MANAGEMENT OF SEXUAL EXPOSURE TO HIV: HIV PEPSE

www.hiv-druginteractions.org

If you require information on **occupational** exposure to blood borne viruses, including HIV, please refer to the NHSGGC board protocol which can be can be downloaded from www.nhsggc.org.uk/phpu.

Key Points

- **If the patients baseline HIV test is positive, PEPSE should be continued until review by HIV team**
- **If the patient has a further high risk exposure in the last two days of PEPSE, they should continue the medication for a further two days at the end of the course**
- **PEPSE is not recommended if the source patient is HIV positive and has a confirmed viral load <40 copies/ml for the preceding 6 months**

Rationale for PEPSE

Pathogenesis studies indicate that there may be a window of opportunity to prevent HIV infection by inhibiting viral replication after an exposure. Once HIV crosses a mucosal barrier it may take up to 72 hours before HIV can be detected within regional lymph nodes and up to five days before HIV can be detected in blood. Initiation of antiretroviral therapy (ART) has been shown to reduce spread and replication of virus in all tissues if initiated quickly after inoculation in an animal model.

Try to establish the HIV status of the source individual (according to appropriate guidance on HIV testing and consent) as early as possible. PEPSE can be averted through assertive HIV testing of the source individual.

Initiation of PEPSE is recommended as soon as possible after exposure, preferably within 24 hours of exposure but can be offered up to 72 hours.
Once 72 hrs have passed since exposure PEPSE should not be started

PEPSE is not recommended where sexual exposure has been protected (condoms used). The recommendations assume condoms were not used or condom failure

The decision to administer PEPSE should be based on the risk of HIV transmission and not to manage a state of acute anxiety following a sexual exposure.

Determining Risk:

Step One: Determine:

1. The gender of the source
2. Whether the source is**:**
   i. HIV positive with a detectable viral load (or viral load unknown)
   ii. HIV positive with a **verifiable** undetectable viral load

(the HIV viral load must have been continuously undetectable for more than 6 months, and the most recent viral load was within the last 6 months, and since the undetectable viral load the source has had high adherence to their HIV medication)

iii. HIV status unknown and from a risk group or country of high HIV prevalence (this is likely to be men who have sex with men, a person migrated to the UK from areas of high HIV prevalence particularly Sub-Saharan Africa or an IDU from high risk countries particularly Eastern Europe or Central Asia). **If the source is on HIV PrEP this should be considered as part of the overall risk assessment.**

iv. HIV status unknown and not from a group or country of high risk

→ **You can now decide which of the 4 vertical columns in the following table are applicable to your patient presenting for PEP**

Step Two: Identify the type of sexual contact

Examples of the estimated risk of HIV transmission according to the likelihood that the source is HIV positive and the risk following a single exposure with someone known to be HIV positive

The Source	The type of sex the patient had with the source	Approximate risk if the source HIV status is not known	Risk if source is HIV positive*
A MSM in Greater Glasgow area	Received anal sex from source	1 in 2000	1 in 90
A MSM in UK outside London, Manchester, Brighton	Received anal sex from source	1 in 2 368	1 in 90
A MSM in Greater Glasgow area	Insertive anal sex to source	1 in 14,800	1 in 666
A MSM in UK outside London, Manchester, Brighton	Insertive anal sex to source	1 in 17 562	1 in 666
A MSM in London	Received anal sex from source	1 in 720	1 in 90
A MSM in London	Insertive anal sex to source	1 in 5 328	1 in 666
A heterosexual man not of Black African ethnicity	Vaginal sex	1 in 1.6 million approximately (1 in 1 666 666)	1 in 1000
A woman not of Black African ethnicity	Vaginal sex	1 in 2 million approximately (1 in 2 031 666)	1 in 1219
A heterosexual man of Black African ethnicity	Vaginal sex	1 in 24 000 (1 in 24 390)	1 in 1000
A heterosexual woman of Black African ethnicity	Vaginal sex	1 in 17 000 (1 in 17 168)	1 in 1219

