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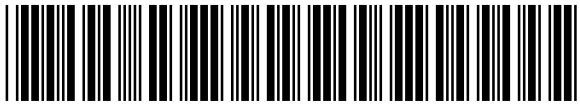

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Emerging infectious diseases and the injection of illicit psychoactive drugs

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The HIV/AIDS epidemic and the outbreak of Ebola virus in Zaire have focused much lay and scientific attention on the problem of emerging diseases in a world with increasing international travel [1,2]. The World Health Organization recently established a new Division of Emerging Viral and Bacterial Diseases Surveillance and Control, and the US National Institutes of Health recently created a Working Group on Emerging Infectious Diseases. In this paper, we review current information on the possible roles of the injection of illicit drugs in the emergence and reemergence of infectious diseases. The terms *emerging* and *re-emerging* infectious diseases have been frequently used without clear definitions. For the purposes of this paper, we include consideration of infectious agents that are 1) new as human pathogens; 2) "old" human pathogens but spreading beyond their traditional geographic areas; 3) new strains of "old" pathogens, particularly drug-resistant strains; and 4) pathogens reemerging as public health problems after decades of declining incidence.

In estimating the potential spread of emerging infectious diseases, it is critical to consider the complex interactions among underlying environmental and social ecologic factors and agent factors such as latency and virulence [3]. Diseases such as classic *Vibrio cholerae* and Ebola virus infection rapidly incapacitate the host, which severely limits the host's ability to transmit to others and the geographic spread of the agent. In contrast, infections that produce a long "healthy" carrier state are more likely to diffuse broadly, because infected persons who are mobile and can travel outside their communities will contact a greater number of potentially susceptible individuals. In addition, their healthy appearance would not deter others from casual or intimate contact. Long-latent infections that culminate in virulent disease are of greatest importance in terms of their individual, social, and economic costs. Many infectious diseases that produce long carrier states and end in severe illness are transmitted through blood-to-blood contact.

The spread of illicit psychoactive drug injection—when accompanied by sharing of drug injection equipment—may provide a globally important ecologic niche for emerging blood-borne infectious agents. Prior to an episode of intravenous drug injection, an injecting drug user typically draws blood into the syringe to determine if a vein has been hit. Multiperson use of the equipment for illicit drug injection is thus a relatively efficient mechanism for transmission of blood-borne viruses among injecting drug users.

Not only is multiperson use (or "sharing") of injection equipment a relatively efficient method of transmission, spread of blood-borne infectious agents can occur with extreme rapidity in populations of injecting drug users. Thus the timing of public health interventions is likely to be critical. As discussed below, interventions implemented before an infectious agent has become well established in a population of injecting drug users are much more likely to be effective than are interventions implemented after an infectious agent has become well established within the population.

As noted in Table 1, illicit drug injection has now been reported in 121 different countries. This is a substantial increase over the 80 countries that were known to have injecting drug use as of 1989 [4]. There are now an estimated 5 million persons throughout the world who inject illicit drugs [5], and this number is probably growing rapidly. The international diffusion of injecting drug use includes spread to geographically remote areas—such as South American and Asian rainforests—where local inhabitants may now be having more frequent contact with animal reservoirs for emerging diseases.

There is still much to be learned about the international diffusion of illicit drug injection. The rapid growth in the use of illicit psychoactive drugs over the past several decades needs to be understood in conjunction with at least the following factors.

Table 1. Countries and territories with injecting drug use and HIV infection among injecting drug users by December 1995

Americas
Argentina,* Bahamas,* Bermuda, Bolivia, Brazil,* Canada,* Chile,* Colombia,* Costa Rica,* Dominican Republic,* Ecuador,* El Salvador,* Guatemala, Haiti, Honduras,* Jamaica, Mexico,* Nicaragua,* Panama,* Paraguay,* Puerto Rico,* Surinam, Uruguay,* United States of America,* Venezuela*
Europe
Albania, Austria,* Belarus,* Belgium,* Boznia-Herzegovina, Bulgaria,* Croatia,* Czech Republic,* Denmark,* Estonia, Finland,* France,* Germany,* Greece,* Hungary,* Iceland,* Ireland,* Italy,* Latvia,* Lithuania, Luxembourg,* Macedonia, Malta,* Moldova, Monaco,* Netherlands,* Norway,* Poland,* Portugal,* Romania, Russia, San Marino,* Slovak Republic, Slovenia,* Spain,* Sweden,* Switzerland,* Turkey,* Ukraine,* United Kingdom,* Yugoslavia*
Africa
Cote d'Ivoire, Egypt,* Gabon, Ghana, Mauritius,* Morocco,* Nigeria, Senegal, South Africa, Tanzania, Tunisia, Uganda, Zambia
Asia
Azerbaijan, Bahrein,* Bangladesh, Brunei,* Cambodia,* China,* Georgia, Hong Kong,* India,* Indonesia,* Iran, Iraq, Israel,* Japan,* Jordan, Kazakhstan, Kirgystan, Korea, Kuwait, Laos,* Macao,* Malaysia,* Myanmar,* Nepal,* Oman, Pakistan,* Philippines,* Saudi Arabia, Singapore,* Sri Lanka,* Sudan, Syria,* Taiwan, Thailand,* Turkmenistan, Vietnam*
Oceania
Australia,* Fiji,* French Polynesia,* Guam,* New Caledonia,* New Zealand*

