Enigma of HIV Control - Modelling a Global Surveillance Network for HIV Infection

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Abstract

It seems control of HIV infection spread is lag behind research for new treatments, especially in developing countries. Intravenous drug use is a major risk factor for HIV infection. Addiction control is a reasonable measure for HIV transmission prevention. Implementing treatments for opiate dependence such as: training drug dependence side effects in schools, omitting behavioral and environmental addiction predispositions, organizations to assist addicted, HIV-infected infected patients to change their lifestyles, and teaching prevention and health maintenance, promoting access to diagnosis and treatment, and to remain in treatment is necessary. More definite protocols for screening and surveillance of at-risk groups by implementing ethical and legal codes, and also better supervision on addiction and harm reduction policies may decrease number of new victims. Estimating addiction patterns and prevalence of HIV infection in different situations may help to model prevention protocols. Lack of routine testing of at-risk populations, data registry screening programs and intervention strategies had lead to confronting HIV-infected subjects lately when presenting with co-morbidities such as advanced liver failure, tuberculosis and opportunistic diseases. It seems in developing countries more policy guidelines for testing, counseling and treatment, and modeling HIV control according to at-risk population such as in the injecting drug users, male homosexual context is needed.

Regarding transmission of HIV infection from undiagnosed cases or by those neglecting treatment to community, it is necessary that prevention methods, receive of appropriate prophylaxis, practical use of recommendations, harm reduction policies, adverse drug side effects, treatment failure, and drug resistance followed and supervised regularly in each country.

Keywords: HIV infection; Global prevalence; Transmission; Intravenous drug use

Introduction

According to 2011 estimates from UNAIDS, WHO and UNICEF around 30.6 million adults and 3.4 million children were living with HIV at the end of 2010. During 2010, some 2.7 million people became infected with HIV, including an estimated 390,000 children. Most of these children are babies born to women with HIV, who acquire the virus during pregnancy, labour or delivery, or through breast milk. Drugs are available to minimize the dangers of mother-to-child HIV transmission, but these are still often not reaching the places where they are most needed. The year also saw 1.8 million deaths from AIDS-related causes. The number of deaths peaked around 2005, and due to the expansion of antiretroviral therapy, it is estimated that 2.5 million AIDS-related deaths have been prevented since 1995 in low- and middle-income countries. By the end of 2009, the epidemic had left behind 16.6 million AIDS orphans, defined as those aged under 18 who have lost one or both parents to AIDS. Around half of people who acquire HIV become infected before they turn 25, and AIDS is the second most common cause of death among 20-24 year olds. The overwhelming majority of people with HIV live in low- and middle-income countries. Sub-Saharan Africa accounts for two-thirds of all infected people. South and South-East Asia has the second highest number of people living with HIV [1-4]. Low- to middle-income countries bear the overwhelming burden of the human immunodeficiency virus type 1 (HIV-1) epidemic in terms of the numbers of their citizens living with HIV/AIDS (acquired immunodeficiency syndrome) [5]. Around 1.5 million people in Russia, Eastern Europe and Central Asia were living with HIV at the end of 2010, with the region having a prevalence of 0.9 percent [3]. Since 2001, HIV prevalence in Russia, Eastern Europe and Central Asia has increased by 250 percent, making the region home to the world’s most rapidly expanding epidemic. In contrast, over the same period, prevalence in sub-Saharan Africa fell from 5.8 percent to 5 percent, and stabilised in South and Southeast Asia at 0.3 percent [3]. The rise of HIV in the region is closely linked with increasing rates of injecting drug use that developed in the mid-1990s during the socioeconomic crisis that followed the break-up of the Soviet Union. At this time, nearby Afghanistan became the world’s largest producer of opium, from which heroin is derived, and drug trafficking increased throughout the region. Initial outbreaks were detected in Ukraine, Russia, Belarus and Moldova [6]. The primary care visit provides an opportunity to screen patients for ongoing high-risk drug and sexual behaviors for transmitting HIV infection, routine screening and symptom-directed testing for and treatment of sexually transmitted diseases (STDs), as recommended by CDC [7].