*The risk will be considerably lower if the source is on treatment, the HIV viral load has been continuously undetectable for more than 6 months, the most recent viral load was within the last 6 months, and since the undetectable viral load the source has had high adherence to their HIV medication

Step Three: Decide if PEPSE is recommended, considered or not recommended

Type of exposure of individual being assessed for PEPSE ↓	**Source HIV positive:**		**Source HIV status unknown:** (Attempts should be made to establish the status of the source)	
	Detectable viral load or viral load unknown	**Verifiable undetectable viral load#**	**From a group or area of high risk**	**Not from a group or area of high risk**
Received anal sex	Recommend	Not recommended	Recommend	Not applicable.
Performed insertive anal sex	Recommend		Consider ‡	
Performed insertive vaginal sex	Consider ‡		Consider ‡	
Received vaginal sex	Recommend		Consider ‡	

the HIV viral load must be verifiable, continuously undetectable for more than 6 months, and the most recent viral load was within the last 6 months, and since the undetectable viral load the source has had high adherence to their HIV medication otherwise manage as per '**detectable viral load or viral load unknown'** If the source is under follow up at the Brownlee most patients results can be accessed from clinical portal (with source patient consent *NB please ensure third-party information is not viewed by the person at risk*) or contact the Sexual Health Adviser at the Brownlee 0141 211 1099.

only recommend if ejaculation took place plus HIV

‡ **Step Four:**
When the advice is 'consider' PEPSE is not normally recommended unless other factors which increase the risk of transmission are present. Patients should be seen by senior clinicians and decisions made on a case to case basis.
Factors which may increase transmission include

- the source may have a high viral load, this may be particularly relevant if the high risk source is thought to have primary HIV infection (has become infected within last six months)
- either person potentially having breaches in the mucosal barrier for example due to genital ulcer disease or trauma
- the high risk source having a sexually transmitted infection
- the male presenting for PEP has not been circumcised
- trauma during sexual assault

Assessment of Individual Presenting for PEPSE

Medical History
A full medical and sexual history should be taken from the individual.

Key questions:

- Is the patient **pregnant or at risk of pregnancy**?
- Is there an existing **medical condition (**eg renal dysfunction**)**?
- Is there potential for **interaction** with other medications that the patient is taking inc. contraception?
- Could the virus be **resistant** to one or more of the drugs?
- Is there a history of recreational drug use – what agents?

IT IS THE RESPONSIBILITY OF THE PRESCRIBING CLINICIAN TO CHECK FOR ANY DRUG INTERACTIONS.

This can be done at **www.hiv-druginteractions.org**. Pharmacists based at the Brownlee can also be contacted for advice Mon- Fri 9-5 on 53383

If a drug-drug interaction exists please discuss this with the GUM consultant on-call, an alternative course of PEPSE may be available.

Baseline Investigations

- HIV – **mark as urgent** – informed choice re future therapies
- U&E
- Urinalysis - if **more than a trace** of protein is present (+, ++ or +++), send urinary protein creatinine ratio (white top pot to biochem). NB. If a client is over the age of 18 then an eGFR is calculated automatically by the labs. If they are under the age of 18 you need a different equation due to lower muscle mass. Please use the following links if required.
  http://labtestsonline.org.uk/understanding/analytes/gfr/tab/test/
  http://nephron.com/bedside_peds_nic.cgi
- LFT
- Syphilis
- Hepatitis B core
- Hepatitis C Ag
- Pregnancy test as appropriate
- Baseline chlamydia and GC *Audit in 2016 showed only 52% of patients presenting for PEPSE had CT/GC tests performed at presentation

Informed Consent for PEPSE

Informed consent should be obtained from the exposed person prior to prescribing PEPSE. The exposed person's understanding of the following should be documented:

- The rationale for PEPSE
- The lack of conclusive data for the efficacy of PEPSE
- The potential risks and side-effects of PEPSE
- The arrangement for early follow-up with an HIV/GU medicine clinician
- Pre-test discussion and HIV test (4th generation laboratory test)
- The need to continue PEPSE for 28 days if the baseline result is negative
- The need to have a follow-up HIV test 4 and 8 weeks post-completion of PEPSE
- The need for safer sex for the following two months
- Coping strategies, assessment of vulnerabilities and social support
- For patients concerned about sexual risk-taking health advisers can offer ongoing risk
- reduction work or referral to psychology
- Recognition of seroconversion symptoms.

