Guidelines
for Post- Exposure Prophylaxis
for
HAV, HBV, HCV & HIV

By

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An exposure that might place health care professional HCP at risk for infection is defined as a percutaneous injury (needlestick or cut with a sharp object) or contact of mucous membrane or non-intact skin (exposed skin that is chapped, abraded, or afflicted with dermatitis) with blood, tissue, or other body fluids that are potentially infectious. In addition to blood and visibly bloody body fluids, semen, vaginal secretions, cerebrospinal fluid, synovial fluid, pleural fluid, peritoneal fluid, pericardial fluid, and amniotic fluid are considered potentially infectious.
Feces, nasal secretions, saliva, sputum, sweat, tears, urine and vomitus are not considered potentially infectious unless they are visibly bloody.
Preventing exposures to blood and body fluids (primary prevention) is the most important strategy for preventing occupationally acquired infection.
Both individual healthcare providers and the institutions that employ them should work to ensure adherence to the principles of standard precautions.

Hepatitis B

• When an occupational exposure occurs; evaluate the source & the exposed persons for HBV,HCV & HIV and the vaccination and vaccine-response status of the exposed person.
• The risk of transmission of HBV and HCV from an occupational exposure is significantly greater than the risk of HIV transmission. The risk of HCV infection following a needlestick is 1.8%, whereas the risk of HBV infection ranges from 1% to 30% depending on the presence of hepatitis e antigen (Table 1). The risk of transmission of HCV from a single mucous membrane exposure is negligible.
• *Decision-making regarding post exposure prophylaxis PEP should not be delayed while testing for antibody status* & is indicated even if the exposed person has received hepatitis B vaccine previously, besides; If the status of the source is unknown, assume infection.
• Administration of prophylactic hepatitis B immune globulin (HBIG) and the initiation of the hepatitis B vaccine series (three-doses of HBV vaccine given at 0, 1-2 months, and 6 months) injected at different injection sites is recommended after exposure & should be ideally administered within 24 hours of exposure; HBIG should not be given later than 14 days post-exposure. This is proved to have 70-90% effective in preventing HBV infection.
• After exposure (Table2):
◘Persons who have written documentation of a complete hepatitis B vaccine series and who did not receive post-vaccination testing should receive a single vaccine booster dose.
◘Persons who are in the process of being vaccinated but who have not completed the vaccine series should receive the appropriate dose of hepatitis B immune globulin (HBIG) and should complete the vaccine series.
◘Unvaccinated persons should receive both HBIG and hepatitis B vaccine.
• Antibody titers should be checked 1-4 months after the completion of a 3rd course of vaccine:
- It is preferable to achieve anti-HBs levels ≥ 100 mIU/mL, however, levels of ≥10 mIU/mL are generally accepted as enough for protection.

- Responders with anti-HBs levels ≥ 100 mIU/mL do not require any further primary doses & further assessment of antibody levels is not indicated. They should then receive the reinforcing booster dose at five years.
- Responders with anti-HBs levels of 10-100 mIU/mL should receive one additional dose of vaccine at that time. Following this, further assessment of antibody levels is not indicated. They should then receive the reinforcing dose at five years.
- An antibody level <10 mIU/mL is classified as a non-response to vaccine, and testing for markers of current or past infection is good clinical practice. In non-responders, a repeat course of vaccine is recommended, followed by retesting 1-4 months after the second course. Those who still have anti-HBs levels below 10 mIU/mL, and who have no markers of current or past infection, will require hepatitis B immunoglobulin (HBIG) for protection if exposed to the virus.
• Neither pregnancy nor lactation should be considered a contraindication to vaccination of women. HBIG is not contraindicated for pregnant or lactating women & pregnant women can safely receive both the HBV vaccination and HBIG.
• HBIG, when given concurrently with hepatitis B vaccine, does not affect the development of active immunity & if infection occurred at the time of immunization, administration of HBIG may still prevent the development of carrier status.
•Though the standard course of active immunization involves three injections at 0, 1 and 6 months; an accelerated course of 0, 1-2 months is possible – the same can be given for the combined hepatitis A and B vaccines (Twinrix).
•Adults who need protection very quickly (within 48 hours of exposure) can have a schedule of 0, 7 and 21 days. After this accelerated course, a booster at one year is recommended.
• The duration of protection provided by the hepatitis B vaccine is still unknown but may give lifelong immunity; still; it is recommended that individuals at continuing risk of infection should be offered a single booster dose of vaccine, once only, five years after primary immunization.

