

## REVIEW ARTICLE

## CURRENT CONCEPTS

## Bacterial Infections in Drug Users

Rachel J. Gordon, M.D., M.P.H., and Franklin D. Lowy, M.D.

ILLICIT DRUG USE IS A WORLDWIDE HEALTH PROBLEM. ANNUALLY, APPROXIMATELY 5 percent of the global population, or 200 million people, use illicit drugs.<sup>1</sup> In a U.S. survey, 19.5 million people 12 years of age or older, or 8.2 percent of the population, had used an illicit drug in the prior month.<sup>2</sup> Injection is one of the most harmful routes of administration. There are an estimated 13 million injection-drug users worldwide, 78 percent of whom live in developing nations.<sup>3</sup>

Infections are among the most serious complications of drug use.<sup>4,5</sup> Drug use plays a major role in the transmission of human immunodeficiency virus (HIV), sexually transmitted diseases, and viral hepatitis. In addition to these infections, drug users risk acquiring a diversity of bacterial infections.<sup>4,6-9</sup> This review summarizes recent information on bacterial infections associated with drug use and examines the interactions among the drug user, the preferred drug, and the method of administration that define the nature of these infections.

## EPIDEMIOLOGY

Most bacterial infections among drug users are caused by the subject's own commensal flora, with *Staphylococcus aureus* and streptococcus species being the most common pathogens.<sup>6-11</sup> Outbreaks among drug users that are caused by unusual organisms, such as clostridia species and *Pseudomonas aeruginosa*, may indicate that a particular drug or drug-use behavior is involved.<sup>12,13</sup>

Skin and soft-tissue infections are some of the most common infections among injection-drug users. Their incidence is difficult to estimate because such infections are often self-treated. A prospective study of injection-drug users in Amsterdam reported an approximate incidence of one abscess per three years of injection-drug use.<sup>14</sup> A cross-sectional study of injection-drug users in San Francisco found that 32 percent had an abscess, cellulitis, or both, as confirmed by physical examination (Fig. 1).<sup>15</sup>

Inexperience with injection may predispose the drug user to soft-tissue infection. Experienced injection-drug users who lack viable veins for use commonly resort to "skin popping" (subcutaneous or intramuscular injection). Binswanger et al.<sup>15</sup> reported that injection-drug users who had skin-popped within the preceding 30 days had a higher risk of soft-tissue infection than those who injected only intravenously. Injecting "speedballs" (mixtures of cocaine and heroin), injecting more frequently, and being positive for HIV infection were also associated with skin abscesses.<sup>14</sup> Using dirty needles, failing to clean the skin before injection, and "booting" (repeatedly flushing and pulling back during injection) may also increase the risk of abscess.<sup>16,17</sup>

An upsurge in skin infections, primarily abscesses, as well as more invasive infections, among injection-drug users in California has been caused by community-associated methicillin-resistant *S. aureus* (MRSA).<sup>18</sup> Six of 14 patients with necrotizing fasciitis due to community-associated MRSA at Harbor-UCLA Medical Center were current or former injection-drug users.<sup>19</sup> Community-associated MRSA infections have also

From the Division of Infectious Diseases, Departments of Medicine (R.J.G., F.D.L.) and Pathology (F.D.L.), Columbia University College of Physicians and Surgeons, New York. Address reprint requests to Dr. Gordon at the Division of Infectious Diseases, Box 82, Columbia University College of Physicians and Surgeons, 630 W. 168th St., New York, NY 10032, or at [rj216@columbia.edu](mailto:rj216@columbia.edu).

N Engl J Med 2005;353:1945-54.

Copyright © 2005 Massachusetts Medical Society.



**Figure 1. Soft-Tissue Abscess on the Leg of an Injection-Drug User.**

"Track" marks from injections extend along the calf.  
Provided courtesy of Robert Gwizdala.

been reported among prisoners, military recruits, and men who have sex with men who use crystal methamphetamine.<sup>20-24</sup> These infections, most of which are positive for the mobile genetic element staphylococcal chromosomal cassette (SCC) *mec* type IV, in part reflect the clonal dissemination of toxin-producing (i.e., Pantón-Valentine leukocidin) strains with a predilection to cause cutaneous and respiratory tract infections.<sup>25</sup>

Infective endocarditis has an estimated incidence of 1.5 to 3.3 cases per 1000 injection-drug users per year.<sup>26,27</sup> Infection at other sites, colonization with *S. aureus*, and a history of infective endocarditis increase the drug user's risk.<sup>14,26,28</sup> The risk appears augmented when the injected drug is cocaine, perhaps owing to the vasoconstrictive effects of the drug or the increased frequency of injection.<sup>29</sup>

HIV infection also predisposes the drug user to infective endocarditis. In a Baltimore cohort of 2946 injection-drug users, the incidence was 3.3 cases per 1000 person-years among HIV-negative subjects and 13.8 cases per 1000 person-years among HIV-positive subjects. Risk factors for infective endocarditis included immunosuppression (defined as fewer than 200 CD4 cells per cubic millimeter) and more frequent injection (at least daily).<sup>26</sup>

Drug users have a 10-fold increase in the risk of community-acquired pneumonia.<sup>30</sup> Drug users, who are often smokers, may have impaired respiratory-clearance mechanisms as well as an increased risk of aspiration.<sup>31</sup> Immunocompromise, resulting from poor nutrition or HIV infection, may also contribute to the increased risk of respiratory tract infection.<sup>6,32,33</sup>

The risk of pulmonary tuberculosis (including drug-resistant cases) appears to be increased among drug users as a result of crowded living conditions (including residence in homeless shelters and drug use in "crack" cocaine houses and "shooting galleries"), delays in diagnosis, poor adherence to treatment (which increases the duration of infectiousness), and the prevalence of HIV infection or the acquired immunodeficiency syndrome (AIDS).<sup>34-37</sup> Tuberculosis and other respiratory pathogens may also be transmitted through a practice known as "shotgunning" (smoking and inhaling a drug and then expelling the smoke into another person's mouth), a common practice among smokers of crack cocaine.<sup>38</sup> Inhaling cocaine also predisposes drug users to upper respiratory tract infections, including sinusitis and, in rare instances, septal abscesses.<sup>39,40</sup>