PEPSE Regimen – recommended by Expert Advisory Group on AIDS

Drug	Dose	Notes
FTC/Tenofovir **FTC/Tenofovir** This is made up of two drugs combined into ONE tablet • Tenofovir disoproxil (245 mg) • Emtricitabine (200 mg)	Take **ONE** tablet, **ONCE** a day, preferably every 24 hours	Take with or just after food or a meal.
Raltegravir 400mg	Take **ONE** tablet, **TWICE** a day, preferably every 12 hours	It does not matter if you take these tablets before or after food or on an empty stomach
FTC/Tenofovir and raltegravir can be taken at the same time.		

A 5-day starter pack is supplied by the clinic. This may be supplied by any of the major city A&E departments. A further 23 day treatment pack will be issued following urgent care review at Sandyford Central or Sandyford Renfrewshire.

Please remind patients that they should only take 28 days of medication in total. (i.e. if they have already taken 5 days treatment from a starter pack, they will only require a prescription for a further 23 days of treatment**).**

Drug Resistance-primary HIV drug resistance in the UK is around 8% and falling. If drug resistance is known or suspected in the source please discuss with the GUM Consultant on-call, it may be necessary to alter the PEPSE regimen.

Refer to Sexual Health Adviser for further discussion around the following:

- The need to complete the four-week course of PEPSE if the baseline result is negative
- The need to have a follow-up HIV test 4 and 8 weeks post-completion of PEP and place the client within a recall system to ensure client is recalled if they do not attend (this also allows for syphilis and hepatitis testing out with window period)
- The side-effects of the drugs and the support available in the clinic and in the community to help adherence
- The need for risk reduction especially for the following three months - consider SRP choices
- Issues around disclosure
- Coping strategies

Follow up

- FTC/Tenofovir / Raltegravir is well tolerated.
- PEPSE should normally be continued for 4 weeks. Published evidence shows that less than 50% of patients complete PEPSE.
- Patients starting PEPSE need to be seen before the end of the starter pack to review baseline HIV test and biochemistry tests, and review risk and verify the need to continue. They do **not** need to be referred to the Brownlee. Routine blood test monitoring is no longer required in the absence of any concerning medical symptoms if baseline bloods are normal.
- Those starting PEPSE should be assessed for eligibility for HIV PrEP – if they are eligible and wish to start, this can be started immediately after PEPSE and this should be arranged with appropriate PrEP follow up (See HIV PrEP protocol).
- Exposed persons should seek medical advice about any acute illness which occurs during the follow up period. Illnesses characterised by **fever**, **rash**, **myalgia**, fatigue, malaise or **lymphadenopathy** may represent a seroconversion illness, or a side effect of the medication.
- A fourth generation HIV test should be done 4 and 8 weeks after completion of PEP – BASHH guidelines 2015. The follow up dates should be added to SHA virtual diary for recall if client does not attend.
- Consider SRP Choices if clinically appropriate.

Other Issues

Anxiety

While it is recognised that individuals may present in a state of acute anxiety following possible exposure to HIV, the decision to administer PEP should be based upon the risk of HIV acquisition and the potential adverse effects of ART. Individuals should be reassured that in general the risk of HIV acquisition is low. Referral to a Sexual Health Adviser for support of individuals reporting anxiety in particular around the risk of transmission may help to alleviate such anxiety. They can also assess for onward referral to other support services as required.

