The option of a medication-based HIV postexposure prophylaxis (HIV-PEP) should be considered

- when injuries from HIV-contaminated instruments or injection equipment occur,
- when contamination of open wounds and mucous membranes by HIV-containing liquids occurs,
- when unprotected sexual intercourse with a (presumably) HIV-infected individual occurred,
- when (presumably) HIV-contaminated injection equipment was used [1, 2]

The risk of an HIV infection depends first and foremost on the amount of pathogens transferred. The statistical probability of an HIV infection in the most frequently occurring situations (injury by contaminated instruments, unprotected sexual intercourse with an individual known to be infected, use of contaminated injection equipment) lies in a comparable range between 1 infection per 100 contacts and 1 infection per 1000 contacts or exposures [3-9].

HIV can be transferred above all via blood, sperm and vaginal secretions. The longer the contact time between infectious liquids and wounds, damaged skin or mucous membranes, the higher is the risk of an infection.

Initiation of an HIV-PEP as early as possible after accidental injury by contaminated instruments or after wound or mucous membrane contamination by HIV-containing fluids can reduce the risk of infection. Prophylactic treatment is usually carried out over a period of 28 days [10, 11].

Since the drugs used for PEP have so far not been approved for this indication, implementation of an HIV-PEP requires explicit approval from the patients who also have to be fully informed about the risks and benefits of the treatment.

There is no guarantee that a prophylactic treatment will be successful. Potential problems associated with an HIV-PEP primarily concern the tolerability of the medications used. Acute side effects are particularly evident during the first two weeks of application (mostly gastrointestinal side effects, nausea), although these normally recede or are reversible upon completion of the therapy [12-14].

A direct or indirect contact between an HIV-negative and an HIV-infected (index) person with a relevant risk of HIV transmission automatically indicates a medical recommendation for an HIV-PEP. If the HIV-serostatus of an index person is unknown, or if the clinical diagnosis of an HIV-infection is not probable, recommendations to initiate HIV-PEP should be handled with caution (see also the PEP-decision tree) [1].

A physician experienced in HIV treatment should be consulted to assess the HIV exposure risk and to weigh up the benefits and risks of an HIV-PEP. This can also be carried out after a provisional, emergency initiation of an HIV-PEP.

1 The costs for an HIV-PEP after occupational exposure are assumed by the provider of the legal accident insurance. The immunization injection guidelines that came into force in 2007 set the limits for compensation for an HIV-PEP after a non occupational exposure. According to §2 (2) the following applies:

1. The postexposure application of sera and chemotherapeutic agents is not subject to the immunization injection guidelines.
2. If the treatment of a patient with a drug is necessary in individual cases to protect against a preventable disease, an obligation for the health insurances to pay exists according to §23 paragraph 1 no. 3 combined with §31 of the SGB V.

In concrete terms this means: postexposure prophylaxis does not fall under the auspices of this guideline, but in individual cases there may be an obligation of the statutory health insurances to cover costs. This is a new ruling which clarifies the previously unclear insurance status for HIV-PEP and other PEPs. HIV-PEP is therefore not a regularly administered preventative measure. If there is an emergency situation or in certain individual cases, however, the statutory health insurances do have an obligation to assume costs according to sentence 2 above for the HIV-PEP (and also for other PEPs such as hepatitis B).
OCCUPATIONAL EXPOSURE

IMMEDIATE MEASURES

After every potential HIV-exposure the following immediate measures should first be introduced without delay (within seconds) and in the following sequence (if necessary further counseling can be obtained by telephone after the immediate measures):

- Prick or cut injury
  - Promote blood flow by applying pressure to the surrounding tissue (≥ 1 minute)
  - Intense antiseptic rinsing and/or fitting of an antiseptic depot
- Contamination of damaged skin, eye, or oral cavity
  - Intense rinsing with the most suitable antiseptic available* (skin) or water (eye, oral cavity)

- Decision on systemic, medication-based postexposure prophylaxis
- Accident documentation (accident and emergency doctor / company doctor)
- Baseline HIV antibody test, hepatitis serology

* for skin, wounds: e.g. ethanol-based combination with PVP iodine (Betaseptic®), AHD 2000® or Amphisept E® solution, 1:1 diluted.
For eye and oral cavity: Water, ringer or saline solution