A unique association exists between clostridial infections and the use of black-tar heroin, a form of heroin produced in Mexico. An epidemic of wound botulism occurred in California during the 1990s in conjunction with the increased use of black-tar heroin. Most patients had injected the drug subcutaneously, suggesting the combined role of black-tar heroin and skin popping in heightening the risk of wound botulism.<sup>13</sup>

The number of tetanus cases climbed in concert with California's epidemic of wound botulism. Twenty-seven (40 percent) of the identified cases occurred in injection-drug users, all of whom reported subcutaneous injection of heroin.<sup>41</sup> Nationally, injection-drug users accounted for 19 of the 130 cases reported from 1998 to 2000 (15 percent).<sup>42</sup> England had an outbreak of eight cases among injection-drug users in 2003. The close clustering of cases suggested contamination of drugs with *Clostridium tetani*.<sup>43</sup>

Necrotizing fasciitis with toxic shock syndrome complicated *C. sordellii* infection in at least six users of black-tar heroin in California.<sup>44</sup> Eighty-eight injection-drug users in England, Scotland, and Ireland were hospitalized with a soft-tissue infection at an injection site and more than 30 died in 2000.<sup>45</sup> Twenty-six percent of patients (9 of 35 patients who

met the case definition) had microbiologic evidence of clostridial infections, including *C. novyi* and *C. perfringens*.

#### PATHOGENESIS

The bacteria responsible for infections in drug users are acquired either from the drug user's commensal flora or from organisms contaminating the drugs, drug adulterants, or paraphernalia. Examples of these different modes of transmission and the pathogenesis of these infections are discussed below.

#### THE ROLE OF COMMENSAL FLORA

The majority of nonpulmonary bacterial infections among drug users are caused by *S. aureus* or streptococcus species.<sup>7,10,11,26,28,46</sup> Drug users may have a higher rate of nasal or skin colonization with *S. aureus* than do those who do not use drugs,<sup>47</sup> perhaps because their nasal epithelium has been damaged by drug inhalation or their skin has been damaged by drug injection. Colonization with *S. aureus* is a risk factor for infection.<sup>47</sup> These infections occur when commensal flora is introduced into the surrounding tissues or bloodstream through injection. Tuazon and Sheagren<sup>48</sup> demonstrated that 12 injection-drug users hospitalized with *S. aureus* infective endocarditis were infected with their own colonizing strain.

Poor hygiene may exacerbate the risk of infection with commensal flora. Before "shooting up," drug users often fail to clean injection sites, or do so insufficiently.<sup>6,15-17</sup> In a study of 1057 injection-drug users in Baltimore, abscesses were twice as common among those who reported never cleaning the skin as among those who reported always cleaning the skin before injection.<sup>16</sup> Injection at heavily colonized sites, such as the femoral vein, may also increase the risk of infection with gram-negative flora.<sup>15,31</sup> Drug users often crush capsules and tablets in their mouth when preparing them for intravenous injection. They also blow out needle clots or lick their needles to facilitate injection. Needle licking may double the risk of cellulitis or abscess with oral streptococcal and anaerobic species.<sup>15</sup>

#### BACTERIAL TRANSMISSION THROUGH SHARING OF DRUG PARAPHERNALIA

Drug users may also transmit bacteria by sharing drug paraphernalia. Such equipment may be rinsed only with water, or if running water is unavailable,

saliva or even toilet water may be used.<sup>31</sup> In the first U.S. outbreak of community-associated MRSA among injection-drug users, the epidemic strain was cultured from a needle used by one of the patients.<sup>49</sup>

In Boston, seven injection-drug users with bacteremia caused by a single strain of *S. aureus* had been injected by a "street doctor" at the same "shooting gallery," using the gallery's drug paraphernalia.<sup>50</sup> In Zurich, 31 injection-drug users were infected and hospitalized with the same MRSA clone.<sup>51</sup> This phenomenon has also been reported with *Streptococcus pyogenes*.<sup>52</sup> Quagliarello et al.<sup>53</sup> reported that 14 of 54 subjects who used inhalational drugs (56 percent of whom also injected drugs) had nasal colonization with *S. aureus* (26 percent) and that 4 of 48 pieces of their inhalational paraphernalia were positive for *S. aureus* (8 percent). Closely related clusters of *S. aureus* strains were present among users of four drug-use networks, all of whom frequented the same crack house.<sup>53</sup> These studies suggest that *S. aureus* is transmitted through drug-use networks and shared drug paraphernalia.

#### TRANSMISSION THROUGH DRUGS OR DRUG ADULTERANTS

The drug of choice and techniques of drug preparation may affect the risk of infection with particular organisms. The association between black-tar heroin and clostridial infections is a case in point. Investigators believe that black-tar heroin becomes contaminated with spores when mixed with adulterants (e.g., methamphetamine or strychnine) or diluted ("cut") with substances such as dextrose or dyed paper. Although black-tar heroin is typically heated in water before use, clostridial spores survive boiling and may even begin to germinate.<sup>13,54</sup>

Intravenous use of black-tar heroin causes venous sclerosis and promotes the practice of skin popping with the loss of usable veins. Repeated injection of the drug into soft tissue leads to local tissue ischemia and necrosis, establishing an anaerobic environment that favors clostridial germination and elaboration of toxin.<sup>42,54</sup> The use of speedballs may potentiate the formation of abscesses and the growth of anaerobic organisms by causing local tissue damage.<sup>14,17,55</sup>

Skin popping may increase the odds of wound botulism by a factor of more than 15. Investigators have also demonstrated a dose-response relationship between the quantities of black-tar heroin introduced by skin popping and the risk of wound botulism. Cleaning the skin, cleaning old needles,

or using new needles before injection were not protective, another indication that black-tar heroin was the source of the infection.<sup>54</sup>

