An Epidemic of Methicillin-Resistant Staphylococcus aureus Soft Tissue Infections Among Medically Underserved Patients

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Hypothesis: A high prevalence of methicillin-resistant Staphylococcus aureus (MRSA) in soft tissue infections presents a treatment challenge.

Design: Retrospective analysis.

Setting: The San Francisco General Hospital Integrated Soft Tissue Infection (ISIS) Clinic.

Patients: Patients treated at the ISIS Clinic from July 1, 2000, to June 30, 2003.

Main Outcome Measures: Information on patient demographics, surgical procedures, microbiologic studies, and antibiotic treatments was obtained for all patients treated in the ISIS Clinic. Microbial data and antibiotic susceptibility pattern of S. aureus, treatment outcome, and antibiotic prescribed were analyzed for all evaluable patients.

Results: The ISIS Clinic treated 6156 unique patients for 12,012 episodes of infection. In this cohort, 5164 (84%) were either homeless or had no health insurance. More than half of the patients (58%) were injection drug users, but most had only 1 prior visit to the clinic (62%). Patients underwent a surgical procedure 7707 times (64%). Of the 837 positive cultures obtained, S. aureus was recovered 695 times (83%), and 525 (63%) of the cultures contained MRSA. Therefore, a full 76% of all S. aureus isolated was MRSA. In a subset analysis of 622 cultures collected prospectively from consecutive patients, 282 (45%) grew organisms, of which 256 (91%) were S. aureus. MRSA represented 59% of all S. aureus isolated. Homelessness and injection drug use were risk factors for infection by S. aureus and MRSA. In another subgroup of patients with soft tissue infections that required admission to the hospital, MRSA was recovered from the cultures in 149 patients. In these patients with MRSA, 44 (30%) only received a β-lactam antibiotic, inactive against MRSA, and had full resolution of their infection.

Conclusions: The prevalence of MRSA soft tissue infections in the medically underserved ISIS Clinic cohort is extremely high. The transmission of the MRSA seems to be in the community. Antibiotic therapy directed at MRSA may not be needed in a large number of patients with these soft tissue infections. Studies to identify the source and cause of this MRSA outbreak are urgently needed. Clinical trials to examine the need for antibiotic therapy in soft tissue infections should be conducted.

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BACTERIAL RESISTANCE TO ANTIBIOTICS is an increasing problem in soft tissue infections. Staphylococcus aureus is the most common organism cultured in soft tissue infections, and resistance of S. aureus to β-lactam antibiotics or methicillin-resistant S. aureus (MRSA) has been an increasing problem. Initially, MRSA was described as a nosocomial pathogen and a problem confined to institutionalized patients. More recently, spread of MRSA to the community setting has been described in injection drug users, prisoners, and children. The prevalence of MRSA in community-acquired soft tissue infections seems to be increasing rapidly worldwide. Even though MRSA soft tissue infections are no more severe than infections caused by methicillin-sensitive S. aureus, antibiotic treatments are more limited in MRSA infections and create special problems in treatment.

The Integrated Soft Tissue Infection (ISIS) Clinic is a specialized center established to treat the large number of soft tissue infections found in the medically underserved, inner-city population of San Francisco, Calif. The ISIS Clinic offers a unique opportunity to observe the natural history of soft tissue infections in a large cohort of patients in a longitudinal fashion. The ISIS Clinic started treating pa-
patients July 2000 and since that time has provided uninterrupted, 7-day-per-week treatment for all patients on a walk-in basis.