Hepatitis C Virus
• Clinicians should consider concurrent exposure to HCV when exposed workers present with an HIV exposure & vice versa.
• Neither immunoglobulin nor antiviral agents are recommended for HCV post-exposure prophylaxis & currently; no effective prophylaxis for HCV has been identified. .
• After exposure; the following baseline tests should be obtained :
◘ Source patient:
HCV antibody test (EIA/ELISA), and if positive; HCV RNA test or recombinant immunoblot assay (RIBA) may be used as the confirmatory test
◘ Exposed worker:

- Week 4: HCV RNA and liver panel
- Week 12: HCV RNA and liver panel
- Week 24: HCV antibody and Liver panel

• If at any time the serum ALT level is elevated; repeat HCV RNA testing; if positive; then consider acute HCV infection & refer for medical management.
• HCV RNA testing can identify acute infection within 2 weeks of exposure, whereas accuracy of the antibody test can be delayed up to several months after acute infection (window period).
• Seroconversion with the ELISA antibody test occurs in 50% of patients within 9 weeks of exposure, 80% of patients within 15 weeks of exposure, and at least 97% of patients within 6 months of exposure.
• The ELISA test is highly sensitive but relatively nonspecific, resulting in a low positive predictive value in low-prevalence populations. Positive HCV ELISA antibody test results require confirmation by a quantitative viral load assay, such as HCV PCR.

HIV infection

• The average risk for HIV transmission after a percutaneous exposure to HIV-infected blood has been estimated to be approximately 0.3% and that after a mucous membrane exposure to be approximately 0.09%
• Increased risk for HIV infection was associated with exposure to a larger quantity of blood from the source person & exposure to blood from source persons with terminal illness, likely reflecting the higher titer of HIV in blood late in the course of the disease.
• Exposure to a source patient with an undetectable serum viral load does not eliminate the possibility of HIV transmission & though this risk is low but PEP and follow-up testing should still be offered.
• Clinicians should consider occupational exposures as ***urgent medical concerns*** *& PEP should be offered as soon as possible*, preferably within one hour of the incident. It may still be worth considering it up to 72 hours after the exposure, but the relative benefit of prophylaxis diminishes with time.
• Initiating therapy after a longer interval (1 week) might still be considered for exposures that represent an extremely high risk of transmission even if the HIV status of a source patient is unknown and the clinician anticipates that hours or days may be required to resolve this issue, antiretroviral medications should be started immediately rather than delayed.
• PEP regimens comprised of 3 (at times more) antiretrovirals for 4 weeks with careful evaluation for drug toxicity, potentially serious drug interactions with other drugs and drug resistance.
•**The current standard recommended regimen for PEP is a 28-day course of:**

Raltegravir (Isentress; RAL) 400 mg PO twice daily Plus

Truvada, 1 PO once daily (Tenofovir [Viread;TDF] 300 mg + emtricitabine [Emtriva; FTC] 200 mg)

TDF has been associated with renal toxicity and an alternative should be sought for those who have underlying renal disease. Zidovudine could be used as an alternative to TDF and could be conveniently prescribed in combination with lamivudine in combination called Combivir to replace both TDF and FTC (Truvada).
Alternatives to RAL include:
Kaletra (lopinavir 200 mg/ritonavir 50 mg) two tablets twice daily OR

darunavir plus ritonavir (RTV), etravirine, rilpivirine, atazanavir plus RTV, lopinivir plus RTV.
When a more cost-efficient alternative to RAL is required, saquinivir plus RTV could be considered.

The decision to offer HIV PEP to a pregnant or breast-feeding healthcare provider should be based on the same considerations that apply to any provider who sustains an occupational exposure to HIV. The risk of HIV transmission poses a threat not only to the mother but also to the fetus and infant, as the risk of mother-to-child HIV transmission is markedly increased during acute HIV infection during pregnancy and breast-feeding.
However, the decision to use antiretroviral drugs during pregnancy should involve both counseling and discussion between the pregnant woman and her clinician regarding the potential risks and benefits of PEP for both the exposed person and her fetus.
- There are potential risks associated with the use of a combination of stavudine and didanosine so this drug combination for PEP is not recommended in pregnancy.
- Efavirenz EFV should not be used during the first trimester. If EFV-based PEP is used in women, a pregnancy test should be done to rule out early pregnancy and she should be counseled to avoid pregnancy while taking FEV until after PEP is completed
- Though only limited data available on the safety of RAL during pregnancy, this regimen could be administered to pregnant woman as PEP.

