Using Antiretrovirals for Post Exposure Prophylaxis against HIV in the Non-occupational Setting -Position Statement of the SCAS

(Scientific Committee on AIDS and STI (SCAS), Centre for Health Protection, Department of Health, March 2006)

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Preamble

Human immunodeficiency virus (HIV) is transmitted by three major routes: blood borne, sexual, and mother-to-child. Early attempts with pharmacologic agents to prevent HIV infection after exposure were in the occupational setting and empiric in nature.

Since 1997, the use of HIV post exposure prophylaxis in the occupational setting (PEP) has been made the standard of care in Hong Kong as well as overseas, following guidelines by the then Scientific Committee on AIDS.[i] In overseas countries, post exposure prophylaxis with antiretrovirals in the non-occupational setting (nPEP) has also been used, mainly targeted against exposure from sexual contact and shared injecting equipment. Although a number of guidelines on nPEP are now available in the US and some countries of Europe,[ii,iii,iv,v] they are noted for their variability in the antiretroviral recommendations and the circumstances where they should be used. This has caused confusion to both the public and health care providers.

The SCAS deliberated on this issue in Nov 2005 by examining the available scientific evidence, reviewing reported experience in local and overseas providers, and considering its ethical implications. This position statement represents the consensus of the Committee regarding nPEP.

Limited scientific basis of nPEP

Proof-of-concept studies with simian immunodeficiency virus (SIV) and HIV-2 in nonhuman primates showed moderate degrees of success if treatment was started very early, preferably at the time of exposure.[vi,vii,viii,ix] Treatment initiated more than 72 hours after exposure would very likely be useless. This essentially imposed a 72-hour window of intervention.

In one retrospective study, zidovudine initiated within 48 h of birth apparently was able to decrease the transmission risk from 26.6% to 9.3%.[x] Human data have otherwise been largely based on a case-control study in health care workers (HCW), in which use of zidovudine was associated with an 81% reduction in transmission risk.[xi] The quality of data however was compromised by the small number of cases (n=31) and controls (n=679) originating from different cohorts. This and other methodological issues with the study may have overestimated the efficacy.[xii] Nevertheless these data formed the basis of one major cost effectiveness study on nPEP.[xiii] This showed that the intervention would be cost-effective only in the event that the source was known to be HIV infected and the exposure was receptive anal sex or shared injecting equipment. Tempering optimism with nPEP is that failures have occurred.[xiv]

All in all, scientific research to date has not matured to the point of recommending nPEP as standard of care. Any use of nPEP would therefore be exceptional and should be considered only in the event of high-risk exposure to a source known to be HIV positive. If 72 hours have elapsed since exposure,

nPEP should not be prescribed. Were nPEP to be given, the recipient should fully understand the toxicity and experimental nature of this intervention.

Antiretroviral regimens

Highly active antiretroviral therapy (HAART) generally comprises at least three drugs from two or more classes. Its potency and durability have been proven in established HIV infection, having significantly lowered morbidity and mortality in Hong Kong. [xv,xvi]

Nevertheless, the studies on which PEP was based largely employed monotherapy. It is rational to the notion that combination regimen, especially HAART, may be more efficacious than monothearpy. Using HAART in prevention against mother-to-child transmission has lowered the risk to less than 2%,[xvii] levels never achieved in any clinical trial using just one drug. In addition, the new generation of antiretrovirals has notably a less severe profile of adverse effects, making the number of drugs *per se* not as important in predicting toxicity in a recipient. In designing a regimen, the toxicity profile should be one that has the least impact on the recipient. For example, efavirenz should be withheld from women of childbearing age because of potential teratogenicity. Nevirapine should not be prescribed for nPEP at all because of pronounced liver toxicity in HIV negative persons.[xviii]

Although certain antiretrovirals have been suggested to be preferable based on inference from their mechanisms of action or in vitro effects, it is unclear if any possesses enhanced prophylactic efficacy. There being no clinical comparative data, one therefore cannot argue convincingly in favour of any particular drug to be included for the purpose of efficacy. Rather, the possibility of drug resistance should be considered and factored in during the selection of drugs. Worldwide, primary drug resistance is emerging as a significant problem, especially in some developed countries where antiretrovirals are widely prescribed. Secondary drug resistance is more common, however, and is usually secondary to poor drug adherence. If available, the treatment history and resistance test results in the source patient are helpful in determining the appropriate antiretroviral regimen. Conceivably, poor adherence to nPEP may impact on the viral resistance profile should transmission occur. It is therefore important to monitor adherence closely and manage toxicity expectantly and appropriately.

