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## Injection Drug Use, Mortality, and the AIDS Epidemic

Long before the AIDS epidemic, injection drug use was known to be associated with a substantially increased risk of morbidity and mortality.<sup>1-4</sup> Numerous published studies of mortality among injection drug users documented increased death rates, in some instances exceeding ten times the expected rates for age-matched non-drug-using populations.<sup>3,5-8</sup> Deaths among drug users were found mostly to result from substance abuse itself (e.g., drug overdose, alcoholic cirrhosis), from violence or unintentional accidents associated with substance abuse, or from infectious complications related to the mode of drug administration (e.g., hepatitis, endocarditis, sepsis).<sup>1-11</sup> In most studies from the pre-AIDS era, drug overdose, violent trauma, and complications of alcoholism accounted for at least 60% of the deaths observed in drug-using populations, with infectious causes and non-drug-related conditions contributing the remainder.<sup>1-11</sup>

With the advent of AIDS, injection drug use has become a critical element in HIV transmission; high levels of HIV infection have been documented among drug users in North America, Europe, and more recently in regions of the developing world, including South America and Southeast Asia.<sup>12-15</sup> In parts of the northeastern United States and southern Europe, injection drug users now constitute the majority of newly reported AIDS cases, and an increasing burden of AIDS-related mortality among drug users has been seen in these areas.<sup>16-18</sup> In addition to recorded AIDS deaths, studies in several countries have also documented that HIV-infected drug users are at increased risk of morbidity—and in some cases, mortality—from non-AIDS-defining ill-

nesses such as severe bacterial infections and pulmonary tuberculosis.<sup>19-27</sup>

The widespread introduction of a lethal bloodborne infection, with its long latent period, virtually inexorable progression to severe disease, and the absence of sustained protective immunity following infection, is a development without precedent in recent memory. As AIDS receives its rightful attention as an important phenomenon among drug users, one should, however, not lose sight of the fact that drug abuse itself is a major cause of premature mortality among young adults in many societies.

Indeed, a recent analysis from the National Institute on Drug Abuse indicated that as AIDS deaths among drug users in the United States increased in the 1980s, the proportion of deaths attributed to drug abuse on death certificates as an underlying cause decreased slightly, a pattern which disappears when codings for multiple causes of death are taken into account.<sup>28</sup> This suggests that as AIDS and HIV-related disease begin to be expressed in drug-using populations, some of the effects of drug abuse on mortality may be underestimated by existing surveillance systems, unless one considers multiple causes of death. This observation has important implications for standards of collection, coding, and analysis of mortality data used for vital statistics and public health surveillance.

The importance of drug abuse, alcoholism, and serious bacterial infections in addition to AIDS itself as causes of death among injection drug users is well demonstrated in the study by Perucci et al. in

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**Editor's Note.** See related article by Perucci et al. on page 1307 of this issue.

this issue of the journal.<sup>29</sup> In this simple but elegant study, the authors defined a historical cohort of 4200 injection drug users enrolled in methadone treatment centers in Rome between 1980 and 1988, and then identified deaths occurring in this population during the same time interval through cross-checks with local vital records data and a national mortality registry. Overall and cause-specific mortality rates were calculated for the sample, on the basis of length of follow-up time since enrollment in the methadone centers. An increase in overall and AIDS-specific mortality was noted by the end of the study period in 1988, with an increase in the last 2 years in deaths from drug overdose (which remained the leading cause of death), AIDS, and other causes, including non-AIDS-defining infectious diseases. The standardized mortality ratio (SMR) for all-cause mortality in this population was 10.10; in addition to deaths from overdose and AIDS, increased SMRs were seen for neoplasms, endocarditis, other heart disease, pneumonia, cirrhosis, trauma, and suicide.

