HHS Public Access

Author manuscript

*Ann Intern Med*. Author manuscript; available in PMC 2019 September 10.

Published in final edited form as:

*Ann Intern Med*. 2019 January 01; 170(1): 68–69. doi:10.7326/M18-3026.

# Drug-Associated Infective Endocarditis Trends: What's All the Buzz About?

**Alysse G. Wurcel, MD, MS**

Tufts Medical Center and Tufts University, Boston, Massachusetts

In the 1930s, a malaria epidemic broke out in New York City. Around 200 cases occurred, at least 120 of which resulted in death, mostly from cerebral edema (1). All the cases developed in persons who injected heroin. Given the high mortality rate, researchers hypothesized that the malaria outbreak was "almost entirely due to the occurrence of the malignant form of the disease among drug addicts" (1). Rigorous experiments ensued, leading researchers to learn that this disease was in no way different from the malaria cases seen in Africa and that late presentation of infected persons to medical care was the reason for the high death rate.

In the context of the current national opioid epidemic, malaria has been replaced by other pressing public health emergencies. The alarming number of fatal and nonfatal opioid overdoses has caused growing concern among clinicians, researchers, and public health officials, leading to collaborative strategizing and interventions. HIV and viral hepatitis outbreaks across the United States have received media attention, with a concerted public health response. Lurking in the shadows, morbidity and mortality from other infections, such as infective endocarditis (IE), have percolated for more than 80 years without much fanfare —until now.

The microbiology, clinical manifestations, and demographic characteristics of IE in persons who inject drugs (PWID) have changed over time. The first reports of bacterial endocarditis in PWID appeared in the 1940s, and by the 1960s most major clinical journals featured case reports in this population. Bacteria colonizing the skin (*Staphylococcus aureus*) or mouth (viridans group streptococci) predominate as the cause of IE in most case studies of sporadic regional outbreaks of gram-negative infections. In the 1980s, the vast majority of PWID with endocarditis were black men living in urban areas (2). Since the turn of the century, most affected persons have been young, white, and rural dwelling, and the percentage of females infected has increased steadily (3). The tricuspid is the valve most commonly affected by IE in PWID, and this manifestation is relatively less severe; however, over time, left-sided and multivalve involvement has increased (2).

In their current *Annals* report, Schranz and colleagues (4) describe their investigation into the epidemiology of IE in North Carolina between 2007 and 2017. Using a statewide

**Corresponding Author:** Alysse G. Wurcel, MD, MS, 136 Harrison Avenue, M and V Building, Room 234, Boston, MA 02111; awurcel@tuftsmedicalcenter.org.

**Disclosures:** Author has disclosed no conflicts of interest.Form can be viewed at www.acponline.org/authors/icmje/ConflictOfInterestForms.do?msNum=M18-3026.

hospital discharge database, they found a staggering 12-fold increase in drug use-associated IE (DUA-IE) and a 13-fold increase in DUA-IE hospitalizations with valve surgery. Similar increases were not seen in the comparison group, which comprised persons with endocarditis but without drug use disorder. In 2017, DUA-IE accounted for almost half of endocarditis valve surgeries. Consistent with previous reports of changing demographic characteristics, most cases occurred in white, female, young persons (median age, 33 years). Less than half the cases affected only the tricuspid valve, confirming shifts in disease pathophysiology.

A 2018 review of endocarditis management considerations listed injection drug use as a risk factor but did not mention the importance of addressing the underlying substance use disorder during hospitalization (5). The hospital-associated characteristics of persons admitted with DUA-IE in this study effectively demonstrate why increased prioritization of substance use disorder during and after hospitalization is urgently needed. About 1 in 10 of the hospitalizations ended with a discharge against medical advice (DAMA). Not only are DAMAs stressful for patients and clinicians, they also may lead to abrupt discontinuation of treatment, disease progression, and death. New data are available that support fewer DAMAs and fewer readmissions among patients hospitalized for infections who receive addiction medicine counseling (6). Clinicians trained in addiction medicine are key partners in treating DUA-IE and need to be involved soon after infected patients are admitted. Initiating medical treatment for substance use disorder during hospitalization is acceptable, feasible, and sustainable after discharge (7).

The length of stay for persons with DUA-IE-a median of 11 days without surgery and 27 days with surgery-reflects the current system’s barriers to treating substance use disorder and IE after the acute illness is stabilized. Advances in outpatient parenteral antibiotic therapy have effectively reduced hospital costs and freed hospital beds for patients who are critically ill. Across the United States, the ability to provide postdischarge intravenous antibiotic therapy on an outpatient basis is limited. Physicians, allied health professionals (including visiting nurses), and rehabilitation staff have voiced several concerns, including that an indwelling intravenous line will facilitate injection drug use and be a “liability” if the patient gets a new infection or overdoses and that persons with a history of substance use cannot reliably administer antibiotics. Of note, no evidence exists to support these concerns. On the contrary, a 2018 review of the literature by Suzuki and colleagues (8) found that 72% of PWID completed antibiotic treatment, a percentage similar to that reported for persons who did not use drugs. Evidence—not anecdotes—should drive decisions on how best to provide antibiotics to PWID.