To our knowledge, previous studies have not reported the prevalence of MRSA in soft tissue infections in such a large cohort in the community setting. Therefore, the data collected from the ISIS Clinic cohort was used to estimate the prevalence of MRSA in this medically underserved population. Although this cohort may not reflect the population as a whole, certain generalizations can be made about the prevalence of MRSA in the medically underserved population.

| Table 1. Demographic Summary of the Integrated Soft Tissue Infection Clinic Cohort* |
|-------------------------------|------------------|
| Variable                      | Patients, No. (%) |
| Total patients                | 6156             |
| Total visits                  | 12,012           |
| Female                        | 1857 (30)        |
| Male                          | 4299 (70)        |
| Ethnicity                     |                  |
| White                         | 2542 (41)        |
| African American              | 1907 (31)        |
| Hispanic                      | 1150 (19)        |
| Native American               | 35 (1)           |
| Asian                         | 402 (7)          |
| Other                         | 89 (1)           |
| Unknown                       | 31 (1)           |
| Uninsured                     | 4980 (81)        |
| Homeless                      | 1876 (30)        |
| Homeless or uninsured         | 5164 (84)        |

*The mean age of patients was 42 years (range, 1-89 years).

Statistical Analysis

Prevalence was calculated using standard equations.20 The Fisher exact test was used to test for significant associations between categorical variables.20 Odds ratios (ORs) and significance testing for S aureus prevalence and methicillin resistance were obtained using logistic regression as implemented in the SAS statistical software package.21

RESULTS

The ISIS Clinic treats a considerable number of patients with soft tissue infections who have limited access to health care and little financial resources. In the 3-year period from July 1, 2000, through June 31, 2003, the clinic treated 6156 unique patients for a total of 12,012 visits (Table 1). There were 4299 men (70%), and the patients had a median age of 42 years (age range, 1-89 years). The racial distribution of the patients is similar to that of the local community. There were 4980 patients (81%) without health insurance coverage, and 1876 (30%) were homeless. A larger number of people lived in marginal situations, such as residential hotels, or stayed with friends, families, or acquaintances but were not considered homeless because they could provide an address. A total of 5164 patients (84%) were either without health care insurance coverage or homeless, indicating that the ISIS Clinic cohort represents a patient population with limited access to health care and financial resources and who are typically regarded as medically underserved.

Most patients had S aureus infections, and most of the isolates in these patients were resistant to methicillin (Table 2). In the study period, 837 positive cultures were obtained. A total of 695 cultures (83%) contained S aureus, and 525 cultures (63%) contained MRSA. Most S aureus isolates were MRSA (76%). Because the total number of cultures obtained (including cultures that did not grow organisms) was not available in the database and the clinical reasons for submitting these cultures was not always clear, this group may represent a heterogeneous group of patients within the ISIS Clinic cohort, and these data may represent a biased sample. Therefore, a subgroup of
patients who underwent microbiologic evaluation in a prospective study was analyzed.

In a prospective study, the rate of MRSA was lower, but still a very high percentage of patients had MRSA (59%). A group of 622 consecutive patients who underwent incision and drainage of an abscess in the ISIS Clinic had a bacterial culture obtained (Table 2). Within this group, information on both positive and negative culture findings was available. A total of 282 (45%) of the cultures obtained grew organisms. Staphylococcus aureus was found in 256 (91%) of all positive culture findings, and 150 (59%) of these were MRSA. The recovery rate of positive culture results in this study (45%) was lower than that generally reported, so our estimate of the prevalence of MRSA of 24% in all cultures obtained from the ISIS Clinic cohort may be an underestimation. Still, MRSA was found in 59% of all cultures positive for S. aureus, making MRSA the predominant isolate in these infections.

This MRSA outbreak in the ISIS Clinic cohort seems to be community acquired and may be related to the unique environment of these patients. Although a large portion of the patient population had prior visits to the ISIS Clinic (2047 [33%] had 2-5 visits, and 291 [5%] had more than 5 visits), most patients were seen for the first time (3818 [62%]). Thus, the MRSA from these patients was isolated from a first visit and did not represent the spreading of MRSA from contact within the ISIS Clinic. The patients’ environment also played a role in infection with S. aureus. Most patients (58%) admitted that the injection of heroin was the direct cause of the infection. The other risk factor was homelessness. In the subset of the first 666 patients with microbiologic culture results, injection drug users had an OR of 1.4 for S. aureus compared with patients who did not inject drugs (P = .04), and homeless patients had an OR of 1.4 for S. aureus compared with patients with stable living situations (P = .04). A risk factor for recovery of MRSA from patients was also associated with injection drug use (OR, 1.8; P = .003) and homelessness (OR, 1.5; P = .03).

