

Epidemiologically targeted post-exposure prophylaxis against HIV: an under-utilized prevention technology

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In many countries, behavioural methods of HIV prevention have been partially effective in decreasing the incidence of HIV infection. They tend to have been more effective in developed countries, where condoms are accessible and affordable, and there have been widespread prevention education campaigns. Behavioural prevention has also had a degree of success in a limited range of developing countries [1]. However, behavioural prevention is nowhere near 100% effective in preventing HIV infection at a population level. In order to prevent further expansion of the HIV epidemic, we are in desperate need of an effective means of biomedical prevention.

While progress on the biomedical front has been promising at a preclinical level, large-scale clinical trials of two of the most promising candidates, vaginal microbicides and vaccines, have failed to show efficacy, and the widespread availability of an effective microbicide or vaccine is many years away [2, 3]. In this context, it is somewhat surprising to realize that we have available today an under-utilized biological means of HIV prevention that has been proved effective in at least some settings: post-exposure prophylaxis (PEP) against HIV using existing antiretroviral drugs.

Currently, PEP is a widely used preventive intervention in two HIV transmission settings. First, in the prevention of occupational HIV transmission, PEP is standard of care, and detailed guidelines for use have been published and widely promulgated [4]. However, only a tiny proportion of all new HIV infections occur in the occupational setting. Second, in the prevention of mother-to-child HIV transmission, part of the effectiveness of antiretroviral therapy relies on PEP rather than the reduction of viral load in the mother [5]. This is demonstrated by the efficacy of single-dose nevirapine given to the mother during labour and to

the neonate at birth, and by observational data that administration of antiretrovirals to the neonate in the first 48 h after delivery substantially reduces the risk of HIV transmission [6]. Most other treatment regimens for prevention of mother-to-child transmission of HIV include treating the neonate for a period of days or weeks as PEP. Thus, in the setting of mother-to-child transmission, 'non-occupational' PEP is already a widely accepted intervention to prevent HIV infection.

However, the vast majority of HIV infections worldwide occur after sexual and injecting exposures. Use of PEP in these 'social' non-occupational settings is far more controversial. Policies vary widely around the world from recommendations that PEP be available after a wide range of such social exposures (e.g. Australia, France, Switzerland, Germany and some other European countries, and Rhode Island in the USA), to those who recommend therapy only after sexual assault or accidental exposures (e.g. Italy, New York State, British Columbia), to those who have neither made a recommendation for nor against use of the therapy (US and UK national guidelines) [7, 8]. However, even in areas without guidelines, PEP is often informally available in a limited range of medical setting clinics [9].

Opponents of increasing the availability of non-occupational PEP after social exposures have raised several concerns. First, it is often stated that there is a lack of evidence for efficacy. It is true that there is no phase III clinical trial evidence that PEP after sexual and injecting exposures works, but this is also true in the occupational setting. Evidence suggesting efficacy comes from animal studies (reviewed in 10), and observational studies of occupational exposures [4]. Second, there has been concern that the availability of PEP may lead to increased sexual risk behaviour and a paradoxical increase in HIV-infection rates. However, in one study that examined this question, knowing that PEP was available was not related to HIV-risk behaviour [11]. Third, there is a concern that such therapy may not prove cost-effective, particularly if the therapy is not highly targeted [12]. Fourth, some antiretroviral drugs such as nevirapine are associated with rare serious adverse effects, and in a prevention context, the risk of these

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adverse effects may outweigh the benefit of therapy. For this reason, only drugs with a very low rate of serious adverse effects should be used in PEP.

Policies on use of PEP need to be evidence based, but the difficulties of performing a randomized controlled trial should not lead to policy paralysis. There are other study designs that may help shed light on the issue. Localities that have introduced non-occupational PEP should collect follow-up data on prescriptions, and report their experiences, so that lessons can be learnt from the application of policies at the population level. By combining follow-up data from observational studies that follow a sufficiently large number of high-risk HIV exposures in which PEP was used, the effectiveness or otherwise of PEP is likely to become apparent.

Policies on the availability of PEP after social non-occupational exposures should be based on a rational analysis of transmission risks and local HIV epidemiology to ensure the maximum cost-benefit from such a therapy. In any setting, PEP is likely to be most beneficial when targeted at the HIV-negative partners of HIV-positive people. In areas where HIV prevalence is high, availability after sexual assault may also be important. In Australia, where HIV prevalence is generally very low, but is high among homosexual men, guidelines recommend that an epidemiological assessment of HIV risk be made before prescription [13]. Thus, PEP is recommended after unprotected male-to-male anal sex with an anonymous partner, but not after heterosexual sexual assault. Policies must be tailored to the local epidemiology of HIV if PEP is to be made available outside the setting of HIV serodiscordant couples.

PEP against HIV in social non-occupational settings is an under-utilized form of HIV prevention. Epidemiologically targeted prescribing guidelines are needed to ensure that the therapy has the maximum potential to decrease HIV transmission at an acceptable economic cost.

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