Post-exposure prophylaxis (PEP): 
A practical guide

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Introduction
Occupational exposure to blood-borne pathogens pose a major threat to health care workers (HCWs), with more than half a million reported cases annually in the USA alone.1 South African statistics are limited, but small studies show exposure rates varying from 48% in medical students2 to 54% among ward staff (including doctors, nurses and support staff), to as high as 91% among junior doctors.3 Of some concern is the fact that over 60% of these incidents are not reported,4 with a higher rate of not reporting exposure among those with a greater number of exposures.5 Risks involved in exposures are summarised in Table 1.

<table>
<thead>
<tr>
<th>South African sero-prevalence without</th>
<th>Transmission risk prophylaxis</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBV 5-18%6,6</td>
<td>HBsAg positive 6-10%7</td>
</tr>
<tr>
<td></td>
<td>HBeAg positive 30-33%7</td>
</tr>
<tr>
<td>HCV 2.0-2.9%8</td>
<td>3%7</td>
</tr>
<tr>
<td>HIV-1 17.64%9</td>
<td>0.3%7</td>
</tr>
</tbody>
</table>

HBV – Hepatitis B Virus  
HCV – Hepatitis C Virus  
HIV-1 – Human Immunodeficiency virus 1

Exposure prevention
The most important step in ensuring the safety of HCWs is by prevention of exposure. This is the responsibility of both the employer and the employee. Standard precautions should be practised at all times where contact with infectious body fluids occurs, and safety should be ensured by the ample availability of equipment ensuring safety (including sharps-containers, protective wear, etc.). Included in prevention strategies is vaccination against HBV of all HCWs exposed to possible infectious material.
An antibody level more than 10 IU/ml is considered to be protective, should an exposure occur. There are currently three vaccines which contain Hepatitis B virus recombinant-DNA surface antigen available in South Africa, namely Energix-B (GlaxoSmithKline Biologicals), Heberbiovac (Biovac) and, in combination with Hepatitis A vaccine, Twinrix (GlaxoSmithKline Biologicals). Should the immune response following vaccination be inadequate (antibody level <10 IU/ml), a modified revaccination approach should be followed to possibly still induce immunity (see Figure 1). Risk factors for non-response include:

- age older than 30 years
- obesity
- immunodeficiency

For management of a true non-responder after an exposure refer to Table IV.

### What constitutes an exposure?

The following should be regarded as infectious material:

- blood or blood-stained tissue, fluid or material
- sexual fluids
- tissue fluids (including cerebrospinal fluid, pleural fluid, effusions, wound secretions, etc.)

If there is no contamination with the above-mentioned fluids, the following may be regarded as non-infectious:

- sweat
- tears
- saliva and sputum
- urine
- stool

### Management of wound site

#### Percutaneous injuries

The exposure site should be washed thoroughly with soap and water. No evidence exists that expressing fluid by squeezing or inducing bleeding reduces the risk of blood-borne pathogen transmission. Avoid too intense a massage or contusions. Use of antiseptics on the wound site has not been shown to reduce transmission risk, but use is not contraindicated. Use of caustic agents like bleach, and injection of antiseptics into the wound site is not recommended.

#### Mucous membrane exposures

The exposed mucous membrane should be flushed with water.

### Initial special investigations

Baseline testing should be performed to determine management as well as for administrative reasons. Most laboratories have protocols available, and would be able to supply this information on request. The following tests are recommended in the latest Southern African HIV Clinicians Society Guidelines, published in 2008.

**Patient (or source of exposure):**

- HIV-1 serology
- Hepatitis B surface antigen
- Hepatitis C serology

**Health care worker (or exposed person):**

- HIV-1 serology
- Hepatitis B surface antibodies
- Hepatitis C serology

**Additional testing:**

- Full blood count with differential count
- UKE (if Tenofovir is used as part of prophylaxis)
- AST and ALT
- Glucose (if a protease inhibitor is used as part of prophylaxis)

### HIV-1 risk determination

The risk of transmission of HIV-1 during an exposure is determined by various factors and should be assessed as stated in Table II.
Table II:
Recommended HIV post-exposure prophylaxis following exposure