#### DRUG PREPARATION

Unique features of drug preparation may predispose drug users to unusual infections. The intravenous combination of pentazocine (an analgesic) and tripeleennamine (an antihistamine), referred to as “Ts and Blues,” or TaBs, which was popular in Chicago in the late 1970s, was associated with an outbreak of infective endocarditis caused by *P. aeruginosa*.<sup>12</sup> The tablets were crushed and then mixed with warm tap water before injection. Unlike heroin-containing mixtures, the mixture was soluble and did not require heating before injection. The presence of *P. aeruginosa* in the tap water often used to

rinse syringes, combined with the solubility of TaBs, was believed to explain the association between TaBs and *P. aeruginosa* infection.<sup>12</sup> A series of groin abscesses due to *S. milleri* was identified in Scotland, where it was common to crush buprenorphine (an opioid) and temazepam (a benzodiazepine) between the teeth and then inject it after cleaning the skin with saliva.<sup>56</sup>

#### HOST SUSCEPTIBILITY

In addition to the role of hygiene, living conditions, and tissue trauma, other factors such as malnutrition and the presence of coexisting conditions may impair host defenses and exacerbate the risk of infection among drug users. HIV infection, a common coexisting medical condition, increases

**Table 1. Organisms Responsible for Bacterial Infections in Drug Users.\***

##### Skin, soft-tissue, and skeletal infections

*Staphylococcus aureus* (including community-associated MRSA)

Streptococcus species — groups A, C, and G; *Streptococcus anginosus* (*milleri*)†; and  $\alpha$ -hemolytic streptococci†

*Pseudomonas aeruginosa*

Other gram-negative bacteria (*Escherichia coli*, enterobacter, klebsiella, proteus, serratia)

Oral anaerobes (bacteroides species, *Eikenella corrodens*, fusobacterium species, peptostreptococcus species)†

*Mycobacterium tuberculosis*

##### Infective endocarditis‡

*S. aureus* (including community-associated MRSA)

Streptococcus species (groups A, B, G, and others)

*P. aeruginosa* and other gram-negative bacteria

##### Toxin-mediated disease

*Clostridium botulinum*, *C. tetani*

Other clostridia species (*C. sordellii*, *C. novyi*, *C. perfringens*)

Group A streptococcus and *S. aureus*

##### Pulmonary infection

Community-acquired pneumonia

*S. pneumoniae*, *S. aureus*, *Haemophilus influenzae*, *Klebsiella pneumoniae*, *Chlamydia pneumoniae*, *Mycoplasma pneumoniae*, *Legionella pneumophila*

Oropharyngeal flora (i.e., due to aspiration)

Opportunistic pulmonary infections (associated with HIV disease)

*M. tuberculosis* (including multidrug-resistant tuberculosis), *M. avium* complex, *P. aeruginosa*, nocardia species, *Rhodococcus equi*

##### Sexually transmitted infections

*Chlamydia trachomatis*, *Neisseria gonorrhoeae*, *Treponema pallidum*, and others

\* This is a selection of likely bacterial pathogens. Other bacterial or nonbacterial pathogens may also be present and should be considered in the differential diagnosis. MRSA denotes methicillin-resistant *S. aureus*.

† These organisms are more likely to be pathogens when oral contamination is present.

‡ Injection-drug users have an increased risk of polymicrobial infective endocarditis.

drug users' susceptibility to bacterial infections.<sup>36,57</sup> First reported by Stoneburner et al.,<sup>58</sup> others have also noted an increased risk of death from bacterial infection among HIV-infected drug users.<sup>59</sup>

#### CLINICAL FEATURES

The clinical presentation of bacterial infections in drug users is generally similar to that encountered in patients who do not use drugs. This section will highlight features that are unique to the drug user. Bacteria associated with infections in drug users are noted in Table 1.

#### SKIN AND SOFT-TISSUE INFECTIONS

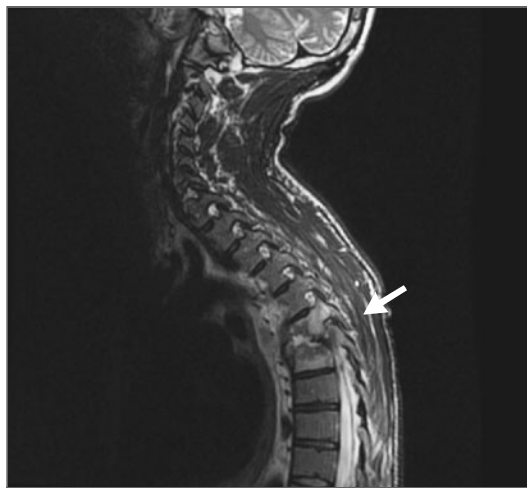
Although the abscesses associated with community-acquired MRSA generally appear similar to other abscesses, they have occasionally been confused with spider bites.<sup>21,23</sup> Community-associated MRSA should be considered as a potential cause in patients who have a history of such infections, patients in potential risk groups who live in high-risk regions who have abscesses (especially complicated ones), and patients with infections that are not responding to conventional antibiotics (photographs of abscesses are available at [http://lapublichealth.org/acd/docs/mrsa\\_colorenhanced.pdf](http://lapublichealth.org/acd/docs/mrsa_colorenhanced.pdf)).<sup>60,61</sup>

#### MUSCULOSKELETAL INFECTIONS

Musculoskeletal infections, including septic arthritis and osteomyelitis, generally result from hematogenous seeding or, less commonly, local extension of a skin or soft-tissue infection in drug users. These infections may be indolent, and the only symptom may be pain without fever.<sup>62,63</sup> Injection-drug users are susceptible to skeletal infections in uncommon places such as the sternoclavicular and sacroiliac joints, in addition to more usual sites, such as the vertebral spine (Fig. 2) and knee.<sup>62,63</sup> These infections may result, in part, from injecting in high-risk areas such as the jugular vein ("pocket shot") and femoral vein ("groin hit").<sup>31,63</sup> Such musculoskeletal infections are also more likely to be polymicrobial or anaerobic, especially if the injection-drug user contaminates the injection site, equipment, or drugs with saliva.

