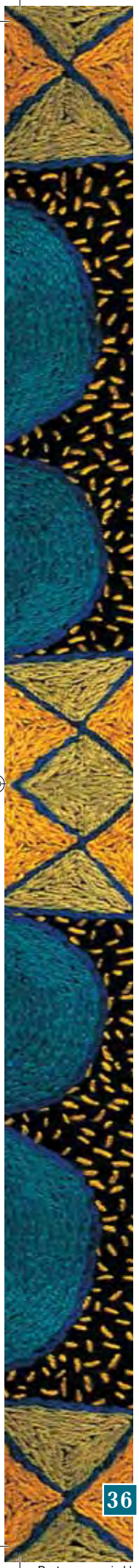

GUIDELINES

POST-EXPOSURE PROPHYLAXIS

KEY SUMMARY POINTS

- Southern Africa differs from other regions, particularly in terms of very high HIV and hepatitis B seroprevalence.
- Post-exposure prophylaxis (PEP) guidelines lack a substantive evidence base to guide advice. It is extremely unlikely that this will change, as randomised studies of different drug regimens for PEP are not feasible owing to the complexity of exposure, low event rate, and inability to ethically have a placebo group. Evolving basic science understanding, along with further studies on animals and prevention of mother-to-child transmission (PMTCT) findings, will continue to guide policy makers.
- Prior PEP guidelines are not user friendly, and rarely acknowledge the complex range of situations that occur with HIV.
- Selecting patients for appropriate PEP administration must be simplified. Algorithmic approaches for highly active antiretroviral therapy (HAART) regimens have simplified ARV management at the treatment and management levels. The same approach is needed for PEP regimens in this region.
- The approach to occupational, sexual and other forms of HIV exposure (bites, assaults, trauma, injecting drug use, etc.) is similar.
- Cases of exposure are often not simple, do not lend themselves to simple categorisation, and require an individualised approach. However, concepts to guide the attending clinician are relatively simple, and allow an effective intervention in most cases.

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Declaration of interests and support in the last 3 years (sponsors, managed care and pharmaceutical organisations)

Dr Venter is supported by PEPFAR, and has received travel and conference support from various pharmaceutical companies.

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The construction of Society guidelines is generally an uncontroversial affair. A panel of experts sits in a room for a few days, argues about a few usually minor issues, and hammers out a consensus document. This document then goes to external reviewers, both local and international, and then becomes standard of care for many organisations and helps inform regional governments' policy.

The post-exposure expert panel has indeed come to a consensus, after a long series of rewrites. However, two key recommendations – that of triple ARV prophylaxis, and treatment for all exposures – are very different from international guidelines, are definitely controversial, and have caused external reviewers to pause.

We have decided to publish the guidelines, and intend to give a detailed critique in the next edition. In future such critiques will be published together with the guidelines, allowing clinicians to see the debate. As with all guidelines, they guide practice, they are not tablets of the law.

We also hope that clincians will take note of the strength of these guidelines, namely the very strong emphasis on occupational prevention and simplified approaches, as well as side-effect and anxiety management, areas usually grossly neglected.

Francois Venter

President, Southern African HIV Clinicians Society

Clinical approach

- Animal data, case control studies and PMTCT data suggest that PEP is highly effective if taken correctly for the full prescribed duration.
- The key outcome in HIV PEP is successful completion of 28 days of uninterrupted appropriate prophylaxis.
- Side-effect management is critical to completion, and is often under-managed. Zidovudine (AZT) and protease inhibitor-based regimens are associated with significant side-effects.
- Anxiety management of the patient must be actively addressed.
- The number of drugs used to treat PEP is often the focus of clinician attention. While number of drugs and specific antiretroviral prescribing are important, completing the full course, through active side-effect and anxiety management, remains the cornerstone of successful management.
- Side-effects due to ART appear to be more common and severe in HIV-negative exposed people than in HIV-positive patients initiated on treatment, especially among health care workers.
- There have been few documented failures of PEP. Many of these failures have been associated with poor adherence, suboptimal dosing or delayed taking of ART.

Drug selection

- Where ART is felt to be justified, three drug regimens should be considered. However, this must never be at the expense of adherence. Monotherapy is known to be effective, and can confidently be used as an alternative where necessary.
- Nevirapine should never be used for PEP, owing to side-effects.
- Boosted protease inhibitors should be used in cases where ARV resistance is suspected, with nucleoside reverse transcriptase inhibitor (NRTI) choices based on medication the patient has not been exposed to. Expert guidance should be sought in these situations.
- Hepatitis B is often not considered after HIV exposure and must be part of any assessment.
- Follow-up must be actively pursued. Advice on further HIV and hepatitis testing, when it is safe to commence unprotected sex, and subsequent primary prevention, are critical. Post-exposure HIV status should be assessed through serial enzyme-linked immunosorbent asay (ELISA) testing. Polymerase chain reaction (PCR) testing does not currently have a role in PEP assessment.

