

# A randomised prospective study to evaluate a rapid HIV-antibody assay in the management of cases of percutaneous exposure amongst health care workers

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## Summary

A rapid start of post-exposure prophylaxis with an antiretroviral regime is recommended after percutaneous exposure to blood from an HIV-positive source. Since the HIV-antibody status of the source is usually not known at the time of injury, antiretroviral treatment is started pending the results of HIV testing of the source.

A randomised prospective study was designed to compare the use of a rapid-screening assay in the management of cases of percutaneous exposure with the conventional procedure. Prior to the comparative study, the accuracy of a rapid-screening assay performed by non-laboratory trained personnel was evaluated.

123 blinded HIV-positive and HIV-negative

samples were correctly identified. In a randomised comparison with the conventional procedure, the application of the rapid-screening assay resulted in a significant reduction of psychological stress, drug use and cost. The estimated net benefit per case was CHF 93.– (62 US\$).

This study strongly supports the use of the rapid-screening assay in the management of post-exposure prophylaxis for HIV after percutaneous exposure in health care workers.

*Keywords: percutaneous exposures in health care workers; post-exposure prophylaxis; HIV-antibody rapid screening assay*

## Introduction

After percutaneous exposure to blood (PE) from an HIV infected patient the risk of a health care worker (HCW) becoming infected by HIV is estimated at 0.2 to 0.5% [1]. Given the significant reduction of HIV transmission by post-exposure prophylaxis (PEP) with zidovudine [2] and the theoretical benefit of combination treatment, PEP with two or three drugs for four weeks after percutaneous exposure is usually recommended [3]. However, in the majority of health care settings, the chances – for a given exposure – of the source having HIV are low. Since PEP should be initiated as soon as possible, and the HIV serostatus of the source is usually not known at the time of the exposure, PEP is usually initiated pending the results of HIV testing of the source. As a consequence, many of the courses of PEP turn out to be unnecessary and can be discontinued after one or two days.

Since 1997, several rapid HIV screening assays (RSA) have become commercially available. Some

of these tests have sensitivities and specificities comparable to standard ELISA tests [4, 5] and some tests are already approved by the US Food and Drug Administration. The newest generation of HIV antibody tests have a total processing time of 15 minutes or less. The first commercially available test was recently also approved in Switzerland for diagnostic use.

The management of PE in HCW represents an ideal situation for the use of such RSAs. To our knowledge, none of these new assays have ever been evaluated in this setting. This study therefore evaluates (1) the performance of RSA by non-laboratory trained staff, (2) the effectiveness of RSA in reducing psychological stress following PE in HCW, and (3) the cost and drug savings by using RSA in the management of PE in HCW.

Abbreviations:  
HCW = health care worker  
PE = percutaneous exposure to blood  
PEP = post-exposure prophylaxis  
RSA = rapid screening assay

## Methods

### Study design and setting

During phase I of the study (April to October 1998), execution of RSA by non-laboratory trained staff (NLTS, emergency nurses) was evaluated. In phase II (November 1998 to August 1999), the value of RSA in the management of percutaneous exposure to blood was tested in a randomised prospective study. The study was conducted in the emergency unit of a tertiary care hospital (Kantons-spital St. Gallen). The unit is responsible for the initial emergency management of PE in HCW including the initiation of PEP for HIV. HCW who experienced PE with blood from an identified source with unknown HIV serostatus were asked to participate in the study (written informed consent). Participants were randomly assigned to either undergo conventional management of the injury (i.e. PEP with antiretroviral drugs – lamivudine, zidovudine, and indinavir – pending the test result of conventional HIV testing, control group) or an alternative strategy, where RSA was used to evaluate the necessity for HIV-PEP at the first contact with the PEP-management team (interventional group). Study endpoints were the rate of false negative results, the HCW's opinion and the reduction of subjective fear and psychological stress. In addition the cost-effectiveness of this procedure was studied. The protocol was approved by the local ethical review board.

### Standard and rapid HIV antibody testing

Standard tests were performed in the routine laboratory using two commercial HIV ELISA assays (Vidas, Cobas) and confirmatory testing by HIV western blot. The RSA used in this study was an enzyme immunoassay (GENIE II from Sanofi-Pasteur) with a specificity of 99.8% and sensitivity of 100%. The assay detects HIV-1 (p24, gp41) and HIV-2 (gp369) antibodies and lacks cross-reactivity with other antibodies (HCV, CMV, HSV, Lupus-anticoagulans, rheumatoid factor, antibodies in pregnancy), and performs as well as the standard ELISA assay in seroconversion panels and with non-B clades and subtype-O samples.