Methods

A review of literature was performed in 2012 to summarize scientific

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reports on epidemiology and transmission of the HIV infection and its association with addiction. Search was performed on MEDLINE, EMBASE, PsycINFO databases, and other sources to identify published studies on social networks. Articles published during recent years (1989-2012) were searched by using the following key words: HIV infection, epidemiology, prevalence, transmission, hepatitis C, hepatitis B, addiction and vulnerability to addiction, injection drug users, and psychology. Exposure group specific information was searched by adding a risk factor name to the search.

**Examples of HIV infection trends**

**Africa**

In 2009, approximately 22.5 million Africans were living with HIV-1, with the worst affected region being southern Africa where about one-third of the world's HIV-infected people reside [4]. The epidemic in Africa is fueled by genetically diverse viral genotypes, which may differ in terms of pathogenicity and rates of transmission [8]. The social, economic, and political factors responsible for the widespread epidemic in southern Africa include poverty, poor social and health infrastructure, lack of education, political and social instability, the low status of women, and sexual violence, as well as lack of political commitment, slow control response, and ineffective preventive measures during critical periods of HIV epidemic in the region. There is no single factor that accounts for the high HIV prevalence observed in certain countries in Africa. Behavioral factors are likely to have contributed, including the number of casual sexual partners, condom usage, age of sexual debut, intergenerational sex, concurrency, and sexual networks [5,8,9-12].

**Asia**

In China, the proportion of MSM in the annual reported HIV cases increased from 12% in 2007 to 33% in 2009 [5,13]. Because of cultural and social pressures, many MSM in Asia are married or otherwise engaged with female partners so as to avoid social stigma and discrimination. For example, approximately one-quarter of the Chinese MSM are married [5,14], and ~30% of these individuals have sex with a steady female partner [5,15].

IDU is a major route of HIV-1 transmission in this region. Afghanistan and Myanmar are the world's largest opiate- and heroin-producing areas. Whereas one-third of the heroin produced in Afghanistan reaches Europe, one-quarter goes to Central Asia and the Russian Federation. The rest is trafficked to other South and Southeast Asia countries. Most of the heroin produced in Myanmar supplies the local and regional markets, including China, South and Southeast Asia, and Oceania [5].

**Latin America and the Caribbean**

The world's largest cocaine-producing area is located in the Andean region, covering Columbia, Peru, and Bolivia, and HIV transmission follows the drug-trafficking routes. High HIV prevalence were found in IDUs in Peru (9.8%-22.3%), Brazil (8%-65%), Argentina (14%-80%), and Uruguay (24%-76%) [5,16].

**Europe**

In a study of AIDS cases diagnosed by transmission group and geographical area, 2004-2010, heterosexual cases in West and then Men who have sex with men outnumber Injecting drug users, while in central Europe Men who have sex with men and then Heterosexual cases outnumber Injecting drug users, and in Eastern Europe Injecting drug users outnumber Heterosexual cases (Data not included from: West: Austria, Monaco, Sweden; East: Russia, Ukraine) [17].

**Data collection of populations at risk**

Voluntary blood donors, military solders, employment seekers, and periodic population-based sero-surveys may regard as representative of young population. Meanwhile the frequency of infection in this group likely is under-estimated.

Pregnant women were originally selected as a sentinel population for HIV surveillance as a way to monitor trends in a population group at low risk of infection. This population was selected because the coverage by prenatal clinics was high in most developing countries and because blood was already being drawn for other purposes [18-19].

Sentinel sites representing at high risk of HIV infection subjects are:

- Injection drug users (IDUs), is probably the most universally marginalized of all HIV-related behaviors, and it is also almost universally illegal. Recent estimates of the number of injection drug users in Russia, for example, vary by a factor of 10 [20].

Other at-risk population are: Drug treatment centres, sexually transmitted infections (STIs) clinics, female sex workers prisoners, men who have sex with men (MSM), Tuberculosis (TB) clinics, Hospital wards, refugees, truck drivers, and in some society's barbers.

In this group their off-springs, spouses, and all intimate contact subjects, detention centres personnel, and the clinics they referred should be screened.

