

## Differences between new United States recommendations and existing European guidelines on the use of postexposure prophylaxis (PEP) following non-occupational exposure

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Last week the United States Department of Health and Human Services published updated recommendations for the use of post-exposure prophylaxis (PEP) following non-occupational exposure to HIV [1]. The evidence is still unclear as to the efficacy of this intervention and this report provides a comprehensive overview of available literature, and discusses the benefits and problems with the administration of PEP in certain circumstances. It also clearly re-emphasises that the most effective way to prevent transmission of HIV is to prevent exposure, and any programme of PEP administration should not replace primary prevention.

In 2004, the Euro-NONOPEP project group published recommendations for PEP use along with the results of their two-year Europe-wide study [2]. Although the two guidelines considered the same intervention in the same circumstances, there are marked differences in their recommendations. Both guidelines state the basic notion that PEP should be administered to people exposed to potentially infectious bodily fluids of a known HIV-infected person, when the exposure represents a substantial risk of transmission. In these cases, a 28-day regimen of highly active retroviral therapy (HAART) should be prescribed. After this point, however, they differ in three main areas.

First, the United States (US) guidelines recommend that PEP is only prescribed when the source person is known to be HIV-infected. For cases where the HIV status of the source is unknown, the guidelines state that the clinician should assess each case individually and use their judgement. The European recommendations lay out the circumstances under which PEP should or should not be considered or prescribed if the status of the source patient is unknown. If the source patient is from a group or area of high HIV prevalence (at least 15%) the European guidelines recommend that PEP be prescribed following receptive anal sex; for other exposures, anal, vaginal or oral (with ejaculation), PEP should be considered. They also state that if the source patient is not from a high-risk group, then PEP should only be considered following receptive anal sex. The US recommendations put a stronger emphasis on the potential side effects of PEP and conclude that these may well outweigh the potential benefits if the infective status of the source patient is unknown.

Second, both guidelines focus on the risk of transmission. For some transmission situations, where the partner is HIV-infected, the transmission values used by each group are similar or the same, e.g. following a blood transfusion: US, 90%; European, 90%-100%. For other exposures, the transmission risk estimates used are very different. In particular, the US document estimates the risk of transmission via receptive anal sex to be 0.5%, while the European group estimates this to be 3%. This large difference in transmission risk may have influenced the recommendations made for PEP usage. As mentioned above, the European guidelines recommend that PEP be considered in any situation where unprotected receptive anal sex has occurred. As long as there is continuing uncertainty as to the true risk of transmission via different exposures, it is difficult to reach consensus on all the situations where PEP should be prescribed.

The final significant difference concerns the advice on the regimen of antiretrovirals to use. The Euro-NONOPEP group recommends the use of triple therapy (treatment with a combination of three drugs belonging to two different classes) but states that a two-drug regimen (treatment with two nucleoside reverse transcriptase inhibitors (NRTI)) is also an option. This is based on

evidence that drugs acting at different stages of the virus' life cycle are superior to monotherapy and that tri-therapy has been shown to treat HIV-infected patients most effectively. However, the US recommendations state that there is no evidence to indicate that a three-drug regimen would be more effective than a two-drug regimen. They place a heavier emphasis on the possible risks of side effects and state that these should be discussed with the patients. They also consider the prescription of medication to treat side-effects of HAART.

The differences in recommendations highlight the ongoing controversy surrounding the use of PEP following a non-occupational exposure. An increasing number of countries are addressing the use of PEP and establishing recommendations (Table).

**Table.** A selection of non-occupational PEP recommendations from European countries.

Country	Web page
Germany	<a href="http://www.rki.de/INFEKT/AIDS_STD/AZ_ENG/HIVPEPL_E.HTM">http://www.rki.de/INFEKT/AIDS_STD/AZ_ENG/HIVPEPL_E.HTM</a> <a href="http://www.rki.de/INFEKT/AIDS_STD/AZ_ENG/AZ_E.HTM?HIVPEPK_E.HTM&amp;1">http://www.rki.de/INFEKT/AIDS_STD/AZ_ENG/AZ_E.HTM?HIVPEPK_E.HTM&amp;1</a>
Italy	<a href="http://www.inmi.it/news/LineeGuida/RecommendationsNONOCC.htm">http://www.inmi.it/news/LineeGuida/RecommendationsNONOCC.htm</a>
Poland	<a href="http://www.msi.com.pl/pub/hiv/vol_1/no_1/3177.pdf">http://www.msi.com.pl/pub/hiv/vol_1/no_1/3177.pdf</a>
Spain	<a href="http://www.msc.es/profesional/preProSalud/sida/pdfs/guia_actuacion_profilaxis.pdf">http://www.msc.es/profesional/preProSalud/sida/pdfs/guia_actuacion_profilaxis.pdf</a>
Switzerland	<a href="http://www.hiv.ch/rubriken/therapie/pep/pepsex/pepsexi.htm">http://www.hiv.ch/rubriken/therapie/pep/pepsex/pepsexi.htm</a> (in Italian) <a href="http://www.hiv.ch/rubriken/therapie/pep/pepsex/pepsexf.htm">http://www.hiv.ch/rubriken/therapie/pep/pepsex/pepsexf.htm</a> (in French) <a href="http://www.hiv.ch/rubriken/therapie/pep/pepsex/pepsexf.htm">http://www.hiv.ch/rubriken/therapie/pep/pepsex/pepsexf.htm</a> (in German)
United Kingdom	<a href="http://www.bashh.org/guidelines/draft_04/pepse[1]_010404.doc">http://www.bashh.org/guidelines/draft_04/pepse[1]_010404.doc</a>

As there cannot be a randomised control trial for this intervention, it is important that countries share data and recommendations to build up the evidence available. Members of the Euro-NONOPEP group are promoting an initiative to analyse cases of high-risk exposure to HIV supplied by registries in Europe, Australia and the United States. The Euro-NONOPEP group has also submitted a protocol for a Cochrane review on NONOPEP to the Cochrane Review Group on HIV Infections and AIDS. Some of these registries have had difficulties sustaining operational funding; some have been discontinued, while others are operating on a voluntary basis of case reporting.

Since the publication of the Euro-NONOPEP recommendations for PEP, some studies of PEP regimens with a better adherence and fewer adverse events have been conducted [3-6]. These studies, and the recent publication of the US guidelines, have highlighted the need to revise and update the Euro-NONOPEP and other national guidelines. Thus, the comprehensive US guidelines will no doubt provide an important focal point in the future.

References:

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