INDICATION FOR AN HIV-PEP AFTER OCCUPATIONAL HIV-EXPOSURE

- Percutaneous injury with a hypodermic needle or other cavity needle (body fluid with high virus burden: blood, CSF, puncture material, organ material, viral culture material) ► recommend
- Deep injury (mostly cut injury), visible blood ► urgently recommend
- Needle after intravenous injection ► urgently recommend
- Superficial injury (e.g. with surgical needle) ► Offer
- Exceptionally, if the index patient has AIDS or a high HIV viral burden ► recommend
- Contamination of mucosa or injured/damaged skin with fluids containing a high viral burden ► Offer
- Contamination of intact skin with blood (also with high viral burden) ► do not recommend
- Skin or mucosa contamination with body fluids such as urine and saliva ► do not recommend
- Percutaneous contact with body fluids other than blood (such as urine or saliva) ► do not recommend
NON-OCCUPATIONAL EXPOSURE

IMMEDIATE MEASURES

Following a possible HIV exposure via a sexual route (e.g. due to a torn condom, or lack of condom use), potentially infectious body fluids should be rinsed from the mucosa as thoroughly and quickly as possible. After exposure via penetrating sexual intercourse the penis should be washed under running water with soap [15]. In doing this, the foreskin should be withdrawn and the glans as well as the inner surface of the foreskin should be cleansed.

However, intravaginal or intrarectal rinsing after an exposure via receptive sexual intercourse is not recommended due to the lack of supporting data. After intake of ejaculate into the mouth, the individual is recommended to spit this out as quickly and thoroughly as possible. After that the oral cavity should be rinsed four to five times briefly with water (for about 15 sec.).

After these immediate measures have been implemented, a specialty practice or hospital emergency department should be consulted as quickly as possible. After examination and consultation a medication-based postexposure prophylaxis can be started if necessary. Baseline HIV antibody testing, hepatitis serology, and if necessary examination for other STDs should also be carried out.

INDICATION FOR HIV-PEP AFTER SEXUAL AND OTHER HIV-EXPOSURE

- Transfusion of HIV-containing blood or receipt of blood products or organs that most probably contain HIV
  - urgently recommend

- Unprotected insertive or receptive vaginal or anal sexual intercourse (e.g. due to a ruptured condom) with an HIV-infected person
  - recommend, except when index person is under a stable HAART (VL<50 copies for at least 6 months)

- Use of HIV-contaminated injection equipment by several drug-users together or after one another
  - urgently recommend

- Unprotected oral sexual intercourse with intake of ejaculate from the HIV-infected partner into the mouth
  - only offer in the presence of additional risk factors - e.g. injuries in the mouth, ulcers

- Kissing and other sexual practices without ejaculate /blood mucosa contact as well as s/m practices without blood to blood contact
  - do not recommend

- Injury from discarded syringe equipment for injecting drugs, medicines or insulin
  - do not recommend

If the HIV status of the potential infection source is not known and cannot be clarified at short notice, a medication-based PEP after a transmission-relevant contact should be initiated only if the demographic group from which the index person originates has an HIV prevalence of approx. 10 % or more (see also PEP decision tree).

A prick injury from a discarded needle (e.g. with playing children) normally does not represent an indication for a medication-based HIV-PEP [16, 17]. In the same way, routine HIV-PEP is not routinely indicated after rape given the epidemiological situation in Germany. This does not exclude that in selected situations the concrete circumstances might dictate that a PEP may indeed be indicated so that evaluation of transmission risks and decision about HIV-PEP is a necessary part of primary care for rape victims.

MEDICATION BASED PEP

If a medication-based postexposure prophylaxis is indicated, the first drug doses should be taken as quickly as possible [18]. In cases of doubt the drugs can also be taken on an emergency basis. Termination of the prophylaxis, when increasing knowledge of the accident event or the surrounding circumstances would appear to render the prophylaxis unnecessary, can be carried out at any time. Otherwise the recommended duration of prophylaxis is 28 days.

Wherever the treatment history or any existing drug resistance is known in the potential infection source, the combination of drugs used for PEP (as defined by an expert consulted on the matter) can be adapted accordingly.

In all other cases one of the standard-combinations listed in the following table can be used [19-27].
Standard combinations for HIV-PEP

<table>
<thead>
<tr>
<th>Combination partner</th>
<th>Lopinavir in fixed combination with Ritonavir (Kaletra®, 2x 400/100mg)</th>
<th>Zidovudine (Retrovir®, 2x 250mg)</th>
<th>Tenofovir (Viread®, 1x 300mg)</th>
<th>Efavirenz* (Sustiva®, Stocrin®, 1x 600mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RTI backbone</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tenofovir + Emtricitabin (Truvada®, 1x 300/200mg)</td>
<td>probable advantage: rapid onset of effect</td>
<td>Possible</td>
<td>not reasonable</td>
<td>possible</td>
</tr>
<tr>
<td>Zidovudine + Lamivudine (Combidiv®, 2x 300/150mg)</td>
<td>Possible</td>
<td>not reasonable</td>
<td>possible</td>
<td>possible</td>
</tr>
</tbody>
</table>

* if standard medicines are unavailable, other medicines approved for HIV therapy can be used - however, Abacavir (Ziagen®) and Nevirapin (Viramune®) should only be used for a PEP in well justified exceptions because of the risk of severe side effects.