One potential reason for the large number of patients infected with MRSA is the widespread use or overuse of antibiotics in this population. We examined the clinical records of the infections treated and determined that the magnitude of the infections seen in the ISIS Clinic was clinically significant and substantial enough to warrant treatment with antibiotics by current standards. Incision and drainage of an abscess or debridement of the wound was used to treat most infections (7707 [64%]). The average area of the abscess with surrounding cellulitis was 25 cm², and the average amount of pus drained from each abscess was 15 mL. (Figure.) In a review of the medical records, we discovered that nearly all patients seen in the ISIS Clinic were given antibiotic therapy (76%). By current medical standards, the patients treated in the ISIS Clinic appeared to require antibiotic therapy, but whether the antibiotics were required for resolution of the infection is an important and unanswered question.

As an initial attempt to determine the efficacy of antibiotics in the treatment of soft tissue infections, a retrospective analysis of the antibiotic therapy matched to the microbiologic isolate was performed in the ISIS Clinic cohort. Although most ISIS Clinic patients were treated solely as outpatients, a subgroup of 2042 patients (17%) had infections deemed severe enough to warrant admission for intravenous antibiotic therapy and close clinical observation. Only patients who had successful treatment of their soft tissue infections were included. From this subgroup, microbiologic data were available from 149 (7%) of these inpatients, and the antibiotic therapy administered was obtained from the hospital pharmacy database. Of this subgroup, 105 (70%) had adequate antibiotic treatment; however, a considerable number of patients (44 [30%]) infected with MRSA were given only antibiotics that were not effective against the organism. By far the most common scenarios were patients with MRSA treated with cefazolin (19 [43%]) or ticarcillin (17 [39%]). Despite the treatment of MRSA with a presumably ineffective antibiotic, all of these infections resolved.

### Table 2. Microbiology Results From the ISIS Clinic Cohort

<table>
<thead>
<tr>
<th>Result</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Entire ISIS cohort</td>
<td>7707</td>
</tr>
<tr>
<td>Total surgical procedures</td>
<td>837 (11)</td>
</tr>
<tr>
<td>Positive culture findings</td>
<td>695 (83)</td>
</tr>
<tr>
<td>Cultures with <em>Staphylococcus aureus</em></td>
<td>525 (63)</td>
</tr>
<tr>
<td>MRSA</td>
<td>150 (59)</td>
</tr>
<tr>
<td>MRSA in all cultures positive for <em>S. aureus</em></td>
<td>150 (24)</td>
</tr>
<tr>
<td>MRSA in all cultures obtained</td>
<td>150 (59)</td>
</tr>
</tbody>
</table>

**Abbreviations:** ISIS, Integrated Soft Tissue Infection; MRSA, methicillin-resistant *Staphylococcus aureus*.

**Typical San Francisco General Hospital Integrated Soft Tissue Infection Clinic:**

Patient with methicillin-resistant *Staphylococcus aureus* soft tissue infection treated with surgical drainage and cefazolin.

Previous studies have described an increasing rate of community-acquired soft tissue infections related to MRSA, but none to our knowledge have described such a high rate as found in the ISIS Clinic cohort. This alarmingly
Clinical trials in this patient population are clearly needed to determine whether the use of β-lactam antibiotics is really beneficial in these soft tissue infections. A randomized, double-blind, placebo-controlled trial to compare cefazolin with an agent known to be effective against MRSA (vancomycin) is currently under way. Previous discussions about conducting a placebo-based trial were rejected as too risky, but our retrospective analysis of antibiotic use and outcomes in the ISIS Clinic cohort has made such a trial more imperative. Understanding the relationship between antibiotic treatments, emergence of resistance, and clinical outcomes will certainly lead to more rational use of antibiotics in the future.