*Countries reporting injecting drug users with HIV infection.

1. In addition to the increasing use of illicit psychoactive drugs, there also has been substantial international growth in the use of licit psychoactive drugs. Use of nicotine and alcohol has spread to many areas of the world where these psychoactive drugs are not part of the traditional culture [6–8]. And there has been international growth in the medical use of psychoactive drugs such as tranquilizers, analgesics, and stimulants [9].

2. Injecting produces a strong drug effect due to the rapid increase in the concentration of the drug in the brain. Because almost all of the drug is actually delivered to the brain, injecting is also highly cost-efficient. On these grounds, intravenous injection can be considered a technologically superior method of psychoactive drug administration. Inexpensive technologic advances tend to disperse widely and are very difficult (though not impossible) to reverse [10].

3. The very large profit margins possible in the sale of illicit addicting substances also mean that substantial profits can be made by selling these drugs, even to "poor" people. The large profit margins from selling illicit drugs in industrialized countries and the economies of scale in the production and distribution of psychoactive drugs for illicit use permit the development of new markets in developing countries.

4. Contrary to popular stereotypes, many drug injectors do travel, including internationally [11]. International drug tourism [12] has been noted, but has not yet been well studied. Additionally, incarceration of injecting drug users from different geographic areas may also contribute to the spread of blood-borne viruses among injecting drug users [13].

Although it is probably possible to improve current efforts to reduce the supplies of illicit psychoactive drugs, the effectiveness of such efforts is likely to vary across time and place. Public health officials should therefore plan for further worldwide increases in illicit psychoactive drug injection and the potential for severe public health consequences, including transmission of many blood-borne pathogens.

HIV-1

HIV-1 is the prototypical emerging virus. HIV-1 infection has been reported among drug injectors in 81 different countries (Table 1), a substantial increase over the 52 countries known to have HIV-1 infection among injecting drug users in 1993 [8]. HIV-1 appears to have spread along drug distribution routes in Southeast Asia [14] and South America [15].

In some local populations of injecting drug users, HIV-1 infection has reached very high prevalence levels, with from 40% to more than 80% of local drug injectors infected. In some cases, these high seroprevalence levels have been reached within a year or two after introduction of HIV-1 into the local injecting drug user population [16]. Factors associated with rapid transmission of HIV-1 among injecting drug users include a lack of awareness of HIV/AIDS as a local problem, scarcity of sterile injection equipment, and the prevalence of mechanisms for rapid, efficient mixing among injecting drug users sharing injection equipment. (*Rapid mixing* refers to a high number of sharing partners within a short time; *efficient mixing* refers to sharing across subgroups within a population.) Drug injections in "shooting galleries" (where injection equipment is rented to successive users), injections with dealers' "works" (injection equipment owned by a drug seller who lends it to successive customers), injections by "hit men" (who are paid to inject others), and injections in prisons all provide occasions for rapid, efficient mixing within drug injector populations.

HIV-1 is important not only because of the specific opportunistic infections associated with it, but also because it can accelerate other infectious disease processes. This can

then lead to the emergence or reemergence of the other infectious agents, as in the case of tuberculosis.

HEPATITIS-ASSOCIATED VIRUSES

Injecting drug users are at high risk for a number of viral infections associated with hepatitis illness. Contamination of drug supplies can transmit hepatitis A virus efficiently and the sharing of injection equipment can transmit hepatitis B virus and a number of viruses previously classified as causing non-A non-B hepatitis. In recent years, some of these non-A non-B hepatitis agents have been identified, including hepatitis C virus and the hepatitis G viruses.