Public health issues

- Occupational exposure is usually avoidable. All cases should be investigated with a view to improving infection control.
- All health and allied institutions where exposure is an occupational risk should have clear, public and accessible PEP protocols.
- Hepatitis B vaccination programmes must be encouraged in all occupational health settings, as primary prophylaxis is very effective.

1. INTRODUCTION

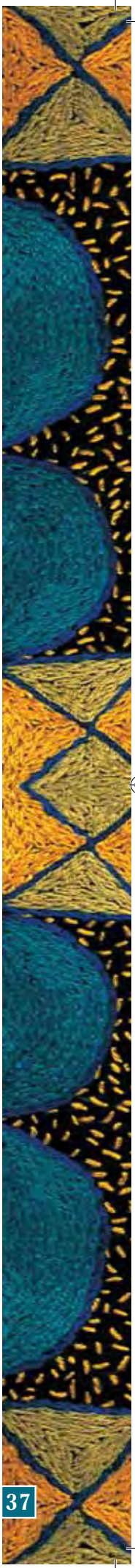
Current guidelines for post-exposure prophylaxis (PEP) are almost exclusively generated in the developed world, where HIV is far less prevalent than in the southern African region.[1] These guidelines largely reflect consensus opinion in regions where co-infection with hepatitis B and C is significantly different from that in our region. All the evidence on which these guidelines are based derives from developed world settings, and is seldom randomised or placebo controlled, except in certain of the prevention of mother-to-child transmission (PMTCT) prophylaxis settings. Much of these data rely on retrospective register analysis, as well as extrapolation from animal data and individual clinical case studies.

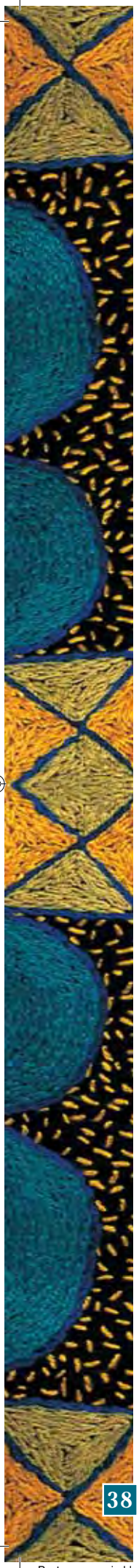
Existing guidelines differentiate between occupational and non-occupational exposures, with a strong emphasis on traditional health care settings. Recent guidelines have combined occupational with sexual assault guidelines, but do not address the broad array of other exposures that clinicians face on a regular basis. Given the very high background prevalence of HIV in the southern African region, HIV exposure risk outside the occupational setting is high and the distinction between occupational and non-occupational exposure less helpful for decision makers. Further complicating the problem is the high rate of sexual assault in the South African region, and the very large number of seroconverters within the community. The generalised nature of the epidemic creates differences in risk group demographics that must be accommodated by local PEP guidelines. Finally, 'non-traditional' exposures, such as pre-mastication, tattoos, roadside cuts from barber's shears and other exposures listed below, often require physician advice.

These guidelines do *not* deal with PMTCT settings, pre-exposure prophylaxis (PREP), or the comprehensive management of sexual assault. Local and HIV Clinicians Society guidelines should be consulted as appropriate.

2. SCALE OF THE PROBLEM: OCCUPATIONAL AND NON-OCCUPATIONAL INJURY

Reported occupational exposure to HIV in the USA alone exceeds half a million health care workers (HCWs) per year, with estimates that over 50% of these exposures are unreported. Data from the southern African region are poor. The largest study from three West African countries documented that 45% of HCWs had sustained at least one accidental blood exposure, over 60% of which went unreported.[2] In 2001, 69% of interns at Chris Hani Baragwanath Hospital in Gauteng, South Africa, had sustained at least one percutaneous injury and 45% had





sustained a mucocutaneous blood risk exposure.[3] Again in this cohort over 60% of exposures were not officially reported. At Tygerberg Hospital, 91% of junior doctors reported needlestick exposures in the prior year, three-quarters of these 'after hours' or during calls.[4]

Despite regulatory frameworks being in place in some countries, management oversight as regards occupational accidental blood exposure is largely lacking in southern African institutions, especially as far as the handling of sharps disposal and training in safe exposure practices are concerned.

In terms of non-occupational exposure, while there are data on many aspects of sexual assualt, with rape a tragic and everyday experience for women, children and many men, HIV transmission data are not as complete. There are almost no data on other forms of exposure; however, the continued high incidence of HIV in southern Africa among the general population suggests that exposure is ongoing and high risk. Advice is frequently sought from clinicians regarding PEP following assault, traffic accidents and other trauma-related events where blood exposure occurs.

