LEAP
GLOBAL MISSIONS

ATTACHMENT - HIV & HEPATITIS C EXPOSURE DETAIL PROTOCOL

The potentially grave consequences of exposure to body fluids from people infected with HIV and Hepatitis C have prompted development of policies and procedures designed to reduce the risk in healthcare personnel (HCP). The most important practice is the use of available measures to prevent such exposures. Although the incidence of needlestick injuries has been reduced by advances in education, needle disposal, engineering changes (e.g., needleless devices, safety needles) and personnel protection, institutions and healthcare professionals must continue to assume responsibility in further lowering the risk.

A. RISK OF TRANSMISSION OF HIV

The risk of transmission of HIV infection following inadvertent exposure varies widely depending upon the type of exposure. The risk is increased when the source has a high viral load, the volume is large, and the exposure is deep. The healthcare personnel (HCP) at highest risk are those who have percutaneously been inoculated with blood from an HIV-infected source. All known seroconversions have occurred with exposure to blood, bodily fluids, or viral cultures.

Risk by exposure type — The risk of becoming infected with HIV after exposure to body fluids from an HIV-infected patient is low. In the United States, there were 58 confirmed and 150 possible cases of occupationally-acquired HIV reported to the Centers for Disease Control from 1985 to 2013; there was only one confirmed case from 2000 to 2012

A review of prospective studies of seroconversion following occupational exposure to an HIV infected source in the era before the introduction of potent antiretroviral therapy (ART) found the following:

- HIV transmission occurred in 20 of 6135 cases (0.33 percent) following percutaneous exposure
- One case of HIV was transmitted out of 1143 exposures (0.09 percent) on the mucosa of HCP
- There were no cases after 2712 intact skin exposures

A similar frequency of HIV seroconversion after needlestick injury (0.36 percent) was found in a later report from the Centers for Disease Control and Prevention (CDC) Cooperative Needlestick Surveillance Group and in another meta-analysis (0.23 percent). The risk of HIV infection following an occupational mucosal exposure was subsequently estimated to be 0.03 percent.

Risk factors for seroconversion — A CDC case-control study of needlestick injuries from an HIV-infected source in the United States, the

United Kingdom, France, and Italy included 33 cases who seroconverted and 655 controls. The study found that the following factors, each of which presumably reflected exposure to a higher number of viral particles, increased the risk of acquiring HIV after a needlestick injury:

- Deep injury (odds ratio [OR]15)
- A device visibly contaminated with the patient's blood (OR 6.2)
- Needle placement in a vein or artery (OR 4.3)
- Terminal illness in the source patient (OR 5.6)

The majority of cases were injured by a hollow bore as opposed to a solid needle.

The HIV load is another important risk factor for transmission based upon studies of sexual transmission in discordant couples and rates of perinatal transmission. Early studies in HCP did not directly address this issue because they were based upon data obtained before viral load measurement was routinely available. The observed correlation of transmission risk with a source with late-stage AIDS is thought to be a surrogate for high HIV viral load.

In addition, long work hours and sleep deprivation among medical trainees result in fatigue, which is associated with a threefold increase in the risk of needle-stick injuries A survey performed among 699 surgeons-in-training at 17 medical centers found that the mean number of needlestick injuries by the fifth (final) year of residency was *7.7* and that 99 percent of residents had at least one needlestick injury.

Furthermore, approximately one-half had a needlestick injury involving a high-risk patient, and more than half of the most recent injuries had not been reported; the most common reason was lack of time. Despite the concerning number of exposures in this study, there has never been a confirmed case of HIV transmitted to a surgeon through occupational exposure in the United States.

Documented seroconversions — In the United States, 58 confirmed cases of occupationally acquired HIV infection were reported to the CDC between 1985 and 2013

In Europe, 35 documented seroconversions following occupational exposure and 85 possible occupationally acquired HIV infections were reported as of 2002

Cases of HIV seroconversion following occupational exposures are not systematically documented and reported in most other regions of the world.