Hepatitis C virus may be a relatively recent human pathogen. Like many other RNA viruses, hepatitis C has a high rate of mutation. Using measurements of the rate of nucleotide change over relatively short periods of time, it has been estimated that the major genotypes of hepatitis C virus diverged as recently as 100 to 200 years ago [17]. Although the timing of the first human infection with hepatitis C virus remains speculative, hepatitis C virus can be considered as a current example of the introduction of an emerging infectious agent into populations of injection drug users without (until very recently) either awareness of the problem or attempts to control its spread.

Although there has been much less research on hepatitis C virus epidemiology than on HIV-1 among injecting drug users, hepatitis C virus is probably even more widespread among injecting drug users than is HIV-1. Hepatitis C virus has been reported among injecting drug users in North America, Europe, Australia, and Asia (Hagan *et al.*, Paper presented at the Sixth North American Syringe Exchange Network Conference, San Juan, Puerto Rico, 1995). It is very unusual to find hepatitis C virus antibody prevalence levels under 40% among any local population of injecting drug users, and anti–hepatitis C virus prevalence rates of 90% and higher are common among persons who have injected for 5 or more years. Hepatitis C virus serves as a prototype pathogen favored for widespread rapid transmission among injecting drug users, because infection results in an asymptomatic carrier state of perhaps 20 years' duration, and also because it is almost exclusively transmitted by parenteral contact.

Present estimates suggest that the majority of persons infected with hepatitis C virus will develop chronic liver disease; approximately one fifth of those with chronic disease will develop cirrhosis and approximately one quarter will develop hepatocellularcarcinoma [18]. Given the possibilities of multiple infections with different strains of hepatitis C virus among drug injectors and of possible interactions with HIV-1, the disease burden of hepatitis C virus infection among injecting drug users may be much greater than that of the general population.

Another blood-borne hepatitis virus has recently been described and designated hepatitis GB virus C [19–24]. Hepatitis GB virus C is an RNA virus with a nucleotide substitution rate similar to hepatitis C virus; infection also tends to be persistent [20]. Hepatitis GB virus C has been found in injecting drug users and other groups with blood exposure and appears to have a global distribution. Its relationship to chronic hepatitis is unclear, but it has been associated with fulminant disease. It appears that hepatitis GB virus C is a newly recognized pathogen. The degree of its penetration into injecting drug user communities and its importance relative to hepatitis B virus and hepatitis C virus require further study.

MALARIA

Drug injectors were once considered to be at relatively high risk for malaria [25]. The first known outbreak of malaria spread through sharing of injection equipment occurred in Cairo in the late 1920s [26]. Outbreaks occurred in the United States in the 1930s [27] and in the 1940s [28]. Friedman *et al.* [29] described an outbreak of malaria among a group of drug addicts in Bakersfield, California, and believe that it was probably transmitted by a Vietnam veteran who had just returned to the United States.

More recently, outbreaks of malaria occurred among drug injectors in Brazil [30,31]. These outbreaks appear to be related to internal migration between the developing areas of the centerwest and south and southeast (where malaria has been very rare). The initial cases apparently became infected in the centerwest and then spread the disease to fellow drug injectors after returning to cities in the south and southeast. The number of cases in these outbreaks was modest (the total was less than 200), but these recent outbreaks in Brazil do illustrate the potential of travel among injecting drug users to facilitate the possible reemergence of malaria.

TUBERCULOSIS

Tuberculosis may be considered a possible prototype reemerging infectious disease among injecting drug users and their personal contacts. Transmission of tuberculosis is air-borne, not blood-borne, but there are important interactions between tuberculosis and HIV-1 [32]. HIV-1 infection greatly increases the probability that persons infected with tuberculosis will develop active disease. Reciprocally, tuberculosis may accelerate the course of HIV disease [33]. The HIV epidemic has had a major impact on the global epidemiology of tuberculosis, causing marked increases in tuberculosis case rates in several countries [34].

The introduction of HIV into injecting drug user communities with high background rates of tuberculosis infection or with prevalent tuberculosis cases has resulted in outbreaks of tuberculosis due to HIV-induced increases in the reactivation of latent infection and to acceleration of the progression to primary disease after exposure [32,34]. Such outbreaks have resulted in the transmission of tuberculosis within social networks of injecting drug users, within institutional settings in which injecting drug users congregate (hospitals, prisons, drug treatment facilities), and from injecting drug users to their non–drug injecting community contacts and health care workers [35]. Travel between injecting drug user communities may contribute to the transcontinental and intercontinental transmission of tuberculosis, including the dissemination of multidrug-resistant strains [36,37]. Cases due to a multidrug resistant tuberculosis strain prevalent in New York City have been documented in several major US cities and in Paris [37,38].