#### ENDOVASCULAR INFECTIONS

Endovascular infections, including infective endocarditis, septic thrombophlebitis, mycotic aneurysms, and sepsis, are among the most serious complications of injection-drug use. An endovas-



**Figure 2.** Sagittal View of Magnetic Resonance Image in an Injection-Drug User with Vertebral Osteomyelitis Involving T6–T7 (Arrow) with an Adjacent Epidural Abscess.

Culture of a biopsy specimen of the involved bone grew *Enterobacter cloacae*.

cular source should be investigated in all injection-drug users with bacteremia. Although left-sided infective endocarditis in drug users is similar to that seen in non-drug users, infective endocarditis in injection-drug users is most commonly due to *S. aureus* and involves the tricuspid valve in 70 percent of patients. Symptoms may include fever, dyspnea, pleuritic chest pain, and cough. A murmur may be absent. The mortality rate in these cases is less than 5 percent.<sup>9,27,28</sup> HIV-infected injection-drug users with fewer than 200 CD4 cells per cubic millimeter have a higher mortality rate than those with less advanced HIV disease.<sup>64</sup> If infective endocarditis is left-sided, complications such as brain and splenic abscess may occur owing to septic embolization. Infective endocarditis associated with injection-drug use is also one of the rare settings in which polymicrobial endocarditis is encountered.<sup>28,64,65</sup>

#### RESPIRATORY TRACT INFECTIONS

Respiratory tract infections are among the most frequent sequelae of drug use, and patients may present with atypical clinical and radiographic findings.<sup>4,6,30,33</sup> A thorough medical history taking includes questions regarding tuberculosis, HIV, and risk factors for aspiration. Aspiration pneumonia as well as pneumonia caused by *S. pneumoni-*



**Table 2. Initial Management of Bacterial Infectious Syndromes among Suspected Drug Users.\***

Clinical Scenario	Selected Diagnostic Tests	Empirical Treatment Options†	
		Oral	Parenteral
Skin or soft-tissue infection in which <i>S. aureus</i> is a likely pathogen	Send drainage for Gram's staining, culture, and susceptibility testing.	Incision and drainage plus wound care may suffice for uncomplicated abscesses  For methicillin-susceptible <i>S. aureus</i> : dicloxacillin or cephalexin,‡ 500 mg every 6 hr  If MRSA suspected: TMP-SMX,‡ 6–10 mg/kg of body weight/day (TMP) in divided doses given every 8–12 hr; clindamycin,§ 300 mg every 6 hr or 450 mg every 8 hr; doxycycline or minocycline, 100 mg every 12 hr; linezolid, 600 mg every 12 hr	For methicillin-susceptible <i>S. aureus</i> : nafcillin or oxacillin, 1–2 g every 4–6 hr; cefazolin,‡ 1–2 g every 8 hr  If MRSA suspected: vancomycin,‡ 15 mg/kg every 12 hr; teicoplanin,‡¶ 6 mg/kg every 12 hr for 3 doses, then 6 mg/kg every 24 hr; linezolid, 600 mg every 12 hr; daptomycin,‡ 4 mg/kg every 24 hr
Infections in which oral contamination is suspected, including skin or soft-tissue and skeletal infections (septic arthritis and bursitis, tenosynovitis, and osteomyelitis)	Send specimens for Gram's staining, culture, and susceptibility testing. Consider imaging to diagnose or define deep-seated infections. A bone biopsy is important when osteomyelitis is suspected regardless of whether blood-culture results are positive. Specimens for anaerobic culture require special handling.	Incision and drainage when appropriate; wound care  Amoxicillin–clavulanate,‡ 875 mg every 12 hr; For serious penicillin allergy: clindamycin and quinolone (dose and route based on type and severity of infection)	Ampicillin–sulbactam,‡ 1.5–3.0 g every 6 hr, plus gentamicin,‡ 1.5–2.0 mg/kg every 8 hr for serious or complicated infections; piperacillin–tazobactam,‡ 3.375 g every 4–6 hr or 4.5 g every 6–8 hr; ticarcillin–clavulanate,‡ 3.1 g every 4–6 hr; cefepime,‡ 1–2 g every 12 hr;  For osteomyelitis, serious infections, and possible MRSA infection, add vancomycin‡ or teicoplanin‡¶
Acute right-sided infective endocarditis	Diagnosis is based on the modified Duke criteria. <sup>71</sup> Culture of multiple blood specimens before the initiation of antibiotic therapy is the optimal approach.	Vancomycin,‡ 15 mg/kg IV every 12 hr (or teicoplanin,‡¶ 12 mg/kg every 12 hr for 3 doses, then 12 mg/kg every 24 hr), plus gentamicin,‡ 1 mg/kg every 8 hr or consider nafcillin or oxacillin, 2 g IV every 4 hr, plus gentamicin,‡ 1 mg/kg every 8 hr, if MRSA not present in the community; consider broadening coverage (pseudomonal, gram-negative, or fungal antibiotics) on the basis of patient risk factors	

*ae*, *Haemophilus influenzae*, *S. aureus*, and *Klebsiella pneumoniae* are among the most common reasons for hospitalization.<sup>4,5,32,33</sup> Undiagnosed HIV can first become evident as the result of an opportunistic infection such as pneumocystis pneumonia. Endovascular infections can cause septic pulmonary emboli producing pneumonias and lung abscesses.<sup>7,31</sup>

Tuberculosis must be considered in drug users presenting with pneumonia and known or suspected HIV infection. Drug users who have tuberculosis associated with HIV disease can present atypically

(i.e., without cavitory lesions), and the purified-protein-derivative test may be negative. Hilar or mediastinal lymphadenopathy may be the only finding.<sup>66</sup>

#### MISCELLANEOUS INFECTIONS

Among the most important of the unusual infections related to drug use are the clostridial infections that have been associated with the use of black-tar heroin. These may have typical presentations, as with the cases of tetanus, or an unusual presenta-

Table 2. (Continued.)