Specialists should be consulted if one of the following points applies:
- The period between possible exposure and onset of prophylaxis is longer than 24 hours
- The nature and infection risk of the instrument causing the accidental injury is largely unclear
- The exposed person is (presumably) pregnant
- The index person has already been pretreated for a long period with antiretrovirals and viral resistance is proven or probable
- Considerable undesirable effects from the initial prophylactic regime cast doubt on whether prophylaxis should be carried out or demand an adaptation

Recommended baseline and follow-up examinations

<table>
<thead>
<tr>
<th>Index person° Exposed person</th>
<th>Baseline examination</th>
<th>2 weeks</th>
<th>4 weeks</th>
<th>6 weeks</th>
<th>3 months</th>
<th>6 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV-antibody</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X (X)</td>
<td></td>
</tr>
<tr>
<td>HBsAg</td>
<td>X</td>
<td>X</td>
<td>X°*</td>
<td>X°*</td>
<td>X°*</td>
<td></td>
</tr>
<tr>
<td>HCV-antibody</td>
<td>X</td>
<td>X°*</td>
<td>X°*</td>
<td>X°*</td>
<td>X°*</td>
<td></td>
</tr>
<tr>
<td>Further STDs</td>
<td>X°</td>
<td>X°*</td>
<td>X°*</td>
<td>X°*</td>
<td>X°*</td>
<td></td>
</tr>
<tr>
<td>medical examination</td>
<td>X°</td>
<td>X°</td>
<td>X°</td>
<td>X°</td>
<td>X°</td>
<td></td>
</tr>
<tr>
<td>Medical history</td>
<td>X°</td>
<td>X°</td>
<td>X°</td>
<td>X°</td>
<td>X°</td>
<td></td>
</tr>
<tr>
<td>Blood count</td>
<td>X°</td>
<td>X°</td>
<td>X°</td>
<td>X°</td>
<td>X°</td>
<td></td>
</tr>
<tr>
<td>Transaminases/ aP/ γ-GT</td>
<td>X°</td>
<td>X°</td>
<td>X°</td>
<td>X°</td>
<td>X°</td>
<td></td>
</tr>
<tr>
<td>Creatinine/ Urea</td>
<td>X°</td>
<td>X°</td>
<td>X°</td>
<td>X°</td>
<td>X°</td>
<td></td>
</tr>
<tr>
<td>Blood sugar</td>
<td>X°</td>
<td>X°</td>
<td>X°</td>
<td>X°</td>
<td>X°</td>
<td></td>
</tr>
</tbody>
</table>

° if the person is known, but his/her infection status is unclear, consent is necessary, and if necessary a rapid test should be applied if indicated/ if an exposure occurred
* if indicated/ if an exposure occurred
** follow-up, if an HCV exposure occurred at the same time
1 Treatment history with antiretroviral drugs (evaluation of potential drug resistance)
2 Taking of other medications? (Beware interactions!) Tolerability of the PEP?

Wherever no consultation can be obtained onsite from specialists or wherever they may not be known, the RKI can be consulted, although only during normal working hours (Mo. - Fr. approx. 9.00 - 17.00, Tel: 030/18754 3467 or -3420). The RKI can also arrange a referral to local specialists. Outside of normal working hours council can also be sought with the Infectious Epidemiology On-Call Service (Infektionsepidemiologische Rufbereitschaft Rat, Tel: 030/18754-0).

An ad-hoc telephone consultation for emergency situations (a screening- and if appropriate referral function to potential therapists, but not for assessing indication for PEP or for obtaining advice on medical interventions) can also be obtained from the Federal Office for Health Information (Bundeszentrale für gesundheitliche Aufklärung, BZgA) with consultation hours daily from 10 a.m. to 10 p.m. (Mo-Th) or 6 p.m. (Fr, Tel: 0221/ 892031).

On the home page of the HIV Report (www.hivreport.de) the German AIDS Help Organization provides a list of clinics that provide emergency consultation on HIV-PEP 24 hours a day (information from the clinics and cold test calls).

