quinolone resistance is primarily class specific. As CA-MRSA quinolone resistance increases, the newer modified quinolones may become less effective. In spite of these theoretical concerns, it is far from a foregone conclusion that the use of moxifloxacin now to treat SSTIs will result in a more rapid antibiotic resistance than the use of any of the other treatment options currently available.

Linezolid, first released in 2000, is active against both HA-MRSA and CA-MRSA and has recently found increased use in the treatment of endemic outbreaks of CA-MRSA infections.

Some studies have shown the effectiveness of linezolid to approach that of vancomycin in the treatment of MRSA.[27,28] Linezolid, like clindamycin, has an inhibitory effect on the production of PVL toxin by *S aureus*.[15] The main limiting factor for the use of linezolid is the cost of $130/day.

Adverse effects of linezolid include myelosuppression, neuropathy, and a particularly high risk of drug interaction with selective serotonin reuptake inhibitors resulting in serotonin syndrome.

Rifampin has long been used as to treat tuberculosis in combination with other medications and is most familiar to clinicians for this use. Although rifampin shows high sensitivities for CA-MRSA, effective cure rates are low when it is used as single-drug therapy. This is at least partially due to the fact that when rifampin is used as a single agent, *S aureus* appears to develop resistance rapidly.[29]

However, numerous studies have shown that when rifampin is used in combination with certain other antimicrobials, cure rates are improved substantially.[19,21,27] In particular, combinations with vancomycin, trimethoprim-sulfamethoxazole (trimeth/sulfa), and minocycline appear to improve clinical outcomes.

Studies of the combined use of linezolid and rifampin showed significant disagreement, but as a whole tended to indicate a lack of antagonism between the two antibiotics, while showing evidence of less induced resistance to rifampin; several studies indicated synergy when using these antibiotics in combination.[27,30]

Rifampin does appear to exhibit synergy with the older quinolones, particularly in reducing inducible resistant. However, we are unaware of any studies addressing possible combination with the newer quinolones in the treatment of CA-MRSA.

Because of the high observed failure rate of single-drug therapy at our facility, we have instituted the following policy:

Mandatory Use of Combination Therapy for CA-MRSA

All patients being treated empirically or with a clinical diagnosis or SSTI due or possibly due to CA-MRSA are to be placed on combination therapy using rifampin and/or clindamycin in addition to one or more of the following: vancomycin, linezolid, trimeth-sulfa, or tetracycline (minocycline, doxycycline). If, in the physician's judgment, there is contraindication to this combination therapy, the rationale for withholding combination therapy must be documented in the patient chart. Alternative appropriate monotherapy includes linezolid or possibly moxifloxacin. Vancomycin should be considered appropriate as either monotherapy or in combination in most serious SSTI.

IN CONSIDERATION OF GAS

Group A *Streptococcus* (GAS) is also an important cause of SSTI. In particular, wounds with predominantly cel-

lulitis or impetigo appearance should be considered possibly due to GAS. Tetracyclines and TMP-SMX are not adequate treatments for suspected GAS infections. Appropriate coverage for GAS includes B-lactams, macrolides or clindamycin.

COMMUNITY RESISTANCE PATTERNS

As the prevalence, virulence, and sensitivities of CA-MRSA vary significantly from region to region, it can be helpful to obtain local antibiogram data. Unfortunately, lab antibiograms routinely combine data from CA-MRSA and HA-MRSA.

Some useful information can still be gleaned by studying community resistance patterns. The diverse phenotypes of these two broad classifications of *S aureus* make it difficult to distinguish them definitively in the laboratory.

In **Table 3**, note the low sensitivities to clindamycin in the only laboratory doing the D-Test for inducible clindamycin resistance. Certainly, without that information, clindamycin would appear to be much more effective than it actually is likely to be in this particular geographic region.

Also, note the falling sensitivities to TMP-SMX when progressing from rural to more urban hospitals. This may reflect a higher percentage of HA-MRSA isolates.

TREATMENT OF UNDERLYING COMORBID FACTORS

Factors regarding certain comorbid conditions bear mention.

Diabetic patients require close monitoring of their glucose measurements during treatment. Infection can predispose these patients to worsening hyperglycemia, making treatment more difficult. Ketosis-prone diabetics are at risk for developing diabetic ketosis. Many, if not most, diabetic patients will require additional insulin, modification of oral regimen, or initiation of temporary insulin therapy during treatment.

Edema states affecting the area of infection can make for very difficult eradication of infection. Therapies including elevation, sequential compression, or graduated compression to affected edematous areas are needed to improve venous return.

CONCLUSION

Failed outpatient therapy is a significant problem in the management of CA-MRSA. Inadequate initial incision and drainage, inadequate wound management after initial I & D, and inadequate antibiotic coverage are potential causes of failed outpatient therapy.

Increased provider attention to these critical aspects of treatment should result in reduced numbers of prolonged outpatient treatment and reduced numbers of outpatient treatment failure.

Currently, the medical literature is very confused on the subject of antibiotic therapy for CA-MRSA SSTIs. Those of us on the front line must continue to assess the literature carefully and with critical thought. Hopefully, as new case series are evaluated, improved evidence and consensus will result.

Continued on page 20.

Table 3. Combined Central Texas Hospital Lab Antibiogram

	Isolates	Oxacillin	Gentamicin	Ciprofloxacin	Levofloxacin	TMP-SMX	Erythromycin	Clindamycin	Vancomycin	Minocycline	Doxycycline	Linezolid
Hospital A (rural)	249	0	98	53	43	100	3	82	100	99	99	100
Hospital B (suburban)	153	0	100	61	50	100	6	93	100	100	97	100
Hospital C (urban)	422	0	99	49	31	99	8	91	100	99	95	NA
Hospital D (urban)	745	0	96	28	23	98	7	66	100	98	95	100
Hospital E (urban-public)	1359	0	98	46	37	66	7	87	100	98	93	100
Hospital F (urban-private)	NA	NA	NA	NA	NA	98	5	17 *D-test	100	NA	NA	NA

(Source: Seton Medical System, Saint David's Medical System; Austin, TX)
*This lab performs D-Test and only reports as sensitive those cultures that do not show inducible clindamycin resistant.

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