Clinical Scenario	Selected Diagnostic Tests	Empirical Treatment Options†	
		Oral	Parenteral
Pulmonary infection (community-acquired pneumonia and aspiration pneumonia, pulmonary tuberculosis, and other opportunistic pathogens) in drug users, including those with HIV or AIDS or risk factors for HIV infection	Radiographic imaging: Gram's and AFB staining of sputum and cultures of sputum and blood. Bronchoscopy may be needed to diagnose pneumocystis pneumonia. In certain cases, performing a PPD test or checking for <i>Streptococcus pneumoniae</i> and legionella urinary antigens may be useful.	Hospitalized with community-acquired pneumonia: ceftriaxone, 1–2 g IV every 24 hr, and azithromycin, 500 mg IV every 24 hr or respiratory fluoroquinolone** Aspiration pneumonia likely: clindamycin, 600–900 mg IV every 8 hr Pneumocystis pneumonia suspected: TMP–SMX,‡ 15–20 mg/kg/day (TMP dose), given in divided doses every 6–8 hr (with or without corticosteroids) For tuberculosis, see treatment guidelines at <a href="http://www.thoracic.org">www.thoracic.org</a> or <a href="http://www.who.int/tb/en/index.html">www.who.int/tb/en/index.html</a>	
Presentation involving septic or neurologic findings of unknown cause with or without skin or soft-tissue infection	Gram's staining, culture, and susceptibility testing should be done if applicable.	For botulism: trivalent antitoxin (type A, B, or E), 1 vial, available from the appropriate public health authority; and penicillin G,‡ 3 million U IV every 6 hr For tetanus-prone wounds or tetanus: human tetanus immune globulin and tetanus toxoid; metronidazole, 500 mg orally or IV every 8 hr For other clostridia species (may be polymicrobial): débridement of skin or soft-tissue infections; ampicillin–sulbactam,‡ 3 g IV every 6 hr plus vancomycin,‡ 15 mg/kg IV every 12 hr (or teicoplanin‡¶)††	
Sexually transmitted infections	Examination and workup are conducted according to local health department guidelines. RPR and VDRL tests may be false positive; confirm results with FTA-ABS test.	Follow CDC treatment guidelines or those of public health authorities (available at <a href="http://www.who.int/topics/sexually_transmitted_infections/en/">www.who.int/topics/sexually_transmitted_infections/en/</a> )	

\* MRSA denotes methicillin-resistant *S. aureus*, TMP-SMX trimethoprim–sulfamethoxazole, AFB acid-fast bacilli, RPR rapid plasma reagin, VDRL Venereal Disease Research Laboratory, FTA-ABS fluorescent treponemal antibody absorption, IV intravenously, and CDC Centers for Disease Control and Prevention.

† Therapy should be adjusted on the basis of the culture results and antibiotic susceptibilities.

‡ The dose must be adjusted in patients with reduced creatinine clearance.

§ Clindamycin should not be used if the isolate is resistant to erythromycin.

¶ This drug is not available in the United States.

|| Therapy is generally continued for four to six weeks. Baddour et al.<sup>72</sup> provide specific recommendations.

\*\* Respiratory quinolones include gatifloxacin, levofloxacin, and moxifloxacin.

†† Hyperbaric oxygen has also been used.

tion, as with the cases of *C. sordellii* infection in which patients presented with toxic shock syndrome (with or without cutaneous lesions).<sup>44,45</sup> Patients should be asked about the use of subcutaneous and intramuscular injections, the use of black-tar heroin, and the date of the last tetanus immunization. Serious toxin-mediated disease, such as botulism, may masquerade as intoxication (e.g., slurred speech).

## PREVENTION

Eliminating drug use is the surest way to control associated infections, but this goal may not always

be possible. Numerous risk-reducing strategies may help prevent bacterial infections among drug users, particularly among new users, the ones at greatest risk. These programs include the provision of medically supervised injection facilities, syringe-exchange programs, and street-based education programs directed at the use of sterile injection practices.<sup>67,68</sup> Safer injection practices include boiling the drug, cleaning the skin with alcohol and the drug paraphernalia with bleach, avoiding contaminating or sharing needles with others, and avoiding the use of dangerous injection sites such as the neck and groin.<sup>17,69</sup> High-risk behavior such as hav-

ing unprotected sex and sex with multiple partners, which facilitates the transmission of HIV, sexually transmitted diseases, and community-associated MRSA, should be discouraged.<sup>22</sup> In a Baltimore study of injection-drug users, 60 percent reported a history of a sexually transmitted infection.<sup>70</sup> Vaccination with pneumococcal, *H. influenzae* type b, and tetanus vaccines<sup>41,42</sup> as well as routine screening for tuberculosis, HIV infection, and sexually transmitted diseases may help prevent bacterial infection and disease transmission.

#### TREATMENT

The medical management of bacterial infections in drug users begins with the recognition of drug use and its associated coexisting conditions. The specific issues of the management of drug withdrawal, adherence to therapy, and difficulties of intravenous access must be a part of the therapeutic strategy. Close attention to local outbreaks and bacterial antibiotic-resistance profiles is important. Management suggestions for selected syndromes related to drug use are included in Table 2.

Although conventional treatment is suggested, short courses of parenteral and oral regimens have been investigated for right-sided infective endocarditis associated with injection-drug use. Selected cases of right-sided infective endocarditis due to methicillin-susceptible *S. aureus* have been successfully treated with a penicillinase-resistant penicillin and an aminoglycoside (for two weeks) or ciprofloxacin and rifampin (for four weeks). Exclusion criteria for short-course or oral therapy for right-sided *S. aureus* infective endocarditis have included infections caused by MRSA, complicated cases characterized by a slow clinical response (more than 96 hours), large valvular vegetations (more than 2 cm), extracardiac complications, or injection-drug use

in a patient with AIDS.<sup>27,73-75</sup> For regimens that require prolonged therapy such as those for tuberculosis, the use of directly observed therapy is now standard.<sup>76</sup> For drug users with sexually transmitted diseases, in addition to the use of standard recommendations, the use of single-dose therapy when possible has been successful.<sup>77</sup>

The choice of therapy also requires consideration of regional differences in antibiotic susceptibility among prevalent bacteria. With the emergence of community-associated MRSA as a virulent pathogen, it is crucial to obtain cultures for sensitivity testing before therapy is initiated.<sup>18,60</sup> As we noted earlier, unlikely pathogens must be considered on the basis of the patient's drug-use behavior, including the type of drug used and the route of administration.