B. RISK OF TRANSMISSION OF OTHER BLOODBORNE PATHOGENS

The risk of transmission of hepatitis B virus (HBV) to unvaccinated healthcare personnel or a vaccinated nonresponder is much higher than HIV. **The risk of hepatitis C virus transmission from an infected source is about sixfold greater compared with HIV (1.8 versus 0.3 percent).** Management of healthcare personnel exposed to these viruses, including post-exposure prophylaxis for hepatitis B virus, is discussed separately. (See "Prevention of hepatitis B virus and hepatitis C virus infection among healthcare providers".)

C. POST-EXPOSURE MANAGEMENT

The management of healthcare personnel (HCP) immediately after a significant exposure to blood or body fluids from HIV-infected patients is critically important in reducing the likelihood of transmission.

1. Initial actions following exposure

The initial response to any exposure of HCP to blood should be immediate cleansing of the exposed site. For skin exposures, the area should be washed with soap and water. Small wounds and punctures may be cleansed with an antiseptic 1 hand hygiene agent, since alcohol is virucidal to HIV, hepatitis B virus (HBV), and hepatitis C virus (HCV). Other antiseptics such as iodophors, chloroxylenol (PCMX) and chlorhexidine (CHG) also inactivate HIV.

For mucosal surface exposure, the exposed mucus membranes should be flushed with copious amounts of water. Eyes should be irrigated with saline or water. There is no evidence that expressing fluid by squeezing the wound will further reduce the risk of bloodborne pathogen transmission. Documentation of the exposure - Clinical information on the source patient for the exposure and the recipient HCP should be documented. This includes risk factors and serologic tests for HIV, and hepatitis B and C. The nature and time of the exposure should also be described.

2. Definition of exposure

In this topic and when evaluating HCP at risk for occupational infection with HIV, "exposure" is defined as contact with potentially infectious blood, tissue, or body fluids in a manner that allows for possible transmission of HIV and therefore requires consideration of post-exposure prophylaxis (PEP).

Such potentially infectious contacts are:

- A percutaneous injury (eg, a needlestick or cut with a sharp object)

• Contact of mucous membrane or nonintact skin (eg, exposed skin that is chapped, abraded, or afflicted with dermatitis)

Body fluids of concern include:

- Body fluids implicated in the transmission of HIV: blood, semen, vaginal secretions, other body fluids contaminated with visible blood.
- Potentially infectious body fluids (undetermined risk for transmitting HIV): cerebrospinal, synovial, pleural, peritoneal, pericardial, and amniotic fluids.
- Fluids that are not considered infectious unless they contain blood include feces, nasal secretions, saliva, gastric secretions, sputum, sweat, tears, urine, and/or vomitus.
- Intact skin is an effective barrier against HIV infection, and contamination of intact skin with blood or other potentially contaminated fluids is not considered an exposure and does not require PEP.

3. Determining HIV status of the source

If unknown, the presence of HIV infection in the source patient should be determined with a rapid HIV test. If testing in the source patient is delayed, PEP should still be initiated while awaiting test results. If the source is found to be HIV negative, PEP should be discontinued. (See 'Indications for prophylaxis' below.)

Clinicians should also be aware of rare case reports where the source patient tested HIV seronegative and was later found to have primary HIV infection. These rare events do not alter guidelines for routine antibody testing but do highlight the importance of testing for HIV RNA if clinically indicated. It is important to be cautious in interpretation of low viral loads (<5000 c/mL) since these are often lab errors and patients with acute retroviral syndrome usually have very high viral loads.

4. Counseling of healthcare personnel

Risk assessment is particularly important for HCP to make educated decisions about PEP since the consequences are great and the stress is extraordinary. They should also be well informed of the benefits and risks of PEP and of the importance of close follow-up. Specifically, the following issues should be discussed with exposed HCP:

HCP should be informed of the risk associated with the specific exposure experienced. (See 'Risk of transmission of HIV' above.)