Intravenous drug users are at risk for nonadherence to tuberculosis-preventive therapy and to treatment of active disease [32,39]. Nonadherence to preventive therapy results in an increased likelihood for developing clinical tuberculosis, and nonadherence to treatment for active disease increases the risks of treatment failure, relapse, and, of particular importance, the risk of developing multidrug-resistant strains of tuberculosis.

TRANSMISSION FROM INTRAVENOUS DRUG USERS TO NON–DRUG INJECTORS

Injecting drug users may have thus become an extremely important ecologic niche for emerging blood-borne infectious agents that produce chronic carrier states. These diseases are not likely to remain confined among injecting drug users. Both sexual and perinatal transmission from injecting drug users to others is almost certain to occur, although with different efficiencies for different agents [40]. Moreover, many female and some male injecting drug users engage in sex work to support their drug addiction, which increases the likelihood for sexual transmission of some agents. Healthcare settings are another situation in which transmission of blood-borne viruses from injecting drug users to others will sometimes occur. Implementation of "universal precautions" against infectious agents would greatly reduce the possibilities of such transmission, but universal precautions have not yet been implemented in most healthcare settings throughout the world. Interactions between HIV-1 and other infectious diseases such as tuberculosis may also contribute to the reemergence of air-borne infectious diseases.

POLITICAL RESPONSES

From our observations over the past 15 years, we propose the following classification system to describe political responses to the international spread of injecting drug use and the problems of emerging and reemerging diseases among drug injectors. The classification system is proposed as an ideal type, and not as a description of the response in any particular country.

Denial

Many political leaders throughout the world simply do not believe that the injection of illicit psychoactive drugs will ever occur in their communities. Noninjecting drug use may be common in these areas, but the leaders do not see the potential for shifts from noninjecting to injecting drug use. They believe that injecting drug use is so foreign to their cultural traditions that it would never be adopted in their communities, and that injecting drug use is a problem only in the rich, decadent, industrialized nations.

These countries at risk for injecting drug use belong to the Single Convention of Narcotics (the primary international treaty governing illicit psychoactive drugs) and often have strict laws against injecting drug use, but are not expecting a problem to develop. They are unprepared for both the health problems that occur with the development of injecting drug use and the social and crime problems that develop as part of large-scale illicit drug distribution.

Law enforcement suppression

After a substantial illicit drug injection problem has developed in an area where injecting drug use did not exist previously, the most common political response is an attempt to eradicate the problem through law enforcement. Drug injectors are often incarcerated and there may be very severe penalties for drug distribution. We are not aware of any assessment of the extent to which strict law enforcement efforts can limit the spread of illicit drug injection. Incarceration certainly is not an effective treatment for addiction, however, so the demand for the illicit drugs will almost undoubtedly continue despite law enforcement efforts against drug users. The analysis by Musto [41] of illicit drug epidemics suggests that it is community experience of the harmful effects of excessive drug use—and not law enforcement efforts—that leads to declines in the use of psychoactive drugs.

Although law enforcement efforts against drug users may or may not lead to reduction in illicit drug use, it is clear that such law enforcement efforts can help set the conditions for rapid transmission of blood-

borne pathogens among injecting drug users. Law enforcement efforts may make it very difficult for injecting drug users to obtain and use sterile injection equipment (for example, by requiring prescriptions for purchasing injection equipment or criminalizing the possession of narcotics paraphernalia [42]. Even where obtaining and possessing injection equipment is legal, drug injectors may not carry equipment with them for fear of becoming known to the police and then being subjected to other charges of possible mistreatment. Additionally, severe laws against drug users help create alienation between drug users and health care workers, reducing the likelihood of effective prevention and care for diseases associated with injecting drug use.

Coping

Although there is little evidence that the denial and law enforcement suppression responses reduce the spread of diseases among injecting drug users, there are strong data showing that other public health responses can dramatically reduce the transmission of many diseases among injecting drug users. We use the term *coping* to describe these responses in that they are predicated on two assumptions: 1) that once injecting drug use has become well established in a community, it is unrealistic to expect to eliminate the problem; and 2) that it is imperative to reduce the individual and social harms associated with injecting drug use even if injecting drug use itself cannot be eliminated. Here we briefly describe four types of public health coping responses to the problems of injecting drug use and disease transmission among injecting drug users: drug abuse prevention programs; long-term, multiple-episode drug abuse treatment; community outreach; and provision of sterile injecting equipment.