Injection-drug users who report having a fever with no localizing findings pose a particular diagnostic problem. Infection is just one of many potential diagnoses in these patients. Infective endocarditis will be diagnosed in up to 20 percent of injection-drug users hospitalized with fever.<sup>29</sup> However, the diagnosis of infective endocarditis in these patients is difficult when based solely on clinical and laboratory criteria.<sup>78</sup> Therefore, it has been recommended that these patients be admitted for further evaluation. Hospitalization of drug users also provides an important opportunity to offer comprehensive medical care.

Supported by grants (DA-09655 and DA-15018) from the National Institute on Drug Abuse and by a grant (CCR223380-01) from the Centers for Disease Control and Prevention.

Dr. Gordon reports having received grant support from GlaxoSmithKline. Dr. Lowy reports having received consulting or lecture fees from Wyeth, Pfizer, and Cubist; having received grant support from GlaxoSmithKline; and holding stock in Merck and Pfizer.

We are indebted to Christine Kubin, Michael Tapper, and Abigail Zuger for their critical review of this manuscript, and to Robert Gwizdala for providing Figure 1.

#### REFERENCES

- World drug report. Vol. 1. Analysis. New York: United Nations Office on Drugs and Crime, 2005.
- 2003 National Survey on Drug Use and Health. Rockville, Md.: Office of Applied Studies, Substance Abuse and Mental Health Services Administration, 2004.
- World drug report. Vol. 1. Analysis. New York: United Nations Office on Drugs and Crime, 2004.
- Scheidegger C, Zimmerli W. Infectious complications in drug addicts: seven-year review of 269 hospitalized narcotics abusers in Switzerland. *Rev Infect Dis* 1989;11:486-93. [Erratum, *Rev Infect Dis* 1990;12:165.]
- Palepu A, Tyndall MW, Leon H, et al. Hospital utilization and costs in a cohort of injection drug users. *CMAJ* 2001;165:415-20.
- Louria DB, Hensle T, Rose J. The major medical complications of heroin addiction. *Ann Intern Med* 1967;67:1-22.
- Cherubin CE, Sapira JD. The medical complications of drug addiction and the medical assessment of the intravenous drug user: 25 years later. *Ann Intern Med* 1993;119:1017-28.
- Levine DP, Sobel JD, eds. Infections in intravenous drug abusers. New York: Oxford University Press, 1991.
- Levine DP, Brown PV. Infections in injection drug users. In: Mandell GL, Bennett JE, Dolin R, eds. *Mandell, Douglas, and Bennett's principles and practice of infectious diseases*. 6th ed. Vol. 2. Philadelphia: Churchill Livingstone, 2005:3462-76.
- Crane LR, Levine DP, Zervos MJ, Cummings G. Bacteremia in narcotic addicts at the Detroit Medical Center. I. Microbiology, epidemiology, risk factors, and empiric therapy. *Rev Infect Dis* 1986;8:364-73.
- Bassetti S, Battagay M. *Staphylococcus aureus* infections in injection drug users: risk factors and prevention strategies. *Infection* 2004;32:163-9.
- Shekar R, Rice TW, Zierdt CH, Kallick



