CARRIAGE OF *STAPHYLOCOCCUS AUREUS* AMONG INJECTION DRUG USERS: LOWER PREVALENCE IN AN INJECTION HEROIN MAINTENANCE PROGRAM THAN IN AN ORAL METHADONE PROGRAM

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ABSTRACT

OBJECTIVES: To compare the prevalence of *Staphylococcus aureus* and methicillin-resistant *S. aureus* (MRSA) carriage among injection drug users (IDUs) treated in an injection heroin maintenance program with that among IDUs treated in an oral methadone program, and to determine predictors of *S. aureus* carriage.

DESIGN: Survey.

SETTING: Two opiate maintenance programs at a psychiatric university clinic.

PARTICIPANTS: A volunteer sample consisting of 94 (74%) of 127 IDUs treated in an injection opiate maintenance program with at least twice daily injections of heroin, and 70 (56%) of 125 IDUs treated in an oral methadone program.

RESULTS: Addicts treated in the intravenous heroin substitution program had a significantly lower overall rate of *S. aureus* carriage (37 of 94 [39.4%] vs 42 of 70 [60%]; $P = .009$) and a significantly lower rate of nasal carriage (21 of 94 [22.3%] vs 30 of 70 [42.9%]; $P = .005$) than did addicts treated in the oral methadone program. Being treated in the oral methadone program was the only independent predictor of *S. aureus* carriage (odds ratio, 2.27; 95% confidence interval, 1.19–4.31; $P = .012$). All *S. aureus* isolates were susceptible to oxacillin.

CONCLUSIONS: The regular use of needles under aseptic conditions did not increase the rate of *S. aureus* carriage among IDUs. Further studies are necessary to investigate whether the lower rate of *S. aureus* carriage among IDUs treated with intravenous heroin leads to a lower incidence of *S. aureus* infections in these patients (*Infect Control Hosp Epidemiol* 2004;25:133-137).

Staphylococcus aureus is the main pathogen causing bacterial infections among injection drug users. The spectrum of infections caused by this organism in injection drug users includes endocarditis, bloodstream infections, arthritis, osteomyelitis, cellulitis, and skin abscesses.[1] Soft tissue infections, predominantly caused by *S. aureus*,[1] are one of the main reasons for emergency department visits and hospital admissions of injection drug users.[2,3] Furthermore, antimicrobial-resistant *S. aureus*, such as methicillin-resistant *S. aureus* (MRSA), may cause outbreaks among injection drug users.[4] Such an outbreak recently occurred in Switzerland.[5]

Colonization with *S. aureus*, particularly nasal carriage of *S. aureus*, plays a key role in the pathogenesis and increases the risk of *S. aureus* infection.[6,7] However, the biological mechanisms of nasal colonization by *S. aureus* are still unclear.[8] Tuazon and Sheagren showed that active injection drug users have a higher rate of *S. aureus* colonization of the skin and nose than does the general population.[9] This finding and the observation of higher rates of *S. aureus* carriage among patients with insulin-dependent diabetes mellitus, patients receiving hemodialysis or continuous ambulatory peritoneal dialysis, and patients undergoing desensitization therapy with allergen injections led to the hypothesis that repeated puncture of the skin by needles or catheters increases the rate of *S. aureus* carriage, even under strict aseptic conditions.[6,10]

The first aim of the current study was to analyze the association between intravenous drug use and *S. aureus* carriage by comparing the rate of *S. aureus* colonization among injection drug users treated in an injection opiate maintenance program with at least twice daily injections of heroin with that among injection drug users treated in a conventional oral methadone program. Second, we assessed the prevalence of MRSA colonization among injection drug users treated in these two opiate maintenance programs in Basel, Switzerland.