The emergence of MRSA in community-acquired soft tissue infections is more significant but certainly not isolated to the medically underserved patients found in the ISIS Clinic cohort. This medically underserved population likely represents the beginning of a wider epidemic of MRSA soft tissue infections in the general population. The ISIS Clinic population may serve as a reservoir of MRSA in the community and continue to challenge health care services for these people and the community at large. Addressing widespread multidrug resistance bacterial infections with rationally designed clinical trials will lead to a better understanding of the pathophysiology of soft tissue infections and to better medical care.

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Dr Charlebois was the validating statistician.

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REFERENCES


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Although I have some concern about defining bacteria relating to their resistance to specific antibiotics, such as methicillin and vancomycin, nevertheless, it is a part of our jargon and is not destined to disappear in the future.

In their presentation, they have treated a cohort of 6000 patients with 12,000 infection episodes. The predictive factors as outlined are not surprising. Eighty-one percent had no health insurance, 84% were either homeless or had no health insurance, and males predominated. Regrettably, these are the shameful facts of our times. Eighty-three percent of this cohort’s subset of patients’ cultures were Staph aureus of which 63% were methicillin resistant. I concur with their conclusions regarding the overuse of antibiotics in today’s practices. Certainly, we know that β-lactam antibiotics used to treat MRSA are inactive and expensive. The overuse of antibiotics is convincingly documented in this manuscript, and we should take notice. A 33% recidivism rate is consistent with reports elsewhere.

There are 2 take-home messages in this manuscript. First, incision and drainage of abscesses may very well be the only thing that is needed and expensive antibiotics are not needed. Second, you should visit this ISIS Clinic. It is designed, clinically effective, and multidisciplinary and has the support of their administration. With these cost-effective figures, it is something you can take back to your administration. It is a creative solution to an expensive problem that takes the strain off of our operating rooms and a number of other cost-effective measures.

The ISIS Clinic is a nugget you can appreciate at your institution and is a small operation and not complex. Going to their ISIS Clinic and meeting the nurse coordinator is worth a visit, because she is really a dynamic individual. In future studies, do you plan to perform additional pulse gel electrophoresis and staphylococcal gene testing?

I have followed this with a great deal of admiration. Your immediate problem, however, is to survive the Archives of Surgery peer review process. Good luck!

Daniel R. Margulies, MD, Los Angeles, Calif: I enjoyed this paper, and I appreciate your bringing our attention to this increasing resistance of antibiotic-resistant bacteria in the outpatient setting. I wonder specifically if you could tell us how you dealt with these infections. Did you drain them in an outpatient setting. I wonder specifically if you could tell us how you dealt with these infections. Did you drain them in an outpatient setting. I wonder specifically if you could tell us how you dealt with these infections. Did you drain them in an outpatient setting. I wonder specifically if you could tell us how you dealt with these infections. Did you drain them in an outpatient setting. I wonder specifically if you could tell us how you dealt with these infections. Did you drain them in an outpatient setting. I wonder specifically if you could tell us how you dealt with these infections. Did you drain them in an outpatient setting. I wonder specifically if you could tell us how you dealt with these infections. Did you drain them in an outpatient setting. I wonder specifically if you could tell us how you dealt with these infections. Did you drain them in an outpatient setting. I wonder specifically if you could tell us how you dealt with these infections. Did you drain them in an outpatient setting. I wonder specifically if you could tell us how you dealt with these infections. Did you drain them in an outpatient setting. I wonder specifically if you could tell us how you dealt with these infections. Did you drain them in an outpatient setting. I wonder specifically if you could tell us how you dealt with these infections. Did you drain them in an outpatient setting. I wonder specifically if you could tell us how you dealt with these infections. Did you drain them in an outpatient setting. I wonder specifically if you could tell us how you dealt with these infections. Did you drain them in an outpatient setting. I wonder specifically if you could tell us how you dealt with these infections. Did you drain them in an outpatient setting. I wonder specifically if you could tell us how you dealt with these infections. Did you drain them in an outpatient setting. I wonder specifically if you could tell us how you dealt with these infections. Did you drain them in an outpatient setting. I wonder specifically if you could tell us how you dealt with these infections. Did you drain them in an outpatient setting. I wonder specifically if you could tell us how you dealt with these infections. Did you drain them in an outpatient setting. I wonder specifically if you could tell us how you dealt with these infections. Did you drain them in an outpatient setting. I wonder specifically if you could tell us how you dealt with these infections. Did you drain them in an outpatient setting.