3. CORE PRINCIPLES FOR PEP

- Occupational exposure prevention requires strong management oversight in all settings.
- Non-occupational exposure requires an understanding of core transmission principles, combined with clinical common sense.
- In the southern African setting, all unknown source exposure should be assumed to be HIV infected.
  - Evidence regarding occupational and non-occupational risks of transmission is limited.
  - Triple antiretroviral (ARV) regimens in treatment and PMTCT settings have been proven superior to mono- or dual therapy regimens.
  - It is recognised, however, that additional ARVs increase the potential side-effect and adherence burden. Risk of adverse effects and toxicities must be weighed against benefit in administering ARVs in the PEP setting. Side-effects must be treated rapidly, effectively and prophylactically.
- PEP should be administered as soon as possible after exposure; efficacy after 72 hours is highly unlikely.
- All PEP regimens must be administered for 28 days. Animal and case control studies suggest that administration for less than 2 weeks is associated with minimal efficacy; administration for more than 28 days confers no added benefit.
- Regimens need to be selected using locally available ARVs.
- A comprehensive infrastructure of counselling and support for the injured party is necessary to facilitate adherence to PEP regimens. Exposure is associated with substantial anxiety for the majority of people. This must be actively dealt with. In many cases, this is most significant for those who do *not* need PEP.
- Counselling must be available to deal with side-effects on an ongoing basis. Zidovudine (AZT) and protease inhibitors (PIs) are commonly associated with side-effects.

Exposure to HIV occurs in a bewildering variety of situations. Exposures where clinicians have requested advice regarding PEP, often where the source HIV and hepatitis status is unknown, include:

- Human bites or exposure to bloody phlegm during bar fights
- Exposure at schools, including biting in crèche
- Contact sports with blood exposure, such as rugby and boxing
- Sharing needles during recreational drug use
- Assaults with several people being stabbed with the same knife
- Bullets travelling through one person and lodging in another
- Animal attacks with repeated blood exposures on several people at once
- Roadside and emergency services exposure – often not just by ambulance staff; police, bystanders who help
- Exposure during home deliveries or during home-based care
- Consensual sexual exposure, burst condoms, mucosal exposure during non-penetrative sex
- Families, home-based carers
- Catering, preparation and serving of food with blood contamination
- Sitting on a needle in a movie theatre
- 'Venoterrorism' – public attacks with needles
- Unconscious drug addict found in a room
- Sex toy exposure.

It is beyond the scope of these guidelines to deal with PMTCT settings, PREP, or the comprehensive legal and clinical aspects of sexual assault.

4. PREVENTION OF EXPOSURE

Awareness of the risks and activities related to transmission of HIV as well as availability of PEP and support is critical, especially in an occupational setting. Health care workers in traditional exposure environments often receive training regarding this hazard. Other potential areas where PEP should be available include, but are not restricted to, home-based carers, day centres and crèches, schools and prisons, where PEP exposure and treatment training are often poorly available.

4.1 PREVENTION OF HIV EXPOSURE IN THE WORKPLACE

Prevention of exposure to HIV and other blood-borne viruses in the workplace is the responsibility of both

employer and employee. It is a legal requirement in many southern African countries for employers to provide a safe working environment and to ensure that employees are adhering to workplace guidelines for infection control.

South Africa has an extensive legal framework and comprehensive codes and guidelines dealing with this issue. Employers have specific and numerous responsibilities with regard to workplace safety and support of staff. The meticulous recording and reporting of incidents is critical and this responsibility usually rests with a medical practitioner. An example of legislation that covers exposure to blood-borne viruses is 'an employer is obliged to provide, as far as is reasonably practicable, a safe working environment'.

A broad range of professionals practising within the health care service and outside the Department of Health are at occupational risk of blood-borne viral exposure (see box below).

Persons at risk of occupational exposure to blood-borne viruses

Health care workers	Non-health care workers
Doctors	Firemen
Dentists	Commercial sex workers
Nurses	Teachers
Traditional healers	Prison warders
Phlebotomists	Bar bouncers
Laboratory workers	
Physiotherapists	
Occupational therapists	
Paramedics	

5. SPECIAL SITUATIONS: OCCUPATIONAL EXPOSURE

Occupational exposure involves potentially hazardous exposure to blood-borne viruses in the workplace.