METHODS

Study Population

All injection drug users treated in two opiate maintenance programs in Basel between April 1 and June 30,

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TABLE 1
CHARACTERISTICS OF THE PATIENTS TREATED IN THE ORAL METHADONE PROGRAM AND IN THE INTRAVENOUS HEROIN MAINTENANCE PROGRAM

Characteristic	Patients Receiving Oral Methadone	Patients Receiving Intravenous Heroin	P
No. of patients	70	94	
Mean age, y (± SD)	35 (± 6)	36 (± 6)	.310
Women	26 (37.1%)	24 (25.5%)	.110
Intravenous drug addiction > 10 y	45 (64.3%)	72 (76.6%)	.085
Staphylococcus aureus carriage			
S. aureus carriers (nose, pharynx, or skin)	42 (60%)	37 (39.4%)	.009
Nasal *S. aureus* carriers	30 (42.9%)	21 (22.3%)	.005
Pharyngeal *S. aureus* carriers (pharynx only)	10 (14.3%)	15 (16%)	.768
Drug use in the month preceding the study			
No injection drug use	24 (34.3%)	1 (1.1%)*	< .001
Heroin use	24 (34.3%)	92 (97.9%)	< .001
Intravenous heroin	17 (24.3%)	88 (93.6%)	< .001
Intramuscular heroin	1 (1.4%)	6 (6.4%)	.240
Heroin smoking	3 (4.3%)	2 (2.1%)	.652
Heroin snorting	6 (8.6%)	2 (2.1%)	.074
Cocaine use	34 (48.6%)	33 (35.1%)	.083
Intravenous cocaine	28 (40%)	32 (34%)	.433
Intramuscular cocaine	2 (2.9%)	2 (2.1%)	1.0
Cocaine smoking	6 (8.6%)	3 (3.2%)	.172
Cocaine snorting	4 (5.7%)	2 (2.1%)	.403
Heroin or cocaine smoking	8 (11.4%)	3 (3.2%)	.056
Oral methadone	58 (82.9%)	46 (48.9%)	< .001
Intravenous methadone	29 (41.4%)	6 (6.4%)	< .001
Intramuscular methadone	1 (1.4%)	0	.427
Cannabis smoking	6 (8.6%)	25 (26.6%)	.004
Intravenous use of street drugs	42 (60%)	42 (44.7%)	.052
Needle exchange	1 (1.4%)	0	.427
Diseases			
HIV infection	14 (20%)	6 (6.4%)	.008
Atopic dermatitis or eczema	9 (12.9%)	9 (9.6%)	.506
Psoriasis	4 (5.7%)	5 (5.3%)	1.0
Skin abscess (at the time of *S. aureus* screening)	11 (15.7%)	9 (9.6%)	.235
Allergic rhinitis	9 (12.9%)	6 (6.4%)	.155
Asthma	5 (7.1%)	8 (8.5%)	.748
History of hepatitis B†	40 (57.1%)	65 (69.1%)	.113
History of hepatitis C†	47 (67.1%)	73 (77.7%)	.133
Medications			
Antibiotics 1 to 6 mo prior to *S. aureus* screening	10 (14.3%)	12 (12.8%)	.778
Antibiotics in the month preceding the *S. aureus* screening	9 (12.9%)	4 (4.3%)	.044
Nasal medications‡	5 (7.1%)	4 (4.3%)	.498
Hospitalizations			
Hospitalization in the year preceding the *S. aureus* screening	12 (17.1%)	16 (17%)	.984
Hospitalization in the month preceding the *S. aureus* screening	7 (10%)	4 (4.3%)	.207

SD = standard deviation; HIV = human immunodeficiency virus.
*At the time of the study, this patient in the intravenous heroin program was treated with oral methadone only, as intravenous or intramuscular injections were not possible.
†Diagnosis could be verified through available results of the determination of antibody to hepatitis C virus and antibody to hepatitis B core antigen IgG for all 94 patients in the intravenous heroin program and for 49 of 70 patients in the oral methadone program.
‡Only 1 of these 9 patients used nasal steroids.

2001, were asked to participate in the study. The first program is a traditional oral methadone program. Patients receive their oral methadone doses every day or at least weekly. The second program is an intravenous heroin substitution program and enrolls severely addicted patients for whom other treatments have failed.[3,11] Participants receive and have to inject the prescribed dose of heroin at the clinic under direct supervision, usually twice daily. They have to use the sterile injection equipment provided. In addition to heroin, patients are given oral methadone if needed.