- CA. Outbreak of endocarditis caused by *Pseudomonas aeruginosa* serotype O11 among pentazocine and tripeleminamine abusers in Chicago. *J Infect Dis* 1985;151:203-8.
13. Werner SB, Passaro D, McGee J, Schechter R, Vugia DJ. Wound botulism in California, 1951-1998: recent epidemic in heroin injectors. *Clin Infect Dis* 2000;31:1018-24.
  14. Spijkerman JJ, van Ameijden EJ, Mientjes GH, Coutinho RA, van den Hoek A. Human immunodeficiency virus infection and other risk factors for skin abscesses and endocarditis among injection drug users. *J Clin Epidemiol* 1996;49:1149-54.
  15. Binswanger IA, Kral AH, Bluthenthal RN, Rybold DJ, Edlin BR. High prevalence of abscesses and cellulitis among community-recruited injection drug users in San Francisco. *Clin Infect Dis* 2000;30:579-81.
  16. Vlahov D, Sullivan M, Astemborski J, Nelson KE. Bacterial infections and skin cleaning prior to injection among intravenous drug users. *Public Health Rep* 1992;107:595-8.
  17. Murphy EL, DeVita D, Liu H, et al. Risk factors for skin and soft-tissue abscesses among injection drug users: a case-control study. *Clin Infect Dis* 2001;33:35-40.
  18. Soft tissue infections among injection drug users — San Francisco, California, 1996–2000. *MMWR Morb Mortal Wkly Rep* 2001;50:381-4.
  19. Miller LG, Perdreau-Remington F, Rieg G, et al. Necrotizing fasciitis caused by community-associated methicillin-resistant *Staphylococcus aureus* in Los Angeles. *N Engl J Med* 2005;352:1445-53.
  20. Methicillin-resistant *Staphylococcus aureus* skin or soft tissue infections in a state prison — Mississippi, 2000. *MMWR Morb Mortal Wkly Rep* 2001;50:919-22.
  21. Public health dispatch: outbreaks of community-associated methicillin-resistant *Staphylococcus aureus* skin infections — Los Angeles County, California, 2002–2003. *MMWR Morb Mortal Wkly Rep* 2003;52:88.
  22. Ly LT, Revuelta MP, Hongo I, Kreiswirth BN, Davis S, Saltzman BR. Clonal outbreak of community-acquired methicillin resistant *Staphylococcus aureus* skin abscesses in men who have sex with men in New York City: possible association with crystal methamphetamine usage. Presented at the annual meeting of the Infectious Diseases Society of America, Boston, September 30–October 3, 2004. abstract.
  23. Methicillin-resistant *Staphylococcus aureus* infections in correctional facilities — Georgia, California, and Texas, 2001–2003. *MMWR Morb Mortal Wkly Rep* 2003;52:992-6.
  24. Zinderman CE, Conner B, Malakooti MA, LaMar JE, Armstrong A, Bohnker BK. Community-acquired methicillin-resistant *Staphylococcus aureus* among military recruits. *Emerg Infect Dis* 2004;10:941-4.
  25. Lina G, Piemont Y, Godail-Gamot F, et al. Involvement of Pantón-Valentine leukocidin-producing *Staphylococcus aureus* in primary skin infections and pneumonia. *Clin Infect Dis* 1999;29:1128-32.
  26. Wilson LE, Thomas DL, Astemborski J, Freedman TL, Vlahov D. Prospective study of infective endocarditis among injection drug users. *J Infect Dis* 2002;185:1761-6.
  27. Miro JM, del Rio A, Mestres CA. Infective endocarditis in intravenous drug abusers and HIV-1 infected patients. *Infect Dis Clin North Am* 2002;16:273-95.
  28. Hecht SR, Berger M. Right-sided endocarditis in intravenous drug users: prognostic features in 102 episodes. *Ann Intern Med* 1992;117:560-6.
  29. Chambers HF, Morris DL, Tauber MG, Modin G. Cocaine use and the risk for endocarditis in intravenous drug users. *Ann Intern Med* 1987;106:833-6.
  30. Hind CR. Pulmonary complications of intravenous drug misuse. 2. Infective and HIV related complications. *Thorax* 1990;45:957-61.
  31. Stein MD. Medical complications of intravenous drug use. *J Gen Intern Med* 1990;5:249-57.
  32. Boschini A, Smacchia C, Di Fine M, et al. Community-acquired pneumonia in a cohort of former injection drug users with and without human immunodeficiency virus infection: incidence, etiologies, and clinical aspects. *Clin Infect Dis* 1996;23:107-13.
  33. Tumbarello M, Tacconelli E, de Gaetano K, et al. Bacterial pneumonia in HIV-infected patients: analysis of risk factors and prognostic indicators. *J Acquir Immune Defic Syndr Hum Retrovirol* 1998;18:39-45.
  34. Crack cocaine use among persons with tuberculosis — Contra Costa County, California, 1987–1990. *MMWR Morb Mortal Wkly Rep* 1991;40:485-9.
  35. Chin DP, Crane CM, Diul MY, et al. Spread of *Mycobacterium tuberculosis* in a community implementing recommended elements of tuberculosis control. *JAMA* 2000;283:2968-74.
  36. Alcibes P, Friedland G. Injection drug use and human immunodeficiency virus infection. *Clin Infect Dis* 1995;20:1467-79.
  37. Malakmadze N, Gonzalez IM, Oemig T, et al. Unsuspected recent transmission of tuberculosis among high-risk groups: implications of universal tuberculosis genotyping in its detection. *Clin Infect Dis* 2005;40:366-73.
  38. Perlman DC, Henman AR, Kochems L, Paone D, Salomon N, Des Jarlais DC. Doing a shotgun: a drug use practice and its relationship to sexual behaviors and infection risk. *Soc Sci Med* 1999;48:1441-8.
  39. Perper JA, Van Thiel DH. Respiratory complications of cocaine abuse. In: Galanter M, ed. Recent developments in alcoholism: alcohol and cocaine. Vol. 10. New York: Plenum Press, 1992:363-77.
  40. Silverman HS, Smith AL. Staphylococcal sepsis precipitated by cocaine sniffing. *N Engl J Med* 1985;312:1706.
  41. Tetanus among injecting-drug users — California, 1997. *MMWR Morb Mortal Wkly Rep* 1998;47:149-51.
  42. Pascual FB, McGinley EL, Zarardi LR, Cortese MM, Murphy TV. Tetanus surveillance — United States, 1998–2000. *MMWR Surveill Summ* 2003;52:1-8.
  43. Cluster of cases of tetanus in injecting drug users in England: update. *Eurosurveill Wkly* 2003;7:5-7.
  44. Kimura AC, Higa JJ, Levin RM, Simpson G, Vargas Y, Vugia DJ. Outbreak of necrotizing fasciitis due to *Clostridium sordelli* among black-tar heroin users. *Clin Infect Dis* 2004;38:e87-e91.
  45. Update: *Clostridium novyi* and unexplained illness and death among injecting-drug users — Scotland, Ireland, and England. *MMWR Morb Mortal Wkly Rep* 2000;49:543-5.
  46. Summanen PH, Talan DA, Strong C, et al. Bacteriology of skin and soft-tissue infections: comparison of infections in intravenous drug users and individuals with no history of intravenous drug use. *Clin Infect Dis* 1995;20:Suppl 2:S279-S282.
  47. Kluytmans J, van Belkum A, Verbrugh H. Nasal carriage of *Staphylococcus aureus*: epidemiology, underlying mechanisms, and associated risks. *Clin Microbiol Rev* 1997;10:505-20.
  48. Tuazon CU, Sheagren JN. Staphylococcal endocarditis in parenteral drug abusers: source of the organism. *Ann Intern Med* 1975;82:788-90.
  49. Saravolatz LD, Markowitz N, Arking L, Pohlod D, Fisher E. Methicillin-resistant *Staphylococcus aureus*: epidemiologic observations during a community-acquired outbreak. *Ann Intern Med* 1982;96:11-6.
  50. Craven DE, Rixinger AI, Goularte TA, McCabe WR. Methicillin-resistant *Staphylococcus aureus* bacteremia linked to intravenous drug abusers using a “shooting gallery.” *Am J Med* 1986;80:770-6.
  51. Fleisch F, Zbinden R, Vanoli C, Ruef C. Epidemic spread of a single clone of methicillin-resistant *Staphylococcus aureus* among injection drug users in Zurich, Switzerland. *Clin Infect Dis* 2001;32:581-6.
  52. Bohlen LM, Muhlemann K, Dubuis O, Aebi C, Tauber MG. Outbreak among drug users caused by a clonal strain of group A streptococcus. *Emerg Infect Dis* 2000;6:175-9.
  53. Quagliarello B, Cespedes C, Miller M, et al. Strains of *Staphylococcus aureus* obtained from drug-use networks are closely linked. *Clin Infect Dis* 2002;35:671-7.
  54. Passaro DJ, Werner SB, McGee J, MacKenzie WR, Vugia DJ. Wound botulism associated with black tar heroin among injecting drug users. *JAMA* 1998;279:859-63.
  55. Hoeger PH, Haupt G, Hoelzle E. Acute multifocal skin necrosis: synergism between invasive streptococcal infection and cocaine-induced tissue ischaemia? *Acta Derm Venereol* 1996;76:239-41.
  56. Hemingway DM, Balfour AE, McCart-