Italy, along with Spain, is among the European countries with the highest number of AIDS cases among injection drug users; and, indeed, drug users constitute the majority of cases in these two countries.<sup>18</sup> Drug use surveillance data suggest that southern Europe was the site of a significant increase in heroin use beginning in the late 1970s, in the period immediately preceding the presumed introduction of HIV into vulnerable populations in that region.<sup>30</sup> One might speculate, as has been done for parts of northern Great Britain,<sup>24</sup> that a burgeoning epidemic of injection drug use, which coincided with the entry of HIV into groups of high-risk drug users, contributed to the rapid spread of HIV among drug injectors in these areas. Although high levels of HIV infection have been noted since the early to mid-1980s in certain populations of European drug users, the pattern of European AIDS cases suggests that the course of the epidemic in drug users there is several years delayed behind that observed in the United States, where large numbers of drug users in the northeast appear to have become infected starting in the late 1970s.<sup>18,31-33</sup>

In the United States, investigators at the Centers for Disease Control have demonstrated that from the early 1980s, states with high AIDS incidence rates also had a parallel increase in deaths from pneumonia, tuberculosis, sepsis, and drug abuse-related causes in young adult populations.<sup>34</sup> Other observations from the mid-

1980s in New York City have shown an increase in HIV-related morbidity and mortality in drug users there, especially from bacterial infections and tuberculosis.<sup>19-23</sup> These studies have now been complemented by studies such as this one by Perucci et al. as well as by reports from Milan, Edinburgh, and Amsterdam, which together suggest that the full spectrum of HIV-related disease in drug users may be underestimated by AIDS surveillance data alone.<sup>24-27,29</sup>

Perucci et al. did not have information regarding the HIV infection status of their study subjects and were thus unable to examine the relationship between HIV and their cause-specific mortality findings. It is of interest, however, that the observation of increased mortality from malignancies in their population supports the findings of other recent studies among HIV-infected drug users in Italy, in which the occurrence of solid neoplasms and other non-AIDS-defining malignancies has been linked to HIV infection.<sup>35,36</sup> As also speculated by Perucci et al., these studies suggest that HIV infection, perhaps in conjunction with the heavy use of tobacco and alcohol, may be a risk factor for the development of certain forms of cancer besides those included in the existing AIDS case definitions.<sup>37</sup> In addition, the presence of human T-lymphotropic retroviruses types I and II (HTLV-I/II) has recently been documented in groups of Italian drug users.<sup>38</sup> Although not yet reported to be a cause of significant morbidity or mortality there, this finding may have clinical consequences in light of recent United States reports, suggests that HTLV-I/II infection may be a risk factor for rapid HIV disease progression and death in drug users coinfecting with HIV.<sup>39,40</sup>

A final point of clinical and public health interest concerns the relationship between treatment for substance abuse and the AIDS epidemic. Perucci and colleagues did not present complete data regarding the duration of drug treatment or the relationship between in-treatment and out-of-treatment mortality for their cohort. They do note, however, that low-dose methadone maintenance was the standard of practice for the treatment centers in which most patients were enrolled. Recent data on the positive correlation between methadone dosage level and retention in treatment, and between retention in treatment and reduced risk of AIDS-related mortality, disease progression, and HIV transmission behaviors, suggest that effective and ongoing treat-

ment for drug abuse can play a key role in the overall medical and public health response to the AIDS epidemic.<sup>24,41-46</sup> With the continuing emergence of HIV-specific therapies and prophylactic regimens,<sup>47</sup> it will become increasingly important to engage HIV-infected drug users in comprehensive systems of care, addressing both medical and drug treatment needs. The fact that, at least in the United States, active drug abusers continue to outnumber treatment slots<sup>48</sup> suggests that the system must continue to develop greater treatment capacity and effectiveness in the face of a growing need for services. Just as the emphasis on AIDS-related mortality in drug users must not obscure the important health effects of drug use itself, so too must any public health strategy regarding AIDS incorporate adequate mechanisms for identifying, treating, and preventing substance abuse if we are to be effective in confronting the connected phenomena of AIDS and drug abuse. □

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