Risk Factors for S. aureus *Carriage*

Information on drug use in and outside the program, medications, medical conditions, and risk factors for *S. aureus* carriage was collected from all participants by questionnaire, and checked by chart review. All of the participants underwent an interview and a skin examination performed by one of the investigators.

Microbiological Studies

Specimens were obtained from the anterior nares, the pharynx, and, if present, skin wounds with a sterile polyester fiber–tipped swab moistened with sterile saline. Swabs were transported to the laboratory in a transport tube (Transwab MW170, Medical Wire & Equipment, Corsham, United Kingdom) and cultured within 24 hours in Chapman broth (7.5% NaCl) at 35°C overnight. A loop was then subcultured on Columbia sheep blood agar with colistin and nalidixic acid. After incubation at 35°C for 24 hours, colonies with morphology consistent with *S. aureus* were identified by Gram stain, catalase test, latex agglutination test for the detection of clumping factor, protein A, and capsular polysaccharides of *S. aureus* (Pastorex Staph-Plus, Bio-Rad, Marnes-la-Coquette,

France), and tube coagulase test. Susceptibility testing for oxacillin was performed with oxacillin screening agar plates (6 mg/L) according to National Committee for Clinical Laboratory Standards guidelines.[12]

Statistical Analysis

Categorical variables were compared using a two-sided chi-square test or Fisher's exact test and continuous variables using a *t* test. Independent predictors of *S. aureus* carriage were determined by multiple stepwise logistic regression analysis. All variables with a *P* value of .10 or less were entered into the model. Statistical analyses were performed using SPSS software (version 10.1.3; SPSS, Inc., Chicago, IL).

The study was approved by the Research Ethics Committee of the Cantons Basel Stadt and Basel Land. Written informed consent was obtained from each study participant.

RESULTS

Study Population

Seventy (56%) of 125 patients from the oral methadone program and 94 (74%) of 127 patients from the intravenous heroin program agreed to participate in the study. The demographic data of study participants and characteristics that could affect the rate of *S. aureus* carriage are presented in Table 1. None of the study participants suffered from insulin-dependent diabetes mellitus. Only 1 patient, an *S. aureus* carrier, used nasal steroids, and 2 female patients used estrogens (1 was colonized with *S. aureus*).

S. aureus *Carriage*

The addicts treated in the intravenous heroin substitution program had a significantly lower overall rate of *S. aureus* carriage (ie, colonization of at least the nose, pharynx, or skin [37 of 94 (39.4%) vs 42 of 70 (60%); $P = .009$]) and a significantly lower rate of nasal carriage (21 of 94 [22.3%] vs 30 of 70 [42.9%]; $P = .005$) than did the addicts treated in the oral methadone program. The prevalence of *S. aureus* carriers with colonization in the pharynx only was similar in the two groups (Table 1). Thirteen (54.2%) of 24 patients from the oral methadone program who did not inject drugs in the month preceding the study were *S. aureus* carriers.

Risk Factors for S. aureus *Carriage*

Characteristics associated with *S. aureus* carriage are presented in Table 2. The following variables were included in the logistic regression analysis model: treatment in the oral methadone program, use of intravenous heroin, heroin smoking, cocaine smoking, use of intravenous methadone, history of hepatitis C, and hospitalization in the month preceding the study. In this model, being treated in the oral methadone program was the only independent predictor of *S. aureus* carriage (odds ratio, 2.27; 95% confidence interval, 1.19 to 4.31; $P = .012$).

Susceptibility to Oxacillin

All *S. aureus* isolates were susceptible to oxacillin.