### Performance of the rapid-screening assay by non-laboratory trained staff

The nursing staff of the emergency unit received simple written instructions on how to perform the RSA and were also instructed by trained personal. During normal working hours, the staff were randomly given small batches of coded serum samples from 50 HIV-positive and 43 HIV-negative individuals. All samples were tested in parallel with the standard HIV antibody test (ELISA) procedure and the results were compared after unblinding of the code.

### Routine management of a percutaneous exposure to blood

After PE, the HCW was immediately referred to the emergency unit for further management. If known, a whole blood sample was drawn from the source and brought to the emergency unit and subsequently tested for antibodies against hepatitis B, C and HIV. A blood sample was drawn from the injured HCW for future reference. Pending the HIV-test result of a known source, the HCW was offered PEP, if the exposure to the source was considered to be of significant risk. After information regarding efficacy, side-effects and correct dosing of PEP, treatment was started with zidovudine, lamivudine and indinavir. A drug supply for 48 hours was given to the HCW. PEP was stopped when a negative HIV antibody test from the source was confirmed by the laboratory, usually within 24-48 hours.

### Management of a percutaneous exposure to blood with the rapid screening assay

The management of HCW randomly assigned to the new test strategy was similar with the sole exception of HIV testing and PEP. The blood of the source was immediately tested in the emergency unit and PEP was only considered if the test result was positive.

### Evaluation of study endpoints

Participants were asked to score their degree of psychological stress following possible exposure to HIV on a scale of 1 to 10. In the experimental group, the question was asked before and after RSA testing. In the control group, the information was obtained at the beginning of the PEP.

Physicians and nurses involved in the early management of PE were asked to document the time spent on managing each case of PE. The total costs of this work were calculated based on an average hourly salary of CHF 38.– and 60.– for nurses or physicians, respectively. The cost for the rapid test was CHF 12.– and the laboratory expenses for the conventional test CHF 35.–. For the calculation of the total costs, the following items were included: cost of screening test, cost of two days of PEP and the time spent by nurses and physicians for the total management of the HCW's PE. We did not include the costs of missed time at work due to side effects.

### Statistics

To compare continuous data between the study arms the two-sample Student's T-test or the Mann-Whitney-U-test were used. For paired data, we used the Wilcoxon matched-pairs sign rank test. Categorical data were compared with the chi-square test or Fischer's exact test. Calculations were performed with the SPSS software package (version 8.0).

## Results

60 HCW (41 females and 19 males) entered the study. Among the injured HCW there were 21 physicians, 36 nurses and 3 other staff. In 47 cases the injury was a percutaneous needle-stick, in 10 cases a cut with a sharp object, a direct cutaneous or mucocutaneous contact in one case, and in 2 cases information was lacking. 25 occurred on the

ward, 23 in the operating theatre, 6 on the intensive care unit and 6 in other places.

### Phase I: Performance of the rapid screening assay by non-laboratory trained staff

A total number of 93 samples (50 HIV pos.) were tested by the NLTS using RSA. One test re-

sult of RSA (1.1%) from an HIV-negative individual was correctly read as “invalid” by the nurse. In one case, the NLTS was aware of a processing error, repeated the assay and gave a correct result. All test results were interpreted correctly resulting in 100% true positive and true negative rates.

### **Phase II: Evaluation of routine vs experimental management with the rapid-screening assay**

A total number of 60 HCW entered the study (30 in each group). All 60 sources tested negative with the conventional HIV ELISA test. All RSA in the 30 cases assigned to the experimental setting were correctly read as negative by RSA.

In the conventional arm, 25 of 30 HCW decided to start with PEP after the recommendation. Four HCW declined to take the drugs and in one case, the physician decided it was not necessary. In the experimental group, one HCW decided to take PEP, until he received the confirmatory negative result of the ELISA. The difference in the PEP uptake was statistically significant (3.3% vs 83.3%;  $p < 0.001$ ).

### **Measures of psychological stress amongst health care workers**

59 of 60 HCW returned the questionnaire (one from the control group did not). On a scale

of 0–10 the median value of the “fear” index was 3.0 in the control and 2.3 in the experimental group prior to true test result (not significant [ns]) and dropped by a median of 2.0 after the RSA was done ( $p < 0.001$ ). The most frequently cited reason for fear was the possibility of being infected with HIV (48% in the control group vs 50% in the experimental group; ns), followed by fear of the side-effects of the drugs (24% vs 33%; ns), having to take the tablets (0 vs 10%; ns) and having to report the accident to the partner (3.4% vs 0%; ns). 24% of HCW in the control group vs 7% in the experimental group did not feel any degree of anxiety or psychological stress ( $p = 0.007$ ).