**At-risk group for HIV infection and co-morbidities**

A review selected of a total of 215 studies, included 43,170 patients, depicted the following prevalence of transmission of drug-resistant HIV in rank order: North America (12.9%), Europe (10.9%), Latin America (6.3%), Africa (4.7%), and Asia (4.2%). Nucleoside reverse transcriptase inhibitor resistance declined over time in North America (p=0.03), Europe (p < 0.001), and Latin America (p < 0.001). The decline in nucleoside reverse transcriptase inhibitor resistance reflects the improvement of treatment regimens in resource-rich settings. In contrast the resistance prevalence increased in Asia (p=0.047) and Africa (p < 0.001). This can be explained by the antiretrovirals becoming more available during recent years in these continents. Nonnucleoside reverse transcriptase inhibitor resistance rose over time in North America (p < 0.001), Europe (p < 0.001), Latin America (p < 0.001), and Asia (p=0.01). Changes include the more wide-spread use of antiretroviral drugs in developing countries and the development of therapies from low-active mono-therapies to highly active antiretroviral regimens in the industrialized countries [21].

HCV co-infection with HIV ranges from 5% to more than 30%, depending on the overall prevalence of HIV in the area [22]. A study conducted in KwaZulu-Natal Province in South Africa where HIV is predominantly a sexually transmitted infection and injection drug use is rare in this region. The prevalence of HCV was 6.4% and that of HIV, 40.2%. There was a significantly higher prevalence of HCV among HIV infected patients as compared to HIV negative patients (13.4% vs. 1.73% respectively, P < 0.001). This study has found that hepatitis C co-infection is more common in HIV positive individuals and is associated with an increased mortality and renal morbidity [23-24]. In a study of 250 injecting drug users (IDUs) from a de-addiction centre, one hundred and forty-nine (59.6%) IDUs were positive for HIV antibody, 226 (90.4%) were positive for anti HCV antibody and
for care. Many co-infected individuals are in need of concurrent ART already developed clinically significant TB by the time they present many individuals in need of therapy initiate ART too late and have involved in HIV care. Despite expanding access to antiretroviral importance of TB diagnosis, treatment and prevention for clinicians The high burden of TB among HIV-infected individuals underlies the introduction of an antiretroviral treatment. However, when treating patients co-infected with TB and HIV, interactions between antiretroviral and membranoproliferative glomerulonephritis (MPGN) [31].

A study of 103 former heroin addicted adults on methadone maintenance therapy in the USA, most methadone-maintained subjects had at least one marker for viral hepatitis. A quarter of subjects had silent HBV infection, defined as the presence of HBV DNA in the absence of HBsAg. These subjects should be considered infectious and pose a public health risk [24,27].

In a study in Switzerland, 78.3% of the 1035 patients entering heroin-assisted treatment were HCVC positive, 53.3% were HBV positive, 41.2% were HAV positive and 12.6% were HBV positive [24,28]. In a study of 433 subjects among a whole population of 900 inmates in the Prison of Bologna, Italy, 147 (33.9%) were injection drug users (IDU) and 286 were not addicts (66.1%). 12.5% of inmates were HBV positive, 8.1% HBV positive and 31.1% HCV positive. In the prison of Bologna drug addiction is prevalent in Italian seropositive persons and it is often associated with HIV and HCV positivity [24,29]. A study conducted on a sample of 210 women from the Montreal detention center, showed that addicted inmates present earlier onsets of both drug use and criminal behaviors compared to other female inmates [24,30].

Renal disease is a complication of heroin addiction. Of 19 patients with serological evidence of HCV infection, 68.4% were found to have membranoproliferative glomerulonephritis (MPGN) [31].

Improved detection of alcohol consumption in the context of HCVC and opiate dependence would allow for earlier intervention in this population that is at particular risk of liver disease and fatal respiratory-depressed overdose [24,32].