- ney AC, Leiberman DP. *Streptococcus milleri* and complex groin abscesses in intravenous drug abusers. *Scott Med J* 1992;37:116-7.
57. Maenza JR, Chaisson RE. Bacterial infections in HIV disease. In: Cohen J, Powderly W, eds. *Infectious diseases*. 2nd ed. Edinburgh: Mosby, 2004:1297-302.
58. Stoneburner RL, Des Jarlais DC, Benzra D, et al. A larger spectrum of severe HIV-1-related disease in intravenous drug users in New York City. *Science* 1988;242:916-9.
59. Petrosillo N, Viale P, Nicastrì E, et al. Nosocomial bloodstream infections among human immunodeficiency virus-infected patients: incidence and risk factors. *Clin Infect Dis* 2002;34:677-85.
60. Charlebois ED, Bangsberg DR, Moss NJ, et al. Population-based community prevalence of methicillin-resistant *Staphylococcus aureus* in the urban poor of San Francisco. *Clin Infect Dis* 2002;34:425-33.
61. Zetola N, Francis JS, Nuernberger EL, Bishai WR. Community-acquired methicillin-resistant *Staphylococcus aureus*: an emerging threat. *Lancet Infect Dis* 2005;5:275-86.
62. Sapico FL, Montgomerie JZ. Vertebral osteomyelitis in intravenous drug abusers: report of three cases and review of the literature. *Rev Infect Dis* 1980;2:196-206.
63. Chandrasekar PH, Narula AP. Bone and joint infections in intravenous drug abusers. *Rev Infect Dis* 1986;8:904-11.
64. Cicalini S, Forcina G, De Rosa FG. Infective endocarditis in patients with human immunodeficiency virus infection. *J Infect* 2001;42:267-71.
65. Levine DP, Crane LR, Zervos MJ. Bacteremia in narcotic addicts at the Detroit Medical Center. II. Infectious endocarditis: a prospective comparative study. *Rev Infect Dis* 1986;8:374-96.
66. Havlir DV, Barnes PF. Tuberculosis in patients with human immunodeficiency virus infection. *N Engl J Med* 1999;340:367-73.
67. Selwyn PA. Illicit drug use revisited: what a long, strange trip it's been. *Ann Intern Med* 1993;119:1044-6.
68. Hart GJ, Carvell AL, Woodward N, Johnson AM, Williams P, Parry JV. Evaluation of needle exchange in central London: behavior change and anti-HIV status over one year. *AIDS* 1989;3:261-5.
69. HIV-prevention bulletin for health-care providers regarding advice to persons who inject illicit drugs. *MMWR Morb Mortal Wkly Rep* 1997;46:510.
70. Nelson KE, Vlahov D, Cohn S, et al. Sexually transmitted diseases in a population of intravenous drug users: association with seropositivity to the human immunodeficiency virus (HIV). *J Infect Dis* 1991;164:457-63.
71. Li JS, Sexton DJ, Mick N, et al. Proposed modifications to the Duke criteria for the diagnosis of infective endocarditis. *Clin Infect Dis* 2000;30:633.
72. Baddour LM, Wilson WR, Bayer AS, et al. Infective endocarditis: diagnosis, antimicrobial therapy, and management of complications: a statement for healthcare professionals from the Committee on Rheumatic Fever, Endocarditis, and Kawasaki Disease, Council on Cardiovascular Disease in the Young, and the Councils on Clinical Cardiology, Stroke, and Cardiovascular Surgery and Anesthesia, American Heart Association: endorsed by the Infectious Diseases Society of America. *Circulation* 2005;111:e394-e434.
73. Dworkin RJ, Lee BL, Sande MA, Chambers HF. Treatment of right-sided *Staphylococcus aureus* endocarditis in intravenous drug users with ciprofloxacin and rifampicin. *Lancet* 1989;2:1071-3.
74. Chambers HF, Miller RT, Newman MD. Right-sided *Staphylococcus aureus* endocarditis in intravenous drug abusers: two-week combination therapy. *Ann Intern Med* 1988;109:619-24.
75. Torres-Tortosa M, de Cueto M, Vergara A, et al. Prospective evaluation of a two-week course of intravenous antibiotics in intravenous drug addicts with infective endocarditis. *Eur J Clin Microbiol Infect Dis* 1994;13:559-64.
76. Treatment of tuberculosis. *MMWR Recomm Rep* 2003;52(RR-11):1-77.
77. Sexually transmitted diseases treatment guidelines 2002. *MMWR Recomm Rep* 2002;51(RR-6):1-78.
78. Marantz PR, Linzer M, Feiner CJ, Feinstein SA, Kozin AM, Friedland GH. Inability to predict diagnosis in febrile intravenous drug abusers. *Ann Intern Med* 1987;106:823-8.

Copyright © 2005 Massachusetts Medical Society.

#### ELECTRONIC ACCESS TO THE JOURNAL'S CUMULATIVE INDEX

At the *Journal's* site on the World Wide Web ([www.nejm.org](http://www.nejm.org)), you can search an index of all articles published since January 1975 (abstracts 1975-1992, full text 1993-present). You can search by author, key word, title, type of article, and date. The results will include the citations for the articles plus links to the full text of articles published since 1993. For nonsubscribers, time-limited access to single articles and 24-hour site access can also be ordered for a fee through the Internet ([www.nejm.org](http://www.nejm.org)).

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.