- All occupational exposure should be regarded as preventable and hence deserving of investigation until proven otherwise.
- Standard precautions should be practised in every setting where blood or infectious body fluid contact is possible. Gloves should be worn, and where appropriate, protective eyewear.
- Clean water or saline should be available to immediately irrigate any mucosal exposure or percutaneous injury. Non-caustic soap should be used unless the exposure involves the eye.
- Needles should NOT be re-sheathed, and manipulation of the needle following withdrawal from the patient must be kept to the absolute minimum.
- Wherever possible, safety equipment for blood taking should be available, particularly in the hospital and clinic setting where the risk of exposure to HIV-infected blood is highest. It is imperative that the cost of cheaper equipment and disposal must be weighed against the potential increased risk of exposure that using such equipment entails.
- Needles and tools for any surgical practice, including traditional circumcision, should never be re-used without rigorous chemical disinfection/sterilisation according to national or local guidelines.
- All needles and sharp objects should be disposed of into a dedicated biohazard sharps bin. Syringes and other blunt instruments should NOT be disposed of in these bins, but rather in regulation biohazard bins for disposal of blunt biohazard objects.
- The number of sharps bins allocated to each workplace area will depend on the setting and the resources available. It is recommended that in hospital settings, designated areas of high throughput of patients who require a large number of invasive procedures, such as intensive care and casualty departments, should have a ratio of sharps bins to beds of either 1:1 or 1:2. Isolation rooms should have their own sharps bin, as should any clinic area in which blood-taking or invasive procedures are undertaken. The ratio of sharps bins to beds in open wards should ideally be 1:2, but be kept to a minimum of 1 bin per bay.
- Once ¾ full, the sharps bin should be sealed and disposed of to prevent obstruction of its orifice; overfull bins are a risk factor for injury during subsequent sharps disposal. In resource-poor settings where sharps bins are unavailable, the safest and most practical method of sharps disposal should be practised as per local or national guidelines.
- Within the hospital or clinic environment, it is the ultimate responsibility of that institution's infection control team to monitor and ensure that sharps bins are being sealed when ¾ full and disposed of correctly. However, on a day-to-day basis this responsibility falls to the nursing sister in charge of the ward or clinic.

Outside of the health care setting, employers must take responsibility for such monitoring and enforce standard practice as laid out above.

- Best practice should be enforced with the aid of unions within the framework of occupational law to ensure that employers and employees are creating a safe working environment with respect to prevention of blood-borne disease acquisition.

Post sexual exposure prophylaxis is indicated for those who present within 72 hours of unprotected risky sexual activity, including but not limited to insertive intercourse, and including but not limited to rape survivors. As a public health intervention equal access to treatment of persons who might otherwise not have been considered to have been raped, but who have definitely sustained a high-risk exposure, is essential to equality of therapy and minimisation of HIV transmission.

- There is often considerable variation in clinical presentation of exposure situations, making it almost impossible to establish standard operating procedures for control of exposure, as may be possible in occupational settings.
- The complications of criminal, civil and medico-legal elements, particularly in the case of criminally defined rape, are specialised elements of care that are beyond the scope of this guideline.
- Given the severe emotional and psychological trauma evinced by many of the patients who present after sexual assault, HIV-specific counselling may be appropriately delayed for 24 - 48 hours after onset of PEP regimens.
- It is recognised that the post sexual assault situation has a high rate of therapy default, complicating all aspects of management.
- The choice of ARVs when multiple other agents are being utilised for pregnancy prophylaxis, sexually transmitted infection (STI) syndromic management, and various medications to treat side-effects of trauma is complicated. Evidence in this setting is lacking, but anecdotal evidence from highly experienced practitioners (Dr A Wulfsson) suggest that the use of triple therapy HAART in this setting may compromise other therapy. Despite the strong empirical arguments for triple ARV therapy in this setting, a default to dual therapy with minimal short-term side-effects may be considered with full disclosure of the potential risk of this strategy to the patient. In addition, prophylactic management such as anti-emetics and anti-diarrhoeals should be considered as upfront therapy, given the high rate of therapy default.
- Issues of potential pregnancy in this scenario should be foremost in the clinician's mind, and use of efavirenz should be carefully weighed against its potential teratogenicity.

6.1 SEXUAL EXPOSURE OUTSIDE OF A RELATIONSHIP, WHERE DISCLOSURE ABOUT THE EXPOSURE IS NOT DESIRED

This is a common and thorny problem faced by clinicians, with ethical and social implications. Marriage and long-term relationships are almost always assumed within our society to be monogamous, although 'straying' from the relationship is very common in all communities. While a single episode of unsafe sex overall carries a low risk of HIV exposure, should the exposed partner become positive, they may have a very high viral load during the seroconversion phase, and unprotected sex will carry a very high risk to the regular partner, whether PEP is given or not. Sudden cessation of regular sexual relationships or introduction of condoms can cause relationship disruption, and the exposed partner may be reluctant to do this. This situation raises issues concerning the duty of the HCW to disclose to the partner, and requires a very careful and individual approach. Any decision to disclose against the wishes of the exposed person to the partner must be carefully discussed with colleagues, representative organisations and medical defence organisations. Patients may require help with strategies around disclosure.

6.2 CHILDREN

Principles around exposure for children are biologically similar to those for adults. However, consent issues are often complicated by legal requirements, and clinicians should be guided by local legislation. Children often do not give accurate histories, and anxious parents, especially in the context of possible sexual assault, may require significant counselling and careful referral.