Tuberculosis (TB) is the most frequent opportunistic infection in patients infected by the Human immunodeficiency virus (HIV). The mortality related to this co-infection can be reduced by the early introduction of an antiretroviral treatment. However, when treating subjects with TB and HIV, interactions between antiretroviral and tuberculosis treatments can be problematic; also, these patients may develop, under treatment, an immune reconstitution inflammatory syndrome (IRIS). This review aims to summarize the necessary therapeutic adjustments which should be performed when treating patients co-infected with TB and HIV, the most important interactions between HIV and TB treatments, and the medical management of the IRIS [33].

Globally, tuberculosis (TB) and HIV interact in deadly synergy. The high burden of TB among HIV-infected individuals underlies the importance of TB diagnosis, treatment and prevention for clinicians involved in HIV care. Despite expanding access to antiretroviral therapy (ART) to treat HIV infection in resource-limited settings, many individuals in need of therapy initiate ART too late and have already developed clinically significant TB by the time they present for care. Many co-infected individuals are in need of concurrent ART and anti-TB therapy, which dramatically improves survival, but also raises several management challenges, including drug interactions, shared drug toxicities and TB immune reconstitution inflammatory syndrome (IRIS). Due to the survival benefits of promptly initiating ART among all HIV-infected individuals, including those with TB, it is recommended that co-infected individuals receive treatment for both diseases, regardless of CD4+ cell count. We review current screening and treatment strategies for TB and HIV co-infection. Recent findings and ongoing studies will assist clinicians in managing the prevention and treatment of TB and HIV co-infection, which remains a major global health challenge [34].

Human immunodeficiency virus (HIV) associated tuberculosis (TB) remains a major global public health challenge, with an estimated 1.4 million patients worldwide. Co-infection with HIV leads to challenges in both the diagnosis and treatment of tuberculosis. Further, there has been an increase in rates of drug resistant tuberculosis, including multi-drug (MDR-TB) and extensively drug resistant TB (XDR-TB), which are difficult to treat and contribute to increased mortality. Because of the poor performance of sputum smear microscopy in HIV-infected patients, newer diagnostic tests are urgently required that are not only sensitive and specific but easy to use in remote and resource-constrained settings. The treatment of co-infected patients requires antituberculosis and antiretroviral drugs to be administered concomitantly; challenges include pill burden and patient compliance, drug interactions, overlapping toxic effects, and immune reconstitution inflammatory syndrome. Also important questions about the duration and schedule of anti-TB drug regimens and timing of antiretroviral therapy remain unanswered. From a programmatic point of view, screening of all HIV-infected persons for TB and vice-versa requires good co-ordination and communication between the TB and AIDS control programs. Linkage of co-infected patients to antiretroviral treatment centers is critical if early mortality is to be prevented. We present here an overview of existing diagnostic strategies, new tests in the pipeline and recommendations for treatment of patients with HIV-TB dual infection [35].

Detecting vulnerability to addiction

According to a study, high stress load in childhood and before puberty, but not in adulthood, was related to negative effect in all participants. In patients, high stress load was related to depressive and posttraumatic symptoms, severity of disorder, and the diagnoses of Major Depressive Disorder (MDD) and personality disorders (PD). Results support the hypothesis of stress-sensitive periods during development, which may interact with genetic and other vulnerability factors in their influence on the progress of psychiatric disorders [24,36]. Depression in older adults is a serious health problem with a poor prognosis [24,37].

Medications which bind to opioid receptors are increasingly being prescribed for the treatment of multiple and diverse chronic painful conditions. The psychological addiction that can occur with the use of these medications, abuse and diversion of these medications is a growing problem as the availability of these medications increases and this public health issue confounds their clinical utility [24,38]. Universal interventions have potential for public health impact by reducing some types of prescription drug misuse among adolescents and young adults [39]. Of 170 schools from seven countries (Austria, Belgium, Germany, Greece, Italy, Spain, Sweden) by European Drug Abuse Prevention trial (EU-Dap) study, 34.9% of students had smoked cigarettes, 24.7% had been drunk, and 8.9% had used cannabis at least once in life [24,40]. In the EU-Dap study of 7079 pupils 12-14 years
of age concluded school curricula based on a comprehensive social-influence model may delay progression to daily smoking and episodes of drunkenness [24,41]. Experimental trials of Project Towards No Drug Abuse (TND), a senior-high-school-based drug abuse prevention program is an effective drug and violence prevention program for older teens, at least for one-year follow-up [42].