### **Cost effectiveness**

The mean time spent for the management of PE was 9 vs 21 minutes by the nurse for the control vs the experimental group, respectively. Physicians spent 15 minutes for both groups. Taking the difference in cost of the two test procedures and the antiviral drugs in to account, the total costs for the two procedures differed significantly favouring the RSA procedure (CHF 140.60 vs 47.30 for the conventional vs the experimental group,  $p < 0.001$ ). This estimate does not include additional time lost from work due to adverse events caused by the PEP drugs.

## **Discussion**

In this study, we tested the performance of a rapid screening assay (RSA) for HIV infection when processed by non-laboratory trained staff (NLTS) of a teaching hospital. Furthermore, the use of this RSA in the management of percutaneous exposure to blood (PE) in health care workers (HCW) was evaluated. All tests were done during routine working hours in an emergency care unit where the acute management of percutaneous exposure is undertaken.

A total number of 123 RSA was completed (50 from HIV-positive sources) and all the final readings matched the corresponding results from conventional testing. No false negative result was reported. The technical performance and interpretation of the RSA did not cause any difficulties in our experience and evaluations performed by the manufacturer of the new RSA have shown that these assays have similar if not higher sensitivities than third-generation ELISA tests [4]. In Switzerland, the RSA are only approved for use by trained laboratory staff [6]. In our study we found that NLTS of an emergency unit can safely use the RSA. Other rapid tests have also been successfully performed by NLTS in emergency departments (e.g., pregnancy-tests, drug-screening) [7]. Thus, RSA appears to be perfectly adequate for implementation in the management of PE of HCW to blood. Even in the unlikely event that the RSA

would be slightly less sensitive, the low prevalence of HIV infection in sources of PE at our and other institutions renders it highly improbable that one single exposure to HIV would be missed.

Since the completion of this study, the Swiss licensing agency has approved the RSA for the screening of HIV infection [6]. In the meantime, 4<sup>th</sup> generation assays for HIV testing have been implemented in routine screening in Switzerland. These tests detect both HIV antibodies and antigen in one test, thus narrowing the diagnostic window period in cases of acute HIV infection. However, in the situation of source testing after PE with its inherent low pre-test probability for HIV infection, the addition of the antigen test does not result in a significant increase in detection rate. However, the management team of PE needs to be informed about the insensitivity of the assay in source cases with suspected acute HIV infection. We think this strategy should not be implemented in other situations of HIV screening, such as transfusion and transplantation services, where priorities regarding promptness of results and safety differ.

In the second phase of this study we tested the value of RSA in the management of PE in a tertiary hospital. From the perspective of HCW the advantages of RSA were obvious: prompt relief of psychological stress (fear and anxiety) and avoid-

ance of a short course of potentially toxic anti-retroviral treatment. Given the low compliance with PEP after PE with a positive source [8] it is likely that the compliance would further decrease in the first few hours pending the result of the HIVtest. Even in this small study 4 of 30 patients refused to take PEP despite its recommendation. Paradoxically, these patients did not take PEP during the most critical early phase of the intervention [9] but might have reconsidered in the setting of an HIV-positive source.

Although in this study an unsophisticated assessment of personal psychological stress was used, a marked and significant reduction of this stress was noted after the disclosure of the rapid test result in the intervention group. The similar rate of psychological stress at the initial assessment in both groups supports the validity of the simple assessment. Notably, only one in 30 HCW expressed a lack of faith in the experimental setting of this assay.

Also from an institutional viewpoint this study clearly demonstrates potential benefits: The source blood testing and management of PEP with RSA is feasible and it is superior to the conventional management in terms of cost savings and acceptance by HCW. It also shortens the acute management of PE since all the required interventions can be performed at one single visit. Responses obtained from HCW enrolled in this study supported the high desirability of this rapid management.

In addition to the many obvious advantages, the cost savings of the use of RSA are relevant. Per single PE the net cost savings were CHF 93.– (US\$ 62.–). The major part of the cost of the conventional methods were contributed by the drugs required for the initial short term treatment pending the HIV-antibody result. Cost-effectiveness of PEP has been documented if it is restricted to cases with a documented positive source [10]. RSA further improves the cost-effectiveness of this procedure.

This study demonstrates that the implementation of RSA in the management of PE in HCW is feasible, safe and cost-effective. In addition it results in a marked relief of psychological stress for injured HCW and avoids the need for PEP in most instances.

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