DISCUSSION

The overall rate of *S. aureus* carriage found in the current study among addicts treated in an intravenous heroin maintenance program (39.4%) is almost identical to the rate previously reported by Tuazon and Sheagren for active injection drug users (35%).[9] The rate of nasal carriage of *S. aureus* (22.3%) is similar to the rate recently found among healthy university students (26.2%),[13] and is lower than the mean rate of carriage of 37.2% in the general population calculated by Kluytmans et al. from 18 published studies involving 13,873 individuals.[6]

The current study also showed that addicts injecting heroin in the setting of a substitution program had a significantly lower overall rate of *S. aureus* carriage and a lower rate of nasal carriage than did addicts treated in an oral methadone program. They had an even lower rate of *S. aureus* carriage than those addicts in the oral methadone program who did not inject street drugs or methadone in the month preceding the study (39.4% vs 54.2%).

These findings suggest that the regular use of sterile needles under aseptic conditions per se does not increase the rate of *S. aureus* carriage. This conclusion is consistent with the results of two previous studies. In the first study involving 217 active and former drug users, Holbrook et al. found no association between injection drug use and nasal colonization by *S. aureus*, although nasal carriage of *S. aureus* was independently correlated with inhalational drug use in individuals infected with human immunodeficiency virus.[14] The second study demonstrated that the higher rate of nasal carriage of *S. aureus* found among patients receiving allergen-injection immunotherapy is probably related to the atopic constitution of these patients, manifested by a high prevalence of atopic dermatitis and eczema, rather than to the regular use of needles for the desensitization therapy.[13]

It is unclear why treatment in the oral methadone program was associated with a higher rate of *S. aureus* carriage. The anterior nares are the ecologic niches of *S. aureus* and provide a reservoir from which the skin is colonized.[6,8] It is not known exactly how *S. aureus* binds to the nasal mucosa. Previous studies described *S. aureus* adhesion to mucin,[15] and to nasal epithelial cells.[16] It is also thought that damaged mucosa is more likely to become colonized with *S. aureus* because underlying surfaces contain tissue constituents, such as microbial surface components recognizing adhesive matrix molecules, that promote colonization.[17] Sixty-six percent of the patients in the oral methadone program continued to use intravenous drugs despite methadone substitution. Addicts treated with oral methadone may inject or smoke contaminated street drugs more frequently and these may cause nasal mucosal damage. This illegal drug use may also take place in settings with poor hygiene and shared use of drug paraphernalia, thus facilitating transmission

TABLE 2
CHARACTERISTICS OF *STAPHYLOCOCCUS AUREUS* CARRIERS (NASAL, PHARYNGEAL, OR SKIN COLONIZATION) AND OF NONCARRIERS

Characteristic	*Staphylococcus aureus* Carriers	*Staphylococcus aureus* Noncarriers	P
No. of patients	79	85	
Mean age, y (± SD)	35 (± 6)	36 (± 6)	.234
Women	27 (34.2%)	23 (27.1%)	.322
Intravenous drug addiction > 10 y	54 (68.4%)	63 (74.1%)	.415
Opiate maintenance treatment			
Intravenous heroin	37 (46.8%)	57 (67.1%)	.009
Oral methadone	42 (53.2%)	28 (32.9%)	.009
Drug use in the month preceding the study			
No injection drug use	14 (17.7%)	11 (12.9%)	.395
Heroin use	54 (68.4%)	62 (72.9%)	.519
Intravenous heroin	45 (57%)	60 (70.6%)	.069
Intramuscular heroin	5 (6.3%)	2 (2.4%)	.263
Heroin smoking	5 (6.3%)	0	.024
Heroin snorting	5 (6.3%)	3 (3.5%)	.484
Cocaine use	31 (39.2%)	36 (42.4%)	.685
Intravenous cocaine	26 (32.9%)	34 (40%)	.346
Intramuscular cocaine	3 (3.8%)	1 (1.2%)	.353
Cocaine smoking	7 (8.9%)	2 (2.4%)	.090
Cocaine snorting	3 (3.8%)	3 (3.5%)	1.0
Heroin or cocaine smoking	7 (8.9%)	4 (4.7%)	.288
Oral methadone	50 (63.3%)	54 (63.5%)	.975
Intravenous methadone	22 (27.8%)	13 (15.3%)	.050
Intramuscular methadone	1 (1.3%)	0	.482
Cannabis smoking	12 (15.2%)	19 (22.4%)	.242
Intravenous use of street drugs	44 (55.7%)	40 (47.1%)	.269
Needle exchange	1 (1.3%)	0	.482
Diseases			
HIV infection	11 (13.9%)	9 (10.6%)	.514
Atopic dermatitis or eczema	10 (12.7%)	8 (9.4%)	.506
Psoriasis	3 (3.8%)	6 (7.1%)	.498
Skin abscess (at the time of *S. aureus* screening)	12 (15.2%)	8 (9.4%)	.259
Allergic rhinitis	6 (7.6%)	9 (10.6%)	.506
Asthma	7 (8.9%)	6 (7.1%)	.670
History of hepatitis B*	50 (63.3%)	55 (64.7%)	.850
History of hepatitis C*	53 (67.1%)	67 (78.8%)	.090
Medications			
Antibiotics 1 to 6 mo prior to *S. aureus* screening	9 (11.4%)	13 (15.3%)	.464
Antibiotics in the month preceding the *S. aureus* screening	7 (8.9%)	6 (7.1%)	.670
Nasal medications†	4 (5.1%)	5 (5.9%)	1.0
Hospitalizations			
Hospitalization in the year preceding the *S. aureus* screening	10 (12.7%)	18 (21.2%)	.147
Hospitalization in the month preceding the *S. aureus* screening	8 (10.1%)	3 (3.5%)	.091