Administration of antiretroviral triple-drug regimens to breast-feeding HIV-infected women has been shown to decrease the risk of transmission to their infants and breast-feeding should not be a contraindication to use of PEP when needed, given the high risk of mother-infant transmission with acute HIV infection during breast-feeding.
However; prolonged maternal antiretroviral drug use during breast-feeding may be associated with some increased infant hematologic toxicity as some of antiretroviral drugs are excreted in breast milk at variable concentrations. Some drugs result in high levels (lamivudine), while other drugs (PIs and tenofovir TDF) are associated with only limited concentrations into milk.
Ultimately, lactating women with occupational exposures to HIV who will take antiretroviral medications as PEP must be counseled to weigh the risks and benefits of continued breast-feeding both while taking PEP and while being monitored for HIV seroconversion.

Drug interactions between antiretroviral & others such as oral contraceptives, H2-receptor antagonists, and proton pump inhibitors, should be looked for.

HIV Postexposure management

• The HIV, HBV& HCV status, of the source patient & exposed worker should be determined.

• Monitor the exposed person for seroconversion after exposure.

After baseline testing at the time of exposure, follow-up testing should be performed at 6 weeks, 12 weeks, and 6 months after exposure for HIV, HBS & HCV & liver function tests should be performed and repeated at 3 & 6 months.

Extended HIV follow-up (for 12 months) is recommended for HCP who become exposed to a source who is coinfected with HIV and HCV.

• Start HIV PEP where appropriate & monitor for drug toxicity by testing at baseline and again 2 weeks after starting PEP. The exposed worker should be evaluated if any acute symptoms develop while receiving therapy (rash, fever, back or abdominal pain, pain on urination, blood in the urine, dark urine, yellowing of the skin or sclera, or symptoms of hyperglycemia).

• Consider the need for antibiotic therapy or hepatitis B immunization accordingly.

• Complete blood counts, renal and hepatic function tests (at baseline and 2 weeks after exposure; further testing may be indicated if abnormalities are detected)

Clinicians should educate the exposed workers to HBV, HCV & HIV about:

- Avoidance of alcohol and, if possible, medications that may be toxic to the liver
- Female workers should have a beta-hCG check to exclude pregnancy.
- Risk of transmission related to:
    - Blood-to-blood contact, including sharing personal care items that may have come in contact with another person's blood, such as razors or toothbrushes.
    - Sexual activity
    - Donating blood, plasma, organs, tissue, or semen
    - Perinatal transmission
- Exposed HCP should be advised to use precautions (barrier contraception and avoidance of blood or tissue donations, pregnancy) to prevent secondary transmission, especially during the first 6–12 weeks after exposure.
- Hepatitis B & C viruses do not spread via food or water and is not transmitted by:
    - Sharing eating utensils
    - Hugging, kissing, or holding hands
    - Coughing or sneezing
    - Breastfeeding: however, clinicians should advise women who may have been exposed to HIV to avoid breastfeeding for 3 months after the exposure

Prevention of avoidable exposure in an occupational setting:

First aid

- Contaminated needlestick, sharps injury, bite or scratch on broken skin: encourage bleeding; wash with soap and running water. *Do Not Squeeze or Scrub.*
- Blood or body fluid in the eyes, mouth & mucous membranes; irrigate with copious quantities of cold water**.**

General measures

- Wash hands before and after contact with each patient and before putting on and after removing gloves. Change gloves between patients.
- Cover with waterproof dressings any existing wounds, skin lesions and all breaks in exposed skin, and wear gloves if hands are extensively affected or contact with blood can be anticipated.
- Avoid sharps usage where possible and, where sharps usage is essential, exercise particular care in handling and disposal.
- Avoid wearing open footwear in situations where blood may be spilt, or where sharp instruments or needles are handled.
- Clear up spillage of blood promptly and disinfect surfaces.
- Pre-employment occupational health assessment should identify those with damaged skin like fissured hand eczema, who may be at higher risk of occupationally acquired infection and ensure that advice is given about minimizing any occupational health risk to which they may be exposed.
- Wear gloves when cleaning equipment prior to sterilization or disinfection, when handling chemical disinfectant and when cleaning up spillages.
- Follow safe procedures for disposal of contaminated waste.
- Use of new, single-use disposable injection equipment for all injections. Sterilisable injection should only be considered if single use equipment is not available and if the sterility can be documented with Time, Steam and Temperature indicators.
- Discard contaminated sharps immediately and without recapping in puncture- and liquid-proof containers that are closed, sealed and destroyed before completely full.
- Document the quality of the sterilization for all medical equipment used for percutaneous procedures.
- Disinfect instruments and other contaminated equipment.
- Handle soiled linen properly. (Soiled linen should be handled as little as possible. Gloves and leakproof bags should be used if necessary. Cleaning should occur outside patient areas, using detergent and hot water.)
- Train and assess all users in the correct use and disposal of sharps and sharps safety devices.