Largely as a result of the length of stay for patients with DUA-IE, their hospital charges far exceed those of persons with IE not associated with drug use. The limited opportunities for intravenous antibiotic infusion after hospitalization has renewed interest in re-evaluating the current dogma demanding 6 weeks of intravenous treatment. Evidence supports short-course treatment as an option for right-sided endocarditis due to S *aureus* in PWID (9). A recent randomized trial showed that partial oral antibiotic treatment was noninferior to full-course intravenous therapy; however, the study did not include many PWID or patients with methicillin-resistant S *aureus* (10). Long-acting injectable antibiotics are being used

increasingly for cases in which outpatient intravenous is not possible. Being mindful of DAMA and suboptimal posthospitalization treatment options, many of us in the infectious diseases community have been using these alternative treatment strategies with successful outcomes. Published research, even at the case-study level, might provide more evidence that long-term intravenous antibiotics are unnecessary.

In the midst of the 1930s malaria outbreak, the population at risk started to cut heroin with quinine to prevent malaria infection (1). They saw a threat and developed a strategy to effectively reduce it. The field is open for innovative patient-centered research on how to prevent endocarditis and provide equitable, evidence-based treatment focusing not only on the microbe but on the underlying substance use disorder. Action is urgently needed to understand and improve the cascade of care for persons with DUA-IE.

## Acknowledgments

**Grant Support:** By National Institutes of Health grants 1KL2TR002545-01 and 1R25DA037190-01.

## References

1. Most H Falciparum malaria among drug addicts-epidemiologic studies. Am J Public Health Nations Health. 1940;30:403–10. [PMID: ] [PubMed: 18015207]
2. Mathew J, Addai T, Anand A, Morrobel A, Maheshwari P, Freels S. Clinical features, site of involvement, bacteriologic findings, and outcome of infective endocarditis in intravenous drug users. Arch Intern Med. 1995;155:1641–8. [PMID: ] [PubMed: 7618988]
3. Wurcel AG, Anderson JE, Chui KK, Skinner S, Knox TA, Snydman DR, et al. Increasing infectious endocarditis admissions among young people who inject drugs. Open Forum Infect Dis. 2016;3: ofw157 [PMID: ] [PubMed: 27800528]
4. Schranz AJ, Fleischauer A, Chu VH, Wu LT, Rosen DL. Trends in drug use-associated infective endocarditis and heart valve surgery, 2007 to 2017: a study of statewide discharge data. Ann Intern Med. 2018 [Epub ahead of print]. doi:10.7326/M18-2124
5. Wang A, Gaca JG, Chu VH. Management considerations in infective endocarditis: a review. JAMA. 2018;320:72–83. [PMID: ] doi:10.1001/jama.2018.7596 [PubMed: 29971402]
6. Marks LR, Munigala S, Warren DK, Liang SY, Schwarz ES, Durkin MJ. Addiction medicine consultations reduce readmission rates for patients with serious infections from opioid use disorder. Clin Infect Dis. 2018 [PMID: ] doi:10.1093/cid/ciy924 [PubMed: 30357363]
7. Trowbridge P, Weinstein ZM, Kerensky T, Roy P, Regan D, Samet JH, et al. Addiction consultation services - Linking hospitalized patients to outpatient addiction treatment. J Subst Abuse Treat. 2017; 79:1–5. [PMID: ] doi:10.1016/j.jsat.2017.05.007 [PubMed: 28673521]
8. Suzuki J, Johnson J, Montgomery M, Hayden M, Price C. Outpatient parenteral antimicrobial therapy among people who inject drugs: a review of the literature. Open Forum Infect Dis. 2018;5: ofy194 [PMID: ] doi:10.1093/ofid/ofy194 [PubMed: 30211247]
9. DiNubile MJ. Short-course antibiotic therapy for right-sided endocarditis caused by Staphylococcus aureus in injection drug users. Ann Intern Med. 1994;121:873–6. [PMID: [PubMed: 7978701]
10. Iversen K, Ihlemann N, Gill SU, Madsen T, Elming H, Jensen KT, et al. Partial oral versus intravenous antibiotic treatment of endocarditis. N Engl J Med. 2018 [PMID: ] doi:10.1056/NEJMoa1808312 [PubMed: 30152252]