In Germany each general practitioner who has completed an additional training in addiction medicine is allowed to prescribe substitution drugs to opioid dependent patients. Also, in the development of research on health care services, guidelines and the implementation of quality assurance measures, implementing substitution treatment with concomitant effects and treatment elements such as drug history-taking, dosage setting, co-use of other psychoactive substances (alcohol, benzodiazepines, cocaine), management of difficult patient populations, and integration into the social environment and psychosocial counseling programs adjuvant has been arranged successfully, there [24,43]. In a study of 26 former male inmates who had recently used drugs within correctional facilities in Vancouver, Canada showed the harms normally associated with drug addiction and injection drug use are exacerbated in prison. The scarcity of syringes has resulted in patterns of sharing amongst large numbers of persons. Continual reuse of scarce syringes poses serious health hazards and bleach distribution is an inadequate solution [24,46]. Harm reduction policies, such as needle exchange programs, injection centers, and substitution treatments, attempt to reduce the health and social damage associated with illegal drug use [24,47].

Harm reduction can be understood as "policies and programs which are designed to reduce the adverse consequences of mood altering substances without necessarily reducing their consumption"; it is consistent with the best traditions of both medicine and public health [24,48]. The success of harm reduction as a unifying concept will depend on its innovative application in both prohibitory and regulatory frameworks, and careful evaluation of its effectiveness in a variety of cultural contexts [47]. In the Western Pacific region, Malaysia has the second highest HIV prevalence after Vietnam among adult populations (0.62%) and the highest proportion of HIV cases resulting from injection drug use (76.3%). Malaysia has lagged behind in the treatment of drug addiction and related disorders, despite experiencing severe drug problems [48]. Methadone pharmacotherapy has been the most widely used treatment for opioid addiction in injection drug users. Methadone has adverse drug-drug interactions with many antiretroviral therapeutic agents that can contribute to nonadherence and poor clinical outcomes in this high-risk population. Buprenorphine has a significant pharmacokinetic interaction with efavirenz but no pharmacodynamic interaction; therefore, simultaneous administration of these drugs is not associated with opioid withdrawal, as has been observed with methadone [24,49].

Secondary syringe exchange (SSE) refers to the exchange of sterile syringes between injection drug users (IDUs). SSE-based networks should be used to improve public health interventions, while minimizing the potential risks associated with the practice of secondary exchange [50]. Network correlates of drug equipment sharing are multifactorial and include structural factors (network size, density, position, and turnover), compositional factors (network member characteristics, role and quality of relationships with members) and behavioural factors (injecting norms, patterns of drug use, severity of drug addiction) [51].

In a comparative study of a group of experimental and control subjects in Argentina, Brazil, Costa Rica, Japan, Jordan, Italy, Malaysia, Singapore and the United States of America (State of New York), and of the results of independent studies conducted in Sweden and the United Kingdom of Great Britain and Northern Ireland, a rather close association was found to exist between drug abuse, criminal behavior and social attitudes to such problems. The study encouraged the review, testing and implementation of alternative measures to penal sanctions, particularly with a view to creating a genuine therapeutic approach to correcting the deviant behavior of drug abusers [52]. According to a study, harm reduction programs (HRP) was associated with a lower incidence of HCV and HIV infection in ever-injecting drug users (DU), indicating that combined prevention measures, but not the use of needle exchange program (NEP) or methadone alone might contribute to the reduction of the spread of these infections [24,53].

In a study of assessing activity and coverage of needle and syringe programmes (NSP) in Central and Eastern Europe and Central Asia, results from 213 sites in 25 countries suggested that overall syringe coverage for the population in contact with NSP was 9.8%. Strategies to increase coverage that may go beyond NSP are urgently required [54,55].