Pre-mastication of food is commonly practised in both developed and developing countries, and several cases of transmission from caregiver to children have been described in the USA. This practice should be actively discouraged.

Another source of potential infection, through breastmilk, is using wet nurses, as well as milk kitchens (the practice

	Status of the Source		
	HIV Positive	Unknown	HIV Negative
Percutaneous exposure to blood or potentially infectious fluids	Triple therapy	Triple therapy	No PEP
Mucocutaneous splash or contact with an open wound, with blood or potentially infectious fluids	Triple therapy	Triple therapy	No PEP
Percutaneous exposure, mucocutaneous splash or contact with an open wound, with non-infectious bodily fluids	No PEP	No PEP	No PEP

Fig. 1. Selecting patients for PEP interventions.

of pooling breastmilk, and then transferring to bottles in health care facilities). These practices have been described in several local environments, and should be actively discouraged.

Finally, children are exposed to other children's behaviours which may theoretically have transmission risks, such as biting. Principles remain the same, although managing parent anxiety is often a huge challenge.

7. SELECTING PATIENTS FOR ARV INTERVENTIONS (FIG. 1)

7.1 POTENTIALLY INFECTIOUS MATERIAL

The following should be regarded as infectious material:

- **Blood** (and ANY bloodstained fluid, tissue or material)
- **Sexual fluids**
  Vaginal secretions
  Penile pre-ejaculate and semen
- **Tissue fluids**
  Any fluid drained from a body cavity, including ascites, embryonic liquor, cerebrospinal fluid, pleural fluid, pericardial fluid and wound secretions
  Breastmilk

Such exposure requires antiretroviral PEP intervention as described in these guidelines.

In the absence of super-contamination with the above fluids, the following may be considered non-infectious:

- **Sweat**
- **Tears**
- **Saliva and sputum**
- **Urine**
- **Stool.**

Exposure to non-infectious material requires reassurance but no PEP. A special circumstance involves human bites and punching. Where a bite or a punch has resulted in the opening of the skin, PEP should be advocated.

7.2 SELECTING ARV REGIMENS FOR PEP

7.2.1 PEP ARV regimens

The choice of NRTI combinations is based on available evidence in both PEP and treatment settings (including PMTCT), side-effect profiles, ease of use, local guidelines and availability.

Twice a day:

- Stavudine (d4T)* + lamivudine (3TC)
- AZT† + 3TC.

Once a day:

- Tenofovir (TDF) + emtricitabine (FTC)‡.

7.2.2. Third agents for PEP regimens

Twice a day:

- Lopinavir/ritonavir
- Saquinavir/ritonavir (400/100 bd).

Once a day:

- Efavirenz§
- Atazanavir/ritonavir
- Lopinavir/ritonavir (800/200).

NOT recommended:

- Nevirapine – owing to high risk of hepatotoxicity.
- Indinavir – this PI is associated with significant side-effects.
- Abacavir – risk of hypersensitivity reaction.

All PEP ARV regimens must be administered for a full 28 days.

7.2.3 Justification for three over two drugs, and for alternatives to AZT

This guideline is a significant departure from previous PEP recommendations, particularly in as much as where PEP is offered, 3 drugs should be administered. This recommendation is predicated on the following:

1. Current North American (Centers for Disease Control (CDC)) and UK guidelines are based on risk assessments in low-prevalence settings, with presumed exclusive clade B data. In contrast, the southern African situation is one of extremely high HIV prevalence (clade C), high volumes of patients, and an attendant very high number of exposures. The individual and cumulative risk of HIV transmission in this setting has never been quantified. There are limited data suggesting that clade C is more infectious in the sexual exposure setting. We assume that this risk is significantly higher than in other settings, and the person who has been exposed should therefore be treated appropriately.
2. While previous guidelines advocate two or three drugs based on clinician assessment of risk, this guideline recommends three drugs in all situations. There is no evidence backing the use of two drugs over the single agent AZT. We further note that the

*d4T is extremely well tolerated in PEP owing to the short duration of intervention.

†AZT is very poorly tolerated in PEP settings owing to headaches, fatigue and gastrointestinal side-effects. It has, however, the best available data for its use in PEP. D4T and tenofovir have been used successfully in PMTCT regimens, and tenofovir is commonly used for PEP in developed-world settings. While theoretically abacavir and didanosine may be used, these agents offer no benefits over the above, and carry significant short-term side-effects.

‡FTC is only available in the fixed-drug combination Truvada (tenofovir + FTC). FTC is not commercially available separately in sub-Saharan Africa

§Care with patients with pre-existing psychiatric illness and in PEP settings where ongoing severe anxiety predominates the clinical picture. Not to be used in pregnancy.