Stephen G. Jolley, MD, Anchorage, Alaska: We have a real problem with the Alaskan native population in terms of methicillin-resistant Staphylococcus aureus. About 80% of the Staph aureus that we isolate is methicillin resistant. It has a little different sensitivity spectrum though. The MRSA we see in the Alaska native population is sensitive to not only Bacitram but also clindamycin and rifampin, as well as vancomycin. The question I have for the authors is do you have a similar sensitivity spectrum to our population, or are your MRSA only sensitive to vancomycin? Although our native population has access to medical care and they do have health care coverage, we don’t think that they necessarily get an exposure to too many antibiotics.

Roger E. Alberty, MD, Portland, Ore: This paper is of interest to me from a historical point of view. Our forbears used to call this laudable pus. They had survived the period of strep infection, which they could do nothing about in the preantibiotic era, and had gotten to where they had a staph infection in which they had considerable success with simple incision and drainage. The data here revisit that old issue.

In the Portland area, we have encountered major problems with orthopedic procedures with methicillin-resistant staph,
and our citywide infectious disease specialists have identified the source as nursing homes, assisted living, and other similar facilities. Seventy percent of the patients in those facilities have methicillin-resistant staph. Coming into our hospitals, they bring it with them. So it is not just an inner-city problem; it is a problem I think for virtually every hospital.

**Ralph W. Aye, MD, Seattle, Wash:** We found that heroin users like being in the hospital, especially a private hospital where the nurses are more naive and they can get narcotics for their dressing changes. So my question is whether the ISIS Clinic is a hospital policy or whether that represents a citywide policy, whether you have seen any of the sort of patient shifting that we see going on in the Seattle area.

**Robert J. Albo, MD, Oakland:** As a member of the staff that cares for national football league injuries, this last year has resulted in an outbreak of MRSA in professional football players who have been injured primarily on artificial turf but not necessarily so. As you probably are well aware, there are many scrapes and lacerations that occur during a football game, and this year there have actually been several admissions of ill players from MRSA infection as well as several players who have missed football games and had to be treated for a period to get rid of infections. This is something entirely new, and a league-wide paper will be reported this next week at the official combined meeting of the NFL. So this is not just being seen in hospital-acquired infections. This is something entirely new, and a leagues-wide paper will be reported this next week at the official combined meeting of the NFL. So this is not just being seen in hospital-acquired organism? The difference in prognosis is major, and it is critical to use appropriate agents for hospital-acquired MRSA infection.

**Samuel Eric Wilson, MD, Orange, Calif:** Methicillin-resistant *Staphylococcus aureus* has been thought to have emerged in acute care hospitals as a result of antimicrobial pressure and to have entered the community via chronic care facilities and perhaps carriage by health care workers. However, your genotype study suggests a community origin for the MRSA in your patients and a different resistance pattern, which allows treatment with routine antimicrobials. I wish to emphasize that one could not extend these observations to nosocomial MRSA infection. Do you, in fact, make this differentiation in your practice between the community-acquired infection and the multidrug-resistant, hospital-acquired organism? The difference in prognosis is major, and it is critical to use appropriate agents for hospital-acquired MRSA infection.