Drug abuse prevention programs

There are numerous examples of programs that have reduced (though not eliminated) initiation into the use of psychoactive drugs [43–45]. Programs that attempt to frighten potential users away from drug use generally are not effective. The effective prevention programs generally include consideration of licit as well as illicit drugs, accurate information about drug effects, development of community norms against drug use, teaching social skills to resist peer pressure to use drugs, and they also address the developmental problems that can predispose youth to developing drug problems.

Long-term, multiple-episode drug abuse treatment

If properly implemented, drug abuse treatment can dramatically reduce illicit drug injection and thereby reduce the incidence of infectious diseases associated with illicit drug injection [46]. Methadone maintenance treatment for narcotic addiction in particular has been associated with reductions in HIV risk behavior and infection with HIV [47].

In order to effectively utilize drug abuse treatment, it is important to recognize the limitations of present forms of drug abuse treatment. Length of time in treatment has been found to be a consistently strong predictor of patients' doing well both while in drug abuse treatment and after leaving treatment [46]. Arbitrary limits on time in treatment are thus likely to be counterproductive. No single episode of treatment is likely to lead to complete abstinence from illicit drug use, thus treatment systems need to provide for multiple episodes of treatment for most drug addicts and will need to provide life-long treatment for some addicts.

An additional important aspect of drug abuse treatment is that it can provide opportunities for assessment of and care for infectious diseases. This can not only improve the health of the individual drug user, but can also reduce transmission to other drug users, to sexual partners, and for, tuberculosis, to community contacts.

Community outreach

Only a relatively modest percentage of drug users are in treatment at any point in time. Outreach programs that contact injecting drug users in the community can play a critical role in reducing the transmission of infectious diseases. Outreach programs have led to substantial reductions in HIV risk behavior among injecting drug users [48]. Outreach programs can also provide HIV counseling and testing and screening for tuberculosis and sexually transmitted diseases. Newer outreach models are now also providing primary medical care and directly observed preventive therapy for tuberculosis (Perlman *et al.*, Unpublished data.)

Community outreach programs have been staffed by current drug users, ex–drug users, street-knowledgeable local community members who have not used drugs, research anthropologists, social workers, and health care professionals. There is no one best category of outreach staff. Training of staff is certainly critical, but the most important aspect of outreach work is developing nonjudgmental and trusting relationships between the outreach workers and the drug users in the community.

Provision of sterile injection equipment

Providing good access to sterile injection equipment has led to dramatic reductions in HIV risk behavior and low rates of new HIV infections among injecting drug users in many cities throughout the world [49–51]. There is also evidence that good access to sterile injection equipment reduces transmission of hepatitis C virus among IDUs [51].

Sterile injection equipment can be provided through syringe exchange programs and pharmacy sales of injection equipment. These two methods have different strengths and weaknesses. Exchanges provide injection equipment at no cost to the user, provide opportunities for additional services, and provide for safe disposal of potentially contaminated injection equipment. Pharmacies have longer hours of operation and usually provide better geographic coverage. These two methods should be considered complementary. Access to sterile injection equipment should include the ability to possess the equipment without fear of arrest or harassment by police.

It is also very important to note that HIV prevention efforts including access to sterile injection equipment have been successful in developing countries. Injecting drug users have used syringes purchased at pharmacies to reduce HIV incidence in Bangkok [52]. There are also well-functioning syringe exchange programs in Kathmandu, Nepal (Maharjan *et al.*, Paper presented at the Tenth International Conference on AIDS, August 7–12, Yokohama, Japan, 1994), northern Thailand [53], and in Madras, India (Kumar, Personal communication).

Timing

It is a fundamental principle in the control of infectious diseases that control efforts are much more likely to be effective if they are begun when the prevalence of these diseases is low. Thus developing programs in anticipation of potential epidemics of emerging infectious diseases among injecting drug users is likely to be the best strategy for preventing epidemics of emerging infectious diseases among injecting drug users, their sexual partners, and—for some diseases—their community contacts.

CONCLUSIONS

The injection of illicit psychoactive drugs has now been reported in 118 different countries. Injecting drug use forms an important ecologic niche for the transmission of emerging and reemerging bloodborne infectious agents and for the transmission of other infectious agents, such as tuberculosis, that have significant interactions with HIV-related immunosuppression. Public health officials need to plan for the continued international diffusion of injecting drug use and the potential transmission of infectious agents among injecting drug users, their sexual partners, and community contacts. For many emerging and reemerging infectious diseases, protecting the health of the community as a whole will depend on protecting the health of injecting drug users.

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