PMTCT trials suggest no added advantage of adding lamivudine to AZT, a finding replicated in various cohort PMTCT studies. However, the use of triple therapy HAART regimens has been shown to have significant benefit in comparison with dual therapy in treatment and PMTCT settings. While no evidence exists to support the use of such combinations in humans in PEP scenarios, all current PEP guidelines advocate triple therapy regimens in 'high-risk scenarios'. The argument is therefore not one of two or three drugs, but of what constitutes 'high-risk scenarios'.

3. Of particular contention are mucocutaneous exposures and oral sex scenarios, which are attributed with lesser risk. The current CDC guideline is based on a single known transmission out of almost 10 000 reported incidents. Once again, no evidence of risk is available in our setting, but evidence of significantly increased exposures in comparison to the US setting (blood spatters on eyeglasses, masks in low-, medium- and high-risk procedures) is available. Furthermore, blood risk exposures are chronically under-reported, a factor that is likely to be particularly true of injuries that are deemed to carry a lesser risk. Hence the incidence may be greater than we think. For these reasons, coupled with the known high background HIV prevalence, we advocate three-drug PEP in these scenarios.
4. Finally, the risk of side-effects increases when additional agents are added to PEP regimens. Three-drug regimens carry more risk of side-effects than simpler drug regimens, although arguably zidovudine-containing regimens carry such a significant side-effect profile that this agent should be avoided if possible. As there is no evidence that prevention of HIV transmission by AZT in the setting of PEP is due to anything other than its inhibition of viral replication, the use of d4T or tenofovir, the potency of action of which is equivalent to AZT, yet which is far better tolerated over 28 days of therapy, should be recommended as first line whenever possible. While the risk of adverse events is undeniably real, it must be balanced against the unquantifiable but equally real risk of transmission associated with high HIV prevalence, high individual viral load levels, and high levels of exposures in the occupational and non-occupational settings.
5. The guideline's powerful emphasis on appropriate choice of agents to minimise side-effects, on close management of the individual patient through the PEP process, and on the aggressive prophylactic and therapeutic management of side-effects allows a great deal of amelioration of the side-effect risk. This then tips the risk/benefit balance back towards the use of the most virologically potent regimen we have, i.e. HAART. Management guidelines to minimise exposure risk also form a large part of these guidelines, but once exposure has occurred, management of side-effects is almost always achievable, while the attendant risks are not.

8. ROUTINE BASELINE AND FOLLOW-UP INVESTIGATIONS

8.1 INVESTIGATING THE SOURCE INDIVIDUAL

The tests that should be performed on blood from the source individual are shown in Table I. If the source is found to be positive on any of the tests undertaken, they should receive post-test counselling and either be treated or referred to their local health care facility for further management.

- If the source individual is unknown, unavailable for testing, or refuses testing after appropriate counselling, the default position should be that the source is seropositive for all blood-borne pathogens.
- Hepatitis testing may not be available in some resource-poor environments. Hepatitis C testing of the source is recommended where resources are available, and omitted in the follow-up of the exposed person if the source is negative.
- If the source is found to be positive on any of the tests undertaken, they should receive post-test counselling and either be treated or referred to their local health care facility for further management.
- If a source individual is unable to give consent because of an impaired level of consciousness, national guidelines allowing testing in such circumstances should be followed.
- Testing of the source should be undertaken as soon after the injury as possible.
- Testing of needles, sharps or other samples that have been implicated in the exposure is not recommended, even when the source is unknown or refuses testing. Such investigations are unreliable and pose a risk of further exposure to the HCWs undertaking the testing.

TABLE I. TIMING OF BLOODS PRE- AND POST PEP

	Source	Exposed				
	Baseline	Baseline	2 weeks	6 weeks	3 months	6 months
HIV	√	√		√	√	√
HBV	√	√				√
HCV		√				√
Hb, WBC PMN		If AZT part of PEP	If AZT part of PEP			

- A nationally approved HIV test should be performed by a HCW who is trained in this procedure, with pre- and post-counselling, and formally documented.
- A positive rapid test should be confirmed, as per national guidelines, and the source patient managed as per guidelines.
- For source patients ON antiretrovirals, HIV RNA PCR should be performed where available. **If the viral load is elevated, genotypic testing should be considered.** This test should, however, not delay instigation of PEP. Raised viral load results should be discussed with an expert. If viral load testing and/or genotyping is not available, and if resistance is expected, a boosted PI should always be used as a third drug.
- Genotypic or phenotypic resistance testing of HIV from a source patient on or previously exposed to ARVs is not recommended in the setting of PEP.
- Testing of the source for HBsAg can be avoided when the exposed individual is known to be protected from hepatitis B acquisition by natural immunity or vaccination.
- In resource-limited settings where treatment for hepatitis C virus (HCV) is unavailable and seroprevalence within the population is low, HCV testing of the source individual can be omitted.
- Malaria blood films should NOT be routinely sent from source patients, unless there is clinical suspicion that the source has malaria.