PEPSE Side Effects

Side effects such as nausea and diarrhoea can occur with PEPSE and clients should be warned about this. It may be necessary to provide clients with symptomatic management such as anti-emetics or loperamide.

PEPSE Adherence

Below are recommendations from BASHH about what to do if a client misses any doses.

Table 5 Recommendations on missed doses of PEP agents

Missed Dose	Recommendation	Comments
<24 hours since missed dose	Take missed dose immediately and subsequent dose at usual time	Reinforce importance of adherence and re-evaluate motivation for continuing PEPSE
24-72 hours since missed dose	Re-start PEPSE	As above
>72 hours since missed dose	Recommend stopping PEPSE	-

Pregnancy
Pregnancy is not a contraindication to PEPSE. If a pregnant woman needs PEPSE please discuss with the GUM Consultant on-call and ask permission of the patient to inform her midwife/ obstetrician.

Skin Rash/ Flu like Illness While on PEPSE or After Completion
Clients with any of the above symptoms must be seen urgently as this may represent HIV seroconversion.

Clients Who Repeatedly Present for PEPSE
Multiple presentations for PEPSE should prompt discussion and review of risk reduction strategies because PEPSE is only a part of this approach. HIV PrEP should be discussed with these individuals.

Further high risk exposure to HIV during PEPSE:
If exposure occurs during the last two days of PEPSE, it should be continued for 48 hours after the last high risk exposure

Positive baseline HIV test on PEPSE:
In the event of a new HIV diagnosis after initiation of PEPSE, PEPSE should be continued pending discussion with an HIV specialist. Long-term ART may be beneficial in the setting of primary HIV infection.

Sexual Health:

STI Screening

All individuals presenting for PEPSE should be comprehensively tested for other sexually transmitted infections at initial presentation.

Contraception

It is also vital to consider the need for emergency and ongoing contraception. The current drug regimes do not include enzyme inducers and so there are minimal drug-drug interactions.

Hepatitis B Vaccination
Hepatitis B vaccination (and immunoglobulin) should be considered in addition to PEP in accordance with existing guidance.

Other Viral hepatitis – please Hepatitis protocols

References

UK Guideline for the use of HIV Post-Exposure Prophylaxis Following Sexual Exposure (PEPSE) 2015. http://www.bashh.org/documents/PEPSE%202015%20guideline%20final_NICE.pdf

HIV prevalence Country specific HIV prevalence can be found in UNAIDS Gap Report:
http://www.unaids.org/en/resources/campaigns/2014/2014gapreport/gapreport

Region-specific estimates for IDU can be found in the UNAIDS Gap Report
http://www.unaids.org

Expert Advisory Group on AIDS. Change to recommended regimen for post-exposure prophylaxis (PEP). Sept 2014
https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/351633/Change_to_recommended_regimen_for_PEP_starter_pack_final.pdf

Has Transmission Risk only occurred in the last 72 hours?

Yes
Is PEPSE "*recommended*" in table 4?

No
PEPSE not to be prescribed.

Consider as appropriate

- Baseline HIV testing.
- Emergency contraception
- STI screening
- Pregnancy test
- Follow up HIV testing after window period
- Hepatitis B vaccination
- Emotional support

No

Discuss PEPSE with client as per guideline.

If accepted review-

- Medical history
- Sexual history
- Drug history inc contraception
- Recreational drug use
- Check for drug interactions.

Discuss with GUM Consultant on-call if any contraindications

Is PEPSE "*considered*" in table 4.

PEPSE may be given if there are other circumstances that may increase HIV transmission such as-

- Following sexual assault
- Presence of other STI
- High HIV viral load

This should be discussed with the GUM Consultant on-call

PEPSE is "*not recommended*" in table 4

PEPSE not to be given.

Manage anxiety and arrange tests and follow up as above.

