

The emerging role of antiretroviral agents in HIV prevention

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There has been increasing focus on the potential for oral antiretroviral agents (ARV) to prevent sexual transmission of HIV. ARVs can theoretically be used in three ways to prevent sexual transmission of HIV: as pre-exposure prophylaxis (PrEP), as post-exposure prophylaxis (PEP) or by effective treatment of those infected with HIV to reduce infectivity and transmission to sexual partners ('treatment as prevention').

The administration of PEP after occupational exposure to HIV has been the standard of care in health care settings in Australia since the early 1990s. In December 1998, New South Wales became the first Australian state to introduce guidelines recommending PEP for HIV in the context of non-occupational exposures (NPEP) such as sexual and injecting exposures.¹ In July 2001, the Australian National Council on AIDS, Hepatitis C and Related Diseases released national guidelines recommending NPEP after high-risk exposures² and these guidelines were revised in 2007.³ Worldwide, many countries have now published guidelines regarding the use of NPEP. Most guidelines recommend that NPEP be commenced within 72 h of exposure, with the exception of European guidelines, which recommend commencement within 48 h. UK and European guidelines recommend three drug regimens for NPEP, whereas the World Health Organization, Australian and USA guidelines recommend two or three drug regimens, prescribed according to the level of risk from the reported exposure.^{3–7}

NPEP is the only biomedical HIV prevention strategy (apart from male condoms) that is widely available and promoted in Australia. NPEP programs that are targeted towards high-risk individuals have been successfully implemented in Australia without evidence of high levels of inappropriate prescription.⁸ Although NPEP is likely to have been successful at preventing HIV on an individual level, it has had very limited population-level impact in terms of the total number of HIV seroconversions prevented.^{8,9} Global implementation of NPEP has been constrained by limited resources and by the absence of data from randomised controlled trials of NPEP efficacy.¹⁰ The likelihood of such trials occurring is remote, given the ethical difficulties of a placebo controlled arm when PEP has been made widely available for prevention in the occupational setting and for maternal-child transmission.^{11,12}

The research from Victoria, Australia, published in this issue of the Journal, reports on a large cohort that comprised nearly all NPEP users in Victoria. The findings of very low rates of

potential NPEP failure are consistent with findings from numerous other observational studies of cohorts of NPEP users.^{8,13–17} Nevertheless, case reports of HIV seroconversions due to NPEP failure have been reported, even after fully adherent NPEP use.^{18,19} In addition, concerns have been raised over the impact of NPEP use on subsequent HIV risk behaviour.¹² Studies examining this issue have concluded that risk behaviour does not increase, particularly when NPEP is combined with behavioural counselling.^{9,13,14}

It has been hypothesised that universal treatment of all HIV-positive individuals within a population may decrease HIV transmission at the population level ('treatment as prevention').^{20,21} This prevention-centred approach to ARV treatment is being explored in a randomised controlled trial of early versus standard ARV therapy of HIV-infected individuals in serodiscordant couples.²² The results of this trial will provide information on the role of HIV treatment in HIV prevention in heterosexuals but no meaningful information for homosexual men. As there are no published studies of HIV viral load and HIV transmission in serodiscordant couples which include homosexual men,²³ we know nearly nothing on HIV treatment as prevention when HIV transmission is occurring through anal intercourse. Studies which quantify the rate of transmission through anal intercourse by HIV viral load are urgently needed.²⁴

ARV agents may also potentially be useful in reducing HIV transmission risk before a risk event. In the USA, expanded PrEP safety studies for men who have sex with men have just concluded. Recently presented data showed no serious adverse events and no significant effect of PrEP on HIV risk.²⁵ Several other PrEP trials are due for completion and will be reported in the near future.²²

It is critical that NPEP policymakers and providers alike now consider what the imminent release of the results of randomised trials of PrEP efficacy will mean for NPEP programs and utilisation in Australia. If PrEP is shown to be effective, the role of NPEP as an HIV prevention strategy may be in question. For example, the delineation between PrEP and NPEP will be unclear, particularly for those people who are possibly exposed to HIV more than once a month where the PrEP and NPEP administration periods may overlap.¹⁰ Australian regulatory authorities and policymakers will need to grapple with the issue of who funds a new expensive HIV

prevention intervention. For community organisations, a multitude of issues will arise including whether resources and community education should be focussed on PrEP promotion rather than NPEP. For health care providers, consideration will need to be given to whether PrEP should be provided to those who present for multiple occasions of NPEP.

At this point in time, there is no question that NPEP provision should be an element of a comprehensive HIV prevention policy. Even though it has been shown that the population level impact of NPEP is low in Australia,⁸ NPEP should be offered when a high risk HIV-prone exposure occurs. Australian observational studies, including the study by Pierce *et al.*, have provided strong evidence that NPEP will never be a stand-alone prevention strategy, and that NPEP should always be prescribed in the context of behavioural counselling and other prevention interventions.^{12,26} It is imperative that all organisations, individuals and government agencies involved in the provision and promotion of NPEP prepare now for the potential introduction of PrEP into the Australian HIV prevention armamentarium.

Conflicts of interest

None declared.

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