8.2 INVESTIGATING THE EXPOSED PERSON

- Except under exceptional circumstances, it is strongly recommended that any investigation on the blood of an exposed person should be requested and taken by an independent third party.
- If infection is proven, baseline investigation for blood-borne viruses forms a vital part of any future compensation claim.

8.2.1 HIV testing

- Pre- and post-test counselling should be offered to all exposed persons at any testing facility.
- A baseline HIV (rapid or similar) test should be performed and the result carefully documented. As many cases have medico-legal or occupational claims implications, it is recommended that formal laboratory testing be done in all cases. Confirmatory testing of a positive result should be undertaken as per standard guidelines.
- Follow-up testing for HIV seroconversion should be undertaken at 6 weeks and 3 and 6 months. We do not advocate routine testing of an exposed worker at 12 months as seroconversion after 6 months is very rare. However, exposed individuals should be properly counselled in this respect and testing provided if the individual requests it.
- Viral load or p24 antigen testing is not recommended in the setting of PEP. Quantitative viral loads may yield false-positive results, and may cause substantial anxiety. Seroconversion on PEP is extremely rare and any exposed individual thought to be experiencing a seroconversion illness on PEP should be discussed with an HIV specialist physician for advice.

8.2.2 Hepatitis B virus (HBV) testing

- If the exposed worker has had natural HBV infection or has been vaccinated and is a known responder, then no investigation or post-exposure therapeutic intervention for HBV is required.
- If the source individual tests HBsAg negative and the exposed individual is not vaccinated or does not know their vaccination/antibody status, they should be referred to a local facility for testing and vaccination.
- In the case of exposure to an HBsAg-positive source, the options for management of unvaccinated individuals or those whose status is unknown are as detailed in Table II.

8.2.3 HCV testing

In resource-limited settings, HCV testing should be undertaken at baseline and 6 months only. There is no known prophylaxis.

8.2.4 Other blood-borne pathogens

Syphilis. Routine testing of source should NOT be performed.

Malaria. Routine testing of a health care worker who has been exposed to a source is NOT recommended unless the source is symptomatic.

8.3 MONITORING FOR ADVERSE DRUG REACTIONS

8.3.1 Co-morbidities

Patients with significant co-morbidities should have regular monitoring of any relevant investigations during therapy. No additional investigations are warranted in otherwise healthy individuals.

8.3.2 Medical co-morbidities and ARV selection for PEP (Table III)

Although many of the co-morbid conditions listed in Table III do not preclude the use of certain ARVs, increased monitoring of the co-morbid condition may be necessary during the 28-day course of PEP. Moreover, whenever a safer regimen is available with equal efficacy, that regimen should be used in preference.

8.4 KEY ISSUES RE COUNSELLING

8.4.1 Anxiety management

Anxiety should not simply be dismissed as baseless with simple reassurance. HIV remains a 'dread disease', despite the success of ART, because it is sexually transmitted, still accounts for significant mortality and morbidity, and has extensive stigma associated with it.

Anxiety management must be part of the adherence or follow-up support, and may need several interventions.

TABLE II. MANAGEMENT OF WORKER EXPOSED TO AN HBsAg-POSITIVE OR UNKNOWN SOURCE*

Vaccinated status of exposed worker	Anti-HBs	HBIG (0.06 ml/kg)	HBV vaccine	Comment
Previous vaccination and known responder	None	None	None	
Not vaccinated	If anti-HBs >10 mUI/ml, no treatment	If anti-HBs <10 mUI/ml, give stat HBIG and repeat at 1 month	1st dose stat and proceed to accelerated schedule 1-2-12 months	HBIG and HBV vaccine can be administered concomitantly at different sites
Incomplete vaccination or unsure	As above	Single dose stat	Complete depending on documentation or restart 0-1-2-12 months	As above
Vaccinated, but unknown response	As above	As above	Single booster stat	As above
Non-responder to primary vaccination	No	1 dose stat repeated after 1 month	1st dose stat and proceed to accelerated schedule 1-2-12 months	As above
Previously vaccinated with 4 doses or 2 completed vaccine series but non-responder		As above	Consider alternative vaccine	

* Adapted from European recommendations for the management of health care workers occupationally exposed to HBV and HCV (*Euro Surveill* 2005; 10(10): 260-264).

TABLE III. CO-MORBIDITIES AFFECTING CHOICE OF ANTIRETROVIRALS FOR PEP

Co-morbidity	Drug	Complication
Pregnancy	Efavirenz	Avoid in the 1st trimester due to teratogenicity
	Indinavir	Hyperbilirubinaemia and nephrolithiasis
Tuberculosis	Kaletra	Additional ritonavir dose of 300 mg bid needed or increase Kaletra dose to 6 tablets bid
Epilepsy	PIs	Increase levels of a number of commonly used anticonvulsants
	Efavirenz	Increased risk of seizures
Psychosis	Efavirenz	Increased risk of psychiatric symptoms
Insomnia	PIs	St John's Wort reduces all PI levels
Migraine	PIs	All PIs increase risk of ergotism with ergotamine co-administration
Renal failure	NRTI	Dose adjustments for AZT and D4T. Avoid tenofovir if creatinine clearance <60 ml/min
Hypertension	PIs	All PIs increase levels of calcium channel blockers. RTV increases beta blocker levels
Diabetes mellitus	PIs	May precipitate hyperglycaemia. Increase monitoring
Asthma	PIs	Decrease levels of theophylline
DVT/PE	PIs	Increase warfarin levels leading to risk of bleeding

Simple telephonic contact and reassurance is almost always adequate.