<table>
<thead>
<tr>
<th>INJURY FACTORS</th>
<th>PATIENT FACTORS</th>
<th>HIV postive</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV negative</td>
<td>HIV positive</td>
<td>• Asymptomatic</td>
</tr>
<tr>
<td>• Solid needle</td>
<td></td>
<td>• Viral load &lt;1500 copies/ml</td>
</tr>
<tr>
<td>• Superficial injury</td>
<td></td>
<td>• Symptomatic</td>
</tr>
<tr>
<td>• Small volume splash</td>
<td></td>
<td>• High viral load</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• AIDS</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Acute seroconversion</td>
</tr>
<tr>
<td>No PEP indicated unless high risk patient</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Large-bore, hollow needle</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Deep puncture</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Visible blood on device</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Needle used in intravascular puncture</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Large volume splash</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

In cases where the status of the source patient is unknown and/or cannot be determined, the source should be regarded as at high risk for infection with HIV and HBV. In patients testing HIV negative the following should be considered:
- The 'window period' for HIV is defined as the time from infection with HIV to actual seroconversion. The implication is that during this period, the patient’s body fluids will be highly infectious, despite a negative HIV serology. Other HIV tests, including HIV-1 DNA and RNA PCR will also be negative in this early stage. Using a 4th generation ELISA (testing for both anti-HIV antibodies and the p24 antigen), the window period is shortened to a minimum of 18 days.
- If the source patient is known to engage in high risk activities (unprotected sexual practices, intravenous drug use, etc.), PEP may be indicated.

Expert consultation
There are various situations where the choice of drugs to use in the PEP regimens is best discussed with an expert in the field, as in the following:
- resistance (or possible resistance) of the source virus to antiretroviral agents
- co-morbid disease, pregnancy or possibility of adverse drug interactions in the exposed
- toxicity to the initial PEP regimen

Hepatitis B risk determination
Of the three viruses discussed, Hepatitis B is the most highly transmissible, and yet preventable by adequate immunisation. Upon exposure, the HCW’s immune status should be evaluated. Any titre above 10 IU/ml is considered adequate for protection. Management is outlined in Table IV.

Timing and duration of PEP
PEP should be initiated as soon as possible; efficacy after 72 hours is unlikely. All PEP regimens should be taken for the full 28 days, as animal studies have proven greatest efficacy for this time period, with limited additional benefit after 4 weeks. Compliance is a big issue and in small studies, PEP default has been as high as 33%, and side effects can occur in up to 50% of cases. Although controversial, there have been case reports where the protease inhibitor was stopped following side-effects, with completion of a two-drug regimen.

Antiretroviral choice
The choice as to which antiretroviral to use should be based on availability, local guidelines, side-effect profile and dosing schedule. Drug regimens are summarised in Table III, as adapted from reference 1.
**Follow-up monitoring**

Testing at two weeks post-exposure specifically focuses on monitoring for toxicity. If toxicity or side-effects occur, the regimen should be altered to facilitate completion of the 28-day PEP. Subsequent testing is for medicolegal documentation and early management (*Table V*).

**Common pitfalls and misconceptions**

- If a patient is HIV negative, an exposed HCW has no risk of contracting HIV.
  - A patient can still be in the window period after HIV exposure with a non-reactive HIV serology test, but high HIV-1 viral load and thus highly infectious.
  - A negative HIV-1 DNA PCR result in HCW while taking PEP can shorten the duration of PEP.
  - In all cases, a full 28-day course is advised since this has been shown to confer the most effective protection from viral transmission.
  - A negative HIV-1 DNA PCR after completion of PEP make further follow-up testing unnecessary.
  - Despite the fact that an HIV-1 DNA PCR is a specific test, it still has a lower limit of detection. This implies that a false negative can be obtained if a small number of cells actually harbour viral nucleic acid. The appropriate follow-up with HIV-serology is still advised at 6 weeks, 3 months and 6 months following exposure.

**Helpful references and contacts**

- Toll-free national HIV health care worker hotline (Mondays to Fridays 8.30am – 4.30pm): Tel: 0800 212506.

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**Table IV:**

<table>
<thead>
<tr>
<th>SOURCE</th>
<th>HBsAg positive</th>
<th>HBsAg negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unvaccinated</td>
<td>HBV*</td>
<td>Start vaccination</td>
</tr>
<tr>
<td>Vaccinated Responder HBsAb&gt;10 IU/ml</td>
<td>No treatment</td>
<td>No treatment</td>
</tr>
<tr>
<td>Vaccinated Non-Responder HBsAb&gt;10 IU/ml</td>
<td>HBV* Start revaccination</td>
<td>No treatment</td>
</tr>
</tbody>
</table>

* HBV – Hepatitis B virus immunoglobulin

If the source status is unknown or unavailable for testing, it should be assumed that the person is HBV positive, and should be managed accordingly. If Hepatitis B immunoglobulin is indicated, it should be administered preferably within 24 hours of exposure. Efficacy after seven days is unlikely. If the HCW is an established non-responder they should receive two doses of HBV, one dose as soon as possible after exposure, and the second dose 1 month later.