**Dr Campbell:** I appreciate the privilege of the floor this morning to respond to the questions from the discussants. I would also like to thank Dr Organ for his insightful comments regarding the ISIS Clinic. I would like to say a bit about the ISIS Clinic. The clinic has really started to take a life of its own since its inception in July 2000. We call it the ISIS juggernaut at San Francisco General Hospital (SFGH) because we have such a high volume that we are able to screen patients quickly and efficiently. The plan of therapy is based on the clinical experience of the surgeon taking care of the patients, because we do not draw blood tests on patients unless we decide to admit them to the hospital. The modality of treatment is all based on clinical impression, so it is really based on the experience of the surgeons who work in the ISIS Clinic and experience is quite tremendous as our data demonstrate.

**Dr Jolley:** thank you for your question regarding MRSA. We switched over quickly to vancomycin to ensure that they get adequate therapy. Treatment depends on whether or not they have persistent septic fivers or persistent elevations in their white count. The plan of therapy is based on the clinical experience of the surgeon taking care of the patients, because we do not draw blood tests on patients unless we decide to admit them to the hospital. The modality of treatment is all based on clinical impression, so it is really based on the experience of the surgeons who work in the ISIS Clinic and experience is quite tremendous as our data demonstrate.

**Dr Alberty:** I am not sure how many of our patients live in nursing homes. You have a tremendous rate of MRSA in your nursing home in your city. I cannot comment on that problem in San Francisco. It is interesting to note that obviously there are other reservoirs of this infection. This community reservoir includes nursing homes and other chronic care facilities in the city.

**Dr Aye asked a question regarding whether or not our patients enjoyed being hospitalized at San Francisco General Hospital. It is true that our patients also like hospitalization at our...
facility. The opportunity to have 3 square meals a day, a pillow under your head, and the chance to watch TV is better than being homeless. Eighty percent of our patients are uninsured or homeless. Our whole approach to treating patients with soft tissue infection is holistic. The patients actually like coming to the clinic; they know when it is open. They also have my call schedule so they know when I am there, which is quite unfortunate because I tend to have a lot more patients than some of the other physicians who work there. The patients like being treated in the clinic. It’s an efficient way to have your infection treated in a humane fashion. They get their infection taken care of, and they don’t have to sit in the emergency room for what is sometimes 10 or 12 hours to get cared for or get admitted to have a procedure. They know that even if they do get admitted that they will come to the ISIS Clinic and be cared for with respect. It’s only in the cases of the severe infections when we think there is necrotizing fasciitis that the patients go on to the operating room to have their abscesses drained. We still have a number of patients who will go to the operating room to have surgery on a regular basis. This volume is a fraction of our volume pre ISIS.

Dr Albo, I don’t think any of our homeless patients are ex-professional athletes the last time I checked. One patient told me in our preprocedure interview that he played a few years of college ball as a running back. The problem of professional athletes and MRSA is an interesting observation. I am really interested in seeing what you have to report from your experience with professional athletes. We appreciate your comments.

Finally, Dr Wilson, I appreciate your comments regarding our paper. You asked, “Do we treat nosocomial infections different than community-acquired infections?” Again, everything really depends on the severity of the illness with the patients. Many times patients do come in and they are already floridly septic, because we have such a hard-core indigent patient population. Our patients typically do not seek treatment until the last possible moment. They present to the clinic, and we make the assessment and make sure they get appropriate therapy. If we think someone has a severe infection, we treat them with vancomycin initially. We will try to drain the large burden of their infection and get rid of it. You may think we only do small cases there in the clinic. Occasionally, we have drained at least a liter or more of pus out of these abscesses in the clinic.

In conclusion, I would like to thank the Pacific Coast Surgical Association for the privilege of the floor and I appreciate all the questions that were generated from the floor.

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**Announcement**

The Archives of Surgery will give priority review and early publication to seminal works. This policy will include basic science advancements in surgery and critically performed clinical research.