The intervention must be individualised, but broadly the following approaches should be integrated:

- Contextualise the risk: emphasise that acquisition of HIV is unusual through a single exposure, unless the injury is severe (sexual assault, blood transfusion of an infected unit, severe penetrating injury with infected tissue).

8.4.2 Risk-taking interventions

PEP is an ideal time to deal with risk-taking environments, whether unsafe sex (e.g. a one-night stand with unprotected sex), poor occupational health (e.g. overfull sharps bins) or other (e.g. injecting drug use).

Counselling should be non-judgemental. Addressing occupational risk must be practical (report over-full bins to infection control, do not tell an exhausted nurse to 'be more careful'). Harm to others (e.g. risk to a spouse after sex with a third party) must be solution focused.

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CASE STUDY 1

A man approaches his doctor 24 hours after having a one-night stand with an unknown woman at a conference. The man is married, and is having regular sex with his wife. He is tearful, and does not want to tell his wife what happened. He does not know the woman at the conference, and has no way of contacting her to determine her HIV status.

Initially, he volunteers that they had mutual oral sex only; the doctor elects not to prescribe PEP, as the exposure sounded very low risk. However, the doctor spends a long time extensively counselling the man, pointing out the severe danger he would put his wife in should he seroconvert and continue to have unprotected sex with her. The man is appalled, and tearfully agrees to see a counsellor.

However, he phones his doctor two hours later, and admits that he had unprotected vaginal sex with the woman. He is extremely anxious and tearful, because he anticipates that his wife will be expecting sex with him that night, as he has been away from home for several weeks. They do not use condoms, the sudden introduction of which is certain to make her suspicious. He asks whether the doctor can concoct a medical condition requiring condoms that may allow him to convince her that usage is legitimate; he also asks whether he could take PEP and therefore not use condoms.

The doctor explains carefully that even though the risk of transmission is very low after a single episode of unprotected sex, it is still present, and that it would have severe consequences for his wife. He suggests that he discuss the case with both of them together. The man is very angry, threatens litigation should the doctor discuss the issue with his wife, and accuses the doctor of scaremongering, as he has seen on the internet that HIV is not readily transmissible. He refuses HIV testing. The doctor elects to prescribe PEP (tenofovir, 3TC and lopinavir/ritonavir), and asks the man to start taking it immediately, promising to phone him immediately after the first dose. During this time he consults with two colleagues, both of whom advise him that he has an ethical duty to warn the man's wife. The doctor carefully documents all the advice and the clinical details.

He phones the man two hours later, under the pretext of asking about side-effects. In the interim the man has confessed to his wife, who is furious. The doctor offers to see the two of them immediately, and explains the threats of unprotected sex and the need for PEP. He also takes the opportunity to do an HIV test on both of them, and both are negative. He refers them to a marriage counsellor. The man develops diarrhoea one week after starting PEP, which does not respond to anti-diarrhoeal agents. However, it stops after the lopinavir/ritonavir is discontinued. The doctor stays in touch with him weekly during his PEP, and facilitates follow-up ELISA testing. The man reconciles with his wife, apologises to the doctor for his behaviour, and uses condoms for 6 months until his final HIV test returns negative.

CASE STUDY 2

An anxious couple arrives at the doctor's rooms with their two-year-old child. Their domestic worker has been looking after the child since soon after birth, and the parents have just found out that she has been chewing food for the child while weaning. The couple is terrified that their child has contracted HIV, despite not knowing the domestic worker's status, and she has refused to test, fearing that they will fire her. The couple demand PEP for the child.

The doctor calms the couple down, carefully explaining that while there is a very small risk, PEP during chronic exposures is not necessary. She tests the child immediately with a rapid test, which is negative. She volunteers to explain to the domestic worker why pre-chewing food is not acceptable, but refuses the couple's request to enforce an HIV test. She also carefully explains to the couple about the law, which in their country does not permit them to discriminate against their employee on the basis of HIV status. The couple is initially dissatisfied; however, after having the low risk of transmission explained, they agree to ask the domestic worker to see the doctor. The domestic worker agrees not to pre-chew food, but again refuses an HIV test. The doctor promises to keep all details confidential from the employers, who appear simply relieved that an independent and trustworthy party has been engaged.