On the home page of the Austrian AIDS Society (www.aidsgesellschaft.at) there is a list of Austrian HIV treatment centers that can be contacted with questions about HIV-PEP.
**Decision Tree for PEP Indication After Occupational Exposure with Unknown HIV-Status of the Potential Infection Source**

1. Considering the type of exposure, is it possible that HIV-contaminated material was inoculated?
   - Yes
   - No: No PEP indication

2. Is the person from whom the material originated known?
   - Yes
     - Can the person still be tested for HIV (after providing consent)?
       - Yes: If necessary start a PEP and terminate if a potential infection source proves to be HIV negative
       - No:
         - Are there concrete reasons to suspect an HIV-infection or does the person belong to a demographic group with increased HIV prevalence?
           - Yes: Individual benefit-risk assessment
           - No: No PEP
     - Both very probable
   - No: Improbable

3. How big is the probability that individuals treated in the facility were infected with HIV and that the inoculated material originated from such a person?
   - No: No PEP indication

**Decision Tree for PEP Indication After Non-Occupational Exposure and Unknown HIV-Status of the Potential Infection Source**

1. Was blood injected or did blood/ejaculate/vaginal secretion contaminate the genital mucosa or the eye, or was there an unprotected contact between penis and the rectal mucosa?
   - Yes
   - No: No PEP indication

2. Can the person from whom the material originated be queried?
   - Yes
     - Query about any possible HIV-test results and/or infection risks, if necessary offer an HIV test or a rapid test. If necessary start PEP and interrupt if the potential infection source proves negative; Otherwise an individual risk assessment just as is the case with an unknown partner
   - No: No PEP indication

3. Does this concern a person from a group with an increased HIV prevalence* (in Germany: men who have sex with men, persons who originate from regions with a high prevalence, especially from Subsaharan Africa, intravenous drug users)?
   - Yes: Individual risk-benefit assessment
   - No: No PEP

---

*HIV prevalence in MSM in Germany: Large cities approx. 10%, rural regions and towns < 200,000 inhabitants below 5%  
HIV prevalence for IDU in Germany: below 5%  
HIV prevalence in the general population in Subsaharan Africa: southern Africa > 10%; East Africa 5-10%; West Africa 1-5%  
HIV prevalence in the general population in South-East Asia (Myanmar, Thailand, Cambodia; Papua-New Guinea) and the Caribbean: 1-5%  
HIV prevalence in the general population in Eastern Europe (Ukraine, Russia, Belorus, Estonia): 1-2% (in IDU approx. 30%)
**Risk Assessment in Case of Unknown HIV-Infected Partner**

With a presumed HIV-prevalence ≥10% in a demographic group to which the index partner belongs, or in a setting in which the exposure occurred, a drug-based HIV-PEP is generally justified. PEP is usually not justified, if the prevalence is below 5%.

In sexual exposures with unknown HIV status of the partner the circumstances surrounding the exposure event should be considered when deciding on a PEP indication: in settings in which sexual contacts occur frequently with anonymous or largely unknown partners, a higher proportion of HIV-infected partners than in the normal population should be reckoned with. In particular amongst newly infected and not yet ART-treated individuals with STI-coinfections the probability of HIV transmission during an unprotected transmission-relevant contact can be 20 -100-fold higher than the values of 1:1,000 - 1:10,000 given in the literature for a single unprotected (heterosexual) sexual intercourse with an untreated, symptom-free HIV-infected partner in the stage of clinical latency [28].

**Literature**

**Centers for Disease Control.** Updated U.S. Public Health Service guidelines for the management of occupational exposures to HBV, HCV, and HIV and recommendations for postexposure prophylaxis. MMWR 2005; 54 (No. R-9) 1-17.


25. DEUTSCHE AIDS GESELLSCHAFT (DAIG). Kon-
sensusempfehlung zur Therapie der HIV-Infektion, Ak-
AIDS_STD/BR_LINIE/BR_LINIE.HTM
27. FLEXNER CW. Principles of clinical pharmacology in
postexposure prophylaxis. Am J Med 1997; 102 (suppl
5B): 32-38.
28. POWERS KA, POOLE C, PETTIFOR AE, COHEN
MS: Rethinking the heterosexual infectivity of HIV-1: a
systematic review and meta-analysis. Lancet Infect Dis
2008; 8:553-63

Address for correspondence:
Nicole Bentrup
Sekretariat der Deutschen AIDS-Gesellschaft
Universitätsklinikum Bonn
Medizinische Klinik und Poliklinik I
Sigmund-Freud-Str. 25
53127 Bonn
Germany
Tel.: +49/228/287-11208
Fax: +49/228/287-15034
E-mail: DAIG@ukb.uni-bonn.de oder
E-mail: Nicole.Bentrup@ukb.uni-bonn.de