Setting purposively selected opioid substitution treatment (OST) sites in Asia (China, Indonesia, Thailand), Eastern Europe (Lithuania, Poland, Ukraine), the Middle East (Iran) and Australia showed all countries demonstrated significant reductions in reported heroin and other illicit opioid use; HIV and other blood-borne virus exposure risk behaviors associated with injection drug users and criminal activity, and demonstrated substantial improvement in their physical and mental health and general wellbeing over the course of the study [56].

Implementing hospice behind bars has some unique challenges in addition to those inherent in hospice work. This series will provide an in-depth look at four hospice programs for inmates in the United States [42]. The synthetic opioids are not routinely assessed in many screening procedures. If a drug screen is positive, but the patient denies drug use, the laboratory should be asked to conduct a confirmatory test using gas chromatography/mass spectroscopy [24,57].

It has been estimated that the burden of illness associated with alcohol dependence is 5 times greater in wealthier countries, compared with less wealthy nations, and that in all cases this burden is significantly greater than the corresponding impact of all illicit drugs [58-59].

Conclusion

HIV surveillance is defined as a systematic data collection about occurrence, distribution, and trends in HIV infection and factors associated with its transmission.

Results of surveillance are used in practice to inform program decisions, judge the effectiveness of the national response, lobby for effective programs, and to provide accurate measures of trends and the absolute state of the epidemic [60].

In the early years of the epidemic, countries were encouraged to set up surveillance systems which had as a primary component AIDS case reporting systems, but also included HIV surveillance in some population groups [60-62].

Many of the developing countries developed and relied on sentinel systems to detect trends in HIV prevalence in groups with high-risk behavior as well as in the general population. This paper focuses on these sentinel surveillance systems. Second generation HIV surveillance aims to tailor surveillance systems to the needs of specific epidemic states [19,61,64]. Second generation systems use behavioral as well as biological data to increase the explanatory power of surveillance systems.
Our proposed HIV Surveillance Form.

Table 1: Our proposed HIV Surveillance Form.
in both predicting and tracking the course of the HIV epidemic in a given country. Within a larger monitoring and evaluation framework, however, data generated by regular surveillance systems can contribute to an understanding of the impact of the combined effect of the national response to HIV [60,63-66].

It is hoped that closer global cooperation from upstream basic research to downstream clinical trials will greatly speed better intervention and treatment strategies as well as the ultimate production of a successful AIDS vaccine [67-68].

In Table 1 our proposed surveillance form for recruitment and follow-up of HIV cases is depicted. In this table one may add other parameters of bheavourial surveillance as about the sexual and drug-injecting behaviours, number of sexual partners, condom use, number of syringe use during one month. Also to assess other characteristics of infected subjects such as occupation and socio-economic state, other infections such as inactive hepatitis B carrier, viral hepatitis B, hepatitis C, anti-HDV, infections and cancers related to immune deficiency state, pregnancy, breast feeding, cirrhosis, hemodialysis, organ transplanted, coagulopathy and other hematologic disorders, recent surgical/medical procedure and seek the possible source of infection and possible transmission. However, we believe informed consent of tested person without their permission in high risk group may be obtained by local ethical/legal rules. Anyway, data of tests, results of biologic and behavioral surveillances, subjects who need to be screened, and feedback of drug abuse/ correction centers/treatment follow-up/ and other referral consult centers for high risk group should be keep secret and just only be accessible by other medical centers with certain precautions.

Lack of routine testing of at-risk populations, data registry screening programs and intervention strategies had lead to confronting HIV-infected subjects lately when presenting with co-morbidities such as advanced liver failure, tuberculosis and opportunistic diseases. It seems in developing countries more policy guidelines for testing, counseling and treatment, and modeling HIV control according to at-risk population such as in the injecting drug users, male homosexual context is needed.

Regarding transmission of HIV infection from undiagnosed cases or by those neglecting treatment, it is necessary that prevention methods, receive of appropriate prophylaxis, practical use of recommendations, harm reduction policies, adjust treatment to changes in more dangerous drug use patterns, adverse drug side effects, treatment failure, and drug resistance followed and supervised regularly in each country. Track HIV infection trends, its biologic and behavioral pattern, implementing strategies according to certain mode of spread of infection, analysis of networking data by supervised epidemiologists are all necessary tools to control the infection.

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