If PEPSE commenced arrange-

- Baseline investigations as per guideline
- Client to see SHA
- Follow up with GUM Dr before end of starter pack

PEPSE Advised by Consultant

Appendix

List of High HIV* Prevalence Countries	
African Continent	
	HIV ≥1%
Angola	2.2
Benin	1.1
Botswana	22.2
Burkina Faso	1.0*
Burundi	1
Cameroon	4.5
Cape Verde	1
Cent. African Rep.	3.7
Chad	2
Congo	3**
Cote d'Ivoire	3.2
Dem. Rep. Congo	1.1*
Djibouti	1.6
Equatorial Guinea	4.9
Ethiopia	1.5**
Gabon	3.8
Gambia	1.8
Ghana	1.6
Guinea	1.6
Guinea-Bissau	3.9**
Kenya	5.9
Lesotho	22.7
Liberia	1.1
Malawi	9.1
Mali	1.3
Mauritius	1.1*
Mozambique	10.5
Namibia	13.3
Nigeria	3.1
Rwanda	2.9
Sao Tome & Principe	1.4**
Sierra Leone	1.3
South Africa	19.2
South Sudan	2.5
Swaziland	28.8
Togo	2.4
Uganda	7.1
United Rep. Of Tanzania	4.7
Zambia	12.9
Zimbabwe	14.7
South America	
Belize	1.5
Guyana	1.5
Suriname	1.1
Caribbean	
Bahamas	3.2
Barbados	1.6
Dominican Republic	1
Haiti	1.7
Jamaica	1.6
Trinidad & Tobago	1.2
E. Europe & Asia	
Estonia	1.3**
Russian Federation	1.4**
Thailand	1.1
Ukraine	1

List of indeterminate or high hepatitis B prevalence (>2%)

Africa	All African countries except the Seychelles
Americas	
Caribbean	All Caribbean Islands
Central America	Belize, Colombia
South America	Ecuador, French Guyana, Guyana, Peru, Suriname +
Northern	Greenland.
Asia	
Central Asia	Kazhakstan, Kyrgyzstan, Tajikistan, Turkmenistan, Uzbekistan.
Eastern Asia	China, Mongolia, North Korea. ,
Southern Asia	Bangladesh, Bhutan, Pakistan Sri Lanka.
SE Asia	Brunei, Cambodia, Myanmar, Philippines, Singapore, South Korea, Taiwan, Vietnam.
Western Asia	Armenia, Azerbaijan, Cyprus, Georgia, Oman, Saudi-Arabia, Syria, Turkey, Yemen.
Europe	Albania, Belarus, Bulgaria, Greece, Kosovo, Moldova, Romania, Russian Federation.
Oceania	New Zealand + all Pacific islands

Data may not be complete for all countries. The purpose of this table is solely to help decide on an offer of risk-based testing where patients originate from or disclose risk in the countries cited

List of indeterminate or high hepatitis C prevalence (>2%)

Africa	Angola, Benin, Burkina Faso, CAR, Cameroon, Chad, Congo, DRC, Egypt, Equatorial Guinea, Gambia, Ghana, Ivory Coast, Gabon, Guinea, Guinea-Bissau, Liberia, Mali, Niger, Nigeria, Senegal, Sierra Leone, Togo, Western Sahara
Americas	Greenland, Puerto Rico
Asia	
Central Asia	Kazakhstan, Kyrgyzstan, Tajikistan Turkmenistan, Uzbekistan.
Eastern Asia	Mongolia.
Southern Asia	Pakistan
SE Asia	Cambodia, Thailand, Taiwan
Western Asia	Armenia, Azerbaijan, Georgia, Israel, Iraq, Yemen
Europe	Belarus, Estonia, Greece, Italy, Latvia, Lithuania, Moldova, Romania, Russian Federation, Slovakia, Ukraine.
Oceania	-

Data may not be complete for all countries. The purpose of this table is solely to help decide on an offer of risk-based testing where patients originate from or disclose risk inthe countries cited.

* HIV prevalence estimates for 15-49 year olds (high estimates used) (Source UNAIDS Global Report 2015)

** 2011-1012 HIV data (no later data available)