SD = standard deviation; HIV = human immunodeficiency virus.
*Diagnosis could be verified through available results of the determination of antibody to hepatitis C virus and antibody to hepatitis B core antigen IgG for all 94 patients in the intravenous heroin program and for 49 of 70 patients in the oral methadone program.
†Only 1 of these 9 patients used nasal steroids.

of *S. aureus*.[17] In fact, in the current study, the patients treated in the oral methadone program snorted heroin, smoked heroin or cocaine, and used intravenous methadone and intravenous street drugs more frequently than did the patients in the intravenous heroin program. These factors and additional factors other than the regular use of needles under aseptic conditions may interact and increase the rate of *S. aureus* colonization among injection drug users. A larger study population would be necessary to identify such factors.

Complications associated with injection drug use are frequently the consequence of the illegal status of street drugs. Therefore, in several countries, harm reduction measures have been developed, including implementation of supervised injecting facilities where injection drug users are provided with sterile injecting equipment, opiate substitution programs, and programs offering intravenous heroin substitution to addicted patients for whom other treatments have failed.[11] It has been shown that injection opiate maintenance programs improve health status and social functioning, reduce the self-reported use of illicit drugs and criminal activity,[11,18] reduce the incidence of hepatitis B and C,[19] and may decrease the incidence of human immunodeficiency virus and hepatitis A virus infection.[20] The current study found a low rate of *S. aureus* carriage among injection drug users in an intravenous heroin maintenance program. This low rate of *S. aureus* carriage may result in a low incidence of *S. aureus* infections in this population. This hypothesis is supported by a previous study showing a significant decrease in the prevalence of skin abscesses and cellulitis, which are predominantly caused by *S. aureus*,[1] among injection drug users in an intravenous heroin program.[21]

All *S. aureus* isolates of the current study in Basel were susceptible to oxacillin. This result is surprising considering the recent MRSA epidemic among injection drug users in the neighboring city of Zurich.[5] However, this

finding mirrors the low MRSA prevalence (4%) among nosocomial *S. aureus* isolates in Basel,[22] and suggests that the injection drug user populations in the two cities are not in close contact. This observation also illustrates the importance of regular surveillance of the local epidemiologic situation regarding antibiotic-resistant organisms.

Addicts treated in an intravenous heroin maintenance program had a lower rate of *S. aureus* carriage than did addicts treated in an oral methadone program. Factors other than the regular use of needles under aseptic conditions may predispose injection drug users to *S. aureus* carriage. Further studies are necessary to investigate whether the lower rate of *S. aureus* carriage leads to a lower incidence of *S. aureus* infections among injection drug users treated with intravenous heroin.

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