Thus members of SCAS are of the view that HAART is preferred were nPEP to be given. Its composition is dictated by the toxicity profile and the possibility of drug resistance. To prevent the emergence of drug resistance, nPEP should be given in settings supervised by physicians experienced in antiretroviral therapy.

Other aspects of managing non-occupational HIV exposure

Exposure to HIV by the sexual route or injecting drug use differs from that of occupational setting in several important aspects. Risk assessment may be difficult because of the often imprecise recount of the sexual act or drug taking episode. Clients present relatively late. Exposure source is not readily available for testing. There are other sexually transmitted infections or blood-borne pathogens which pose significant, if not more, threats. As exposure is behaviour-mediated, there is also a high likelihood of repetition.

nPEP is but one facet of the overall management of non-occupational exposure to HIV. In fact, over-emphasis on nPEP by the client or the health care provider risks overlooking the importance of risk-reduction counselling on safer sex and safe injection practice. Most STIs are of higher transmissibility than HIV and should be screened for after sexual exposure. Depending on circumstances, blood-borne pathogens such as hepatitis B and C should also be managed by serology

testing and immunisation where applicable. Tetanus vaccination history should also be reviewed after percutaneous exposure.

A frontline health care provider may not be equipped to handle all aspects of management and referral to specialists is advised after immediate management.

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1. Which of the following is not transmission route of HIV?
   (a) Sexual contact
   (b) Sharing of eating utensils
   (c) Sharing toilet
   (d) Mother-to-child
   (e) (b) and (c)

2. Which of the following does not constitute HIV prophylaxis after non-occupational exposure?
   (a) Sexual exposure
   (b) Sharing of injection equipment
   (c) Mother-to-child exposure
   (d) Needle-stick injury of health care worker in hospital
   (e) All of the above

3. What is the reduction in transmission risk with use of zidovudine (AZT) after percutaneous injury in a case-control study?
   (a) 50%
   (b) 60%
   (c) 70%
   (d) 80%
   (e) 90%

4. What is true about recommendations on non-occupational post-exposure prophylaxis (nPEP) by the Hong Kong Scientific Committee on AIDS and STI?
   (a) nPEP is only exceptionally considered for high risk exposure to known HIV positive source
   (b) Monotherapy be prescribed were it to be given
   (c) nPEP is indicated for any sexual exposure
   (d) nPEP is indicated for any drug injection exposure
   (e) none of the above

5. What is the time limit for prescription of HIV post exposure prophylaxis?
   (a) 12 hours
   (b) 24 hours
   (c) 48 hours
   (d) 72 hours
   (e) 96 hours

6. Which of the following factors can impact on the choice of regimen of post exposure prophylaxis?
   (a) Toxicity profile
   (b) Drug treatment history of the source
   (c) Teratogenicity potential for women
   (d) Potency
   (e) All of the above

7. Which of the following is not true regarding efficacy of non-occupational exposure prophylaxis?
   (a) Conclusive data of one drug more superior than the other is not available
   (b) Presence of drug resistance impairs efficacy
   (c) Efficacy same despite poor adherence
   (d) There were failure cases even with prophylaxis
   (e) None of the above

8. Which of the following is not a concern of non-occupational exposure?
   (a) Late presentation
   (b) Difficult risk assessment
   (c) Unavailability of source
   (d) Low risk of repetition
   (e) Presence of other sexually transmitted or blood-borne pathogens

9. What is the scenario that non-occupational exposure prophylaxis is cost-effective according to one study?
   (a) Receptive anal sex exposure to known HIV-infected
   (b) Sharing injection equipment with unknown source
   (c) Vaginal sex with uninfected
   (d) Oral sex with infected
   (e) None of the above

10. What is true regarding management of non-occupational exposure?
   (a) Post exposure is only one component
   (b) Attention to other concomitant infections is needed
   (c) Risk reduction counseling is of paramount importance
   (d) Tetanus vaccination history be reviewed after percutaneous exposure
   (e) All of the above