Hepatitis A

● Vaccination with the full, two-dose series of Hepatitis A vaccine is the best way to prevent HAV infection; this vaccine has been licensed for use in persons 12 months of age and older.
● Protective levels of antibody to HAV could be present for at least 25 years in adults and at least 14–20 years in children.
● Immune globulin IG is available for short-term protection (approximately 3 months) against Hepatitis A, both pre- and post-exposure but must be administered within 2 weeks after exposure for maximum protection.
● Vaccine can be used if IG cannot be obtained.
● Persons who have recently been exposed to HAV and who have not been vaccinated previously should be administered a single dose of single-antigen Hepatitis A vaccine or IG (0.02 mL/kg) as soon as possible, *within 2 weeks after exposure.*
The guidelines vary by age and health status:
◘ for healthy persons aged 12 months–40 years, single-antigen Hepatitis A vaccine at the age-appropriate dose is preferred to IG because of the vaccine's advantages, including long-term protection and ease of administration, as well as the equivalent efficacy of vaccine to IG.
◘ for persons aged 40 years and older, IG is preferred because of the absence of information regarding vaccine performance in this age group and because of the more severe manifestations of Hepatitis A in older adults. The magnitude of the risk of HAV transmission from the exposure should be considered in decisions to use vaccine or IG in this age group.
◘ IG should be used for persons with expected decreased response to hepatitis A vaccine or those at increased risk of severe or fatal hepatitis A infection; including children ≤ 12 months & adults ≥ 40 years of age (particularly adults ≥ 75 years), persons who are allergic to the vaccine or a vaccine component, those with chronic liver disease and immunocompromised persons.

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Table 1: Risk for Transmission of Hep. B, C & HIV Viruses after Needlestick

Source	Risk
HBV HBeAg + HBeAg -	 22.0% - 30.0% 1.0% - 6.0%
HCV+	1.8%
HIV+	0.3%

Table 3: Hepatitis C Post-Exposure Management According to Baseline Test Results

Clinical Scenario	Follow-Up
Source patient is HCV-antibody negative	No further testing or follow-up is necessary for source patient or the exposed worker[a]
Source patient is unavailable or refuses testing	Exposed worker: Follow-up HCV antibody at 3 & 6 months[a]
Source patient is HCV-antibody positive and HCV RNA negative	Manage the exposed worker as if the source patient has chronic hepatitis C [b]
Source patient is positive for both HCV antibody and HCV RNA & Exposed worker is HCV-antibody negative	Source patient: Manage as chronic hepatitis C regardless of status of exposed worker Exposed worker: Follow up
Exposed worker tests positive for both HCV antibody and HCV RNA	Counsel and manage as chronic hepatitis C

[a] If at any time the serum ALT level is elevated in the exposed worker, the clinician should test for HCV RNA to assess for acute HCV infection.
[b] A single negative HCV RNA result does not exclude active infection.

Table2: Recommended Post-Exposure Prophylaxis for Hepatitis B Virus

Vaccination and/or antibody response status of exposed person[a]	Treatment when source patient is:		
	HBsAg positive	**HBsAg negative**	**Source unknown or not available for testing**
Unvaccinated/non-immune	HBIG[b] ×1; initiate HBV vaccine series	Initiate HBV vaccine series	Initiate HBV vaccine series
Previously vaccinated,[c] known responder[d]	No treatment	No treatment	No treatment
Previously vaccinated,[c] known non-responder[d]	HBIG[b] ×1 and initiate revaccination[e] or HBIG[b] ×2	No treatment	No treatment unless known high-risk source; if high-risk source,[f] then treat as if source were HBsAg positive
Previously vaccinated,[c] antibody response unknown	Single vaccine booster dose	No treatment	No treatment unless known high-risk source; if high-risk source,[f] then treat as if source were HBsAg positive
If still undergoing vaccination	HBIG[b] ×1; complete series	Complete series	Complete series

[a] Persons who have previously been infected with HBV are immune to re-infection and do not require PEP.
[b] Dose 0.06 mL/kg intramuscularly.
[c] Vaccinated with full three-dose series.
[d] Responder is defined as person with previously documented adequate levels of serum antibody to HBsAg (serum anti-HBs ≥10 mIU/mL); non-responder is a person with previously documented inadequate response to vaccination (serum anti HBs < 10 mIU/mL).
[e] The option of giving one dose of HBIG and re-initiating the vaccine series is preferred for non-responders who have not completed a second three-dose vaccine series.
For persons who previously completed a second vaccine series but failed to respond, two doses of HBIG are preferred.
[f] High-risk is defined as sources who engage in needle-sharing or high-risk sexual behaviors, and those born in geographic areas with HBs-Ag prevalence of ≥ 2%.