**Hepatitis C risk determination**

The actual risk of contracting Hepatitis C upon exposure within the South African context is quite low, if one takes into consideration both the low seroprevalence rate (2.0-2.9%) and the low transmission rate (3.0%). Exposure to body fluids from a HCV infected patient does not warrant immunoglobulin or antiviral administration. Serial monitoring of the HCW should be performed, and should seroconversion occur, the person should be referred to a specialist in the field early during the course of the disease.

**Risk of contracting Hepatitis C upon exposure within the South African context is quite low**

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**Table V:**

<table>
<thead>
<tr>
<th>Timing of bloods during PEP</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Baseline</strong></td>
</tr>
<tr>
<td>HIV</td>
</tr>
<tr>
<td>HBV</td>
</tr>
<tr>
<td>HCV</td>
</tr>
<tr>
<td>FBC &amp; differential</td>
</tr>
<tr>
<td>AST/ALT</td>
</tr>
<tr>
<td>UKE</td>
</tr>
<tr>
<td>Glucose</td>
</tr>
</tbody>
</table>
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**Evaluate the source:**
- Obtain informed consent and perform:
  - HIV-serology
  - Hepatitis B surface antigen
  - Hepatitis C serology

**Evaluate the exposed person:**
- Baseline testing (at Casualties)
  - HIV-serology
  - Hepatitis B surface antibodies
  - Hepatitis C serology
  - FBC and differential
  - AST and ALT
  - UKE
  - Glucose
- Determine HBV immune status
  - HBsAb > 10 IU/ml considered protective

### Table: Exposure type vs. PEP

<table>
<thead>
<tr>
<th>Exposure type</th>
<th>HIV positive Low risk</th>
<th>HIV positive High risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Solid needle splatter</td>
<td>3 Drug PEP</td>
<td>3 Drug PEP</td>
</tr>
<tr>
<td>Hollow needle splash</td>
<td>3 Drug PEP</td>
<td>3 Drug PEP</td>
</tr>
</tbody>
</table>

### Table: Vaccination response vs. Source

<table>
<thead>
<tr>
<th>Vaccination response</th>
<th>Source HBsAg positive</th>
<th>Source HBsAg negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unvaccinated</td>
<td>HBV x1 and start vaccination</td>
<td>HIV vaccination</td>
</tr>
<tr>
<td>Vaccinated and known responder</td>
<td>No treatment</td>
<td>No treatment</td>
</tr>
<tr>
<td>Vaccinated and known non-responder</td>
<td>HBV x2</td>
<td>No treatment</td>
</tr>
</tbody>
</table>

### Figure 2:
Summary on PEP in a health care worker

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**Summary on practical management of PEP**

This is the current protocol implemented at the Department of Orthopaedics, University of Pretoria (see also Figure 2).

**Upon exposure:**
1. Wash the wound site or irrigate mucous membrane exposures as described above.

Also see: CDC. Notice to Readers: Updated Information Regarding Antiretroviral Agents Used as HIV Post exposure Prophylaxis for Occupational HIV Exposures. MMWR 2007;56(49);1291-2
Available from: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5649a4.htm

2. Take the first dose of PEP from the starter pack which should be readily available. Taking PEP can always be stopped later if not indicated. It is current practice at the Department of Orthopaedics, University of Pretoria to keep PEP drugs available to its personnel. Upon exposure, they have immediate access to these drugs and can therefore complete any administrative procedures as time permits. It is emphasised however, that the appropriate channels should be followed to ensure proper legal liability from the hospital.

3. Obtain consent from your patient and take the appropriate bloods from both the patient and the HCW. Most laboratories should have a protocol in place on which special investigations are indicated, based on the South African PEP guidelines. It is therefore possible to contact your local laboratory and ask for the appropriate test names as indicated in both the injured and patient.

4. Report the incident to the authorities tasked with handling these incidents and finish the necessary paperwork, e.g. ‘Injury on Duty’ forms.

5. Follow up on Hepatitis B immune status and follow up blood investigations as indicated.

6. Monitor for side-effects – if severe, consider converting to two-drug regimen, to ensure completion of PEP.

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References
7. WHO. Aide-Memoire - Health care worker safety. Department of Blood safety and clinical technology - WHO.