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The Feasibility of HIV Vaccine Efficacy Trials among Russian Injection Drug Users

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Summary

IDU exposure remains a primary driver of the Russian HIV epidemic, and recent incidence data provide little evidence that this epidemic is slowing. While there are multiple important challenges that need to be further explored before starting vaccine trials, most importantly access to evidence-based drug treatment services for trial participants, the current context of high HIV incidence and low genetic diversity of HIV strains, suggests the need for intensified prevention strategies and supports the feasibility of mounting efficacy trials of HIV vaccines among IDUs in the Russian Federation.

Keywords

HIV; Injection Drug use; St. Petersburg; Molecular Epidemiology; Vaccines

Introduction

There are estimated to be over 13 million injection drug users (IDUs) worldwide, and IDU in many settings are at high risk for HIV-1 acquisition [1]. IDU risks have been the predominant mode of HIV-1 spread in much of the Former Soviet Union and explosive spread of HIV among IDUs was documented through 1998–2001 in several Russian cities [2;3]. Current estimates are that some 70–90% of HIV infections in the Russian Federation are attributable to injection drug use [4]

There is a growing consensus that a preventive HIV vaccine would be a key component in the global control of HIV spread [5]. Given the epidemiology of HIV in countries such as Russia, where parenteral exposure through IDU is the predominant mode of spread, it may be essential to investigate this route of transmission in HIV vaccine efficacy trials. If vaccine efficacy does differ by route of exposure, HIV vaccine candidates and strategies which have

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not been evaluated in the context of parenteral transmission could have limited utility in regions where this risk factor accounts for the majority of spread. One efficacy trial has been conducted in IDU, the Thai AIDSVAX trial among Bangkok IDU, but this remains an under-studied research domain. No efficacy trials with later-generation HIV vaccine candidates are currently underway among IDU.

The Russian Context

The HIV Prevention Trial Network (HPTN) of the U.S. NIH conducted a multi-site cohort preparedness trial among IDUs in 2 Chinese cities and in St. Petersburg, Russia. This trial in Russia, which was funded by a grant to the University of North Carolina and the Biomedical Center (BC) in St. Petersburg, enrolled 520 IDUs between March and December of 2002 and followed them through to 2004. This study demonstrated a baseline HIV prevalence of 30% among IDUs and a measured HIV-1 incidence of 4.5/100 person-years (95% CI 2.7–7.0)[6;7]. A more recent collaboration between the BC and the Johns Hopkins School of Public Health is a randomized controlled trial of the Russian IDU Peer Network HIV Prevention Intervention which prospectively followed 534 IDUs beginning in December of 2004. Though this study is still ongoing, preliminary analyses of available results have demonstrated an HIV incidence rate of 14/100 person-years (95% CI 8.5–22.1) among IDUs[8]. Finally, a study using the BED capture enzyme immunoassay for incidence rate estimation among 1031 IDUs between the years of 2004 to 2006, resulted in an estimate of HIV incidence rate of 17.5/100 person-years (95% CI 14.2–20.8)[9]. Given other reports of performance with this assay, this is likely to be an overestimate of incidence [10].

Molecular epidemiological studies have also characterized the dominant HIV strains among Russian IDUs[11;12]. One such study among 18 IDUs in 2002–2004 suggested a very homogenous distribution of virus in this population with 16/18 being infected with subtype A, the dominant subtype across Russia, and 2/18 infected with CRF03_AB, a recombinant strain originating in Kaliningrad[13]. A more recent study initiated in 2005 analyzed 44 IDUs from St. Petersburg and demonstrated that 100% were infected with subtype A. Furthermore, genetic diversity studies comparing the subtype A viruses isolated in 2002 and 2005 suggest that the sequences are relatively well conserved, only the *env* gene increased significantly in genetic diversity during this time period (3.7% vs. 2.1%) [14]. These data are confirmed by other HIV-1 molecular epidemiology investigations among IDUs in St. Petersburg in 1997–2006 which also demonstrate the predominance of subtype A and its low genetic diversity [15–17].

Site-Specific Challenges

There are many challenges in designing an effective HIV vaccine trial, particularly one implemented in a marginalized population such as IDUs. However, there are some challenges that are specific to the Russian context that need to be further explored and overcome before vaccine trials can proceed. UNAIDS has published a comprehensive guidance document outlining the specific ethical considerations when designing preventive HIV vaccine protocols[18]. One of the guidance points specifically refers to providing access to risk reduction counseling and evidence based preventive methods. In terms of IDU, evidence-based preventive measures include, but are not limited to, needle and syringe exchange, HAART availability for those who become infected during trials, and opioid substitution therapy. While both of the former are legal in Russia, substitution therapy currently is not. Methadone is explicitly prohibited and although others agents, such as buprenorphine, are not banned; they are not permitted for use in substitution therapy. Agents such as naltrexone are actively being used in Russia, though detoxification remains a

prerequisite for naltrexone prescription. This may diminish the acceptability of naltrexone among active injectors[19].

Conclusions

IDU exposure remains a primary driver of the Russian HIV epidemic, and recent incidence data provide little evidence that this epidemic is slowing. Studies of molecular epidemiology of the infecting strains have shown significant homogeneity of subtype A and relatively little increase in genetic diversity over the last 4 years. A preventive HIV vaccine would be an important addition to the arsenal used to prevent HIV transmission. And there are already vaccine candidates in the pipeline both in the US and Russia that might in the near future allow for the comparison of clade matched versus non-clade matched HIV vaccines. Research groups in Russia have demonstrated their capacity and infrastructure to recruit, follow, and evaluate this vulnerable population in a manner consistent with the highest standards of clinical research, as well as the laboratory capacity to conduct molecular epidemiology and genetic diversity studies. The Russian government has supported the plan for an HIV vaccine trial among IDUs in Russia. At the 16th International Conference “AIDS, Cancer, and Public Health” and NIH Office of AIDS Research sponsored workshop “Status of AIDS Vaccine Research: An Exploratory Workshop on Perspectives and Potential for HIV Vaccine Development” held in St. Petersburg in June of 2007, representatives from numerous international institutions, including WHO, endorsed the concept of developing HIV vaccine protocols among IDUs. While there are multiple important challenges that need to be further explored before starting vaccine trials, most importantly access to evidence-based drug treatment services for trial participants, the current context of high HIV incidence and low genetic diversity of HIV strains, suggests the need for intensified prevention strategies and supports the feasibility of mounting efficacy trials of HIV vaccines among IDUs in the Russian Federation.

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