With percutaneous or sharps injuries from an HIV-infected source, the risk of HIV infection averages 3/1000 but varies greatly depending on the inoculum size (source viral load and volume of blood), the depth of penetration, and exposure to a hollow bore versus suture needle.

- Exposure of source blood to intact skin is considered "no risk". There are no confirmed cases of HIV transmission in HCP with skin abrasions, cuts, sores, or other breaches in skin integrity, but a theoretical risk is estimated at 1/1000.
- All documented transmissions have involved source blood, bloody body fluids, or laboratory cultures of HIV. Bites have never been implicated in transmission to HCP, but have resulted in HIV transmission in other settings.
- The risk is likely considerably lower if the source has unknown HIV status or if prior tests were negative.
- The HCP may also be at risk for other bloodborne pathogens, such as hepatitis B or C.
- The HCP should be advised to practice safe sex or abstain until serologic testing in the source is reported negative.
- The efficacy and disadvantages of PEP should be discussed. (See 'Post-exposure prophylaxis' below.)
- Indirect evidence shows that post-exposure prophylaxis with zidovudine alone can reduce the risk of HIV infection. Current multidrug regimens are likely much more effective in preventing infection. However, even when properly provided, PEP does not assure complete prevention of HIV infection.

The goal is to initiate PEP within one to two hours of exposure; the benefit of PEP is diminished with each hour delay in initiation. PEP is typically not recommended after a delay of more than 72 hours. Risk reduction strategies should be employed to prevent transmission of HIV should the HCP acquire infection,

In the event of HIV infection post-exposure, the greatest risk of transmission to other individuals is in the first 6 to 12 weeks. Exposed HCP should be instructed on measures to reduce the potential risk of HIV transmission to others. This usually means condom use or abstinence from sex and refraining from blood, plasma, organ, tissue, and semen donation until the six-month serologic test is negative.

There is no need to modify a healthcare provider's patient-care responsibilities after an exposure.

Follow-up is important to identify HIV infection or adverse effects of the PEP regimen, if administered. (See 'Testing for HIV' below and 'Patient monitoring' below.)

Baseline and follow-up testing for HIV should be performed to see if seroconversion occurred. The frequency and duration of follow-up testing depends upon the type of HIV test being used (eg, third versus fourth generation test). (See 'Testing for HIV' below.)

- Exposed HCP should report any febrile or "mononucleosis-like" illness so they can be evaluated for an acute retroviral syndrome. This should include testing for HIV RNA since early antiretroviral therapy has important potential benefits. (See "Acute and early HIV infection: Clinical manifestations and diagnosis".)

For those who opt to take PEP, blood testing should be done at two and four weeks to evaluate for drug toxicity.

Specific counseling is warranted for women of childbearing age. (See 'PEP during pregnancy' in the complete UptoDate article.)

5. Testing for HIV

Baseline and follow-up serologic testing for HIV should be performed in all HCP exposed to HIV to see if seroconversion occurred. The majority of individuals who seroconvert will do so within the first three months. Testing should be performed even among those who receive PEP. (See 'Selection of antiretroviral therapy' below.)

All exposed individuals should have a baseline HIV test immediately after the exposure. The frequency and duration of follow-up testing depends upon the type of HIV test being used. A fourth generation antibody-antigen test is preferred since this test will detect seroconversion earlier. If this assay is used, follow-up testing should be performed at six weeks and four months after the exposure. If a third generation antibody test is used, repeat HIV testing should occur at six weeks, three months, and six months following the exposure. A detailed discussion on the different types of HIV assays is found elsewhere. (See "Screening and diagnostic testing for HIV infection".)

Extended follow-up for HIV testing (eg, for 12 months) is recommended for any HCP who becomes infected with HCV after exposure to a source coinfected with HIV and HCV This recommendation is based upon a case report of delayed HIV seroconversion in a HCP who acquired HIV and HCV infection simultaneously through a needlestick exposure. Extended follow-up may also be considered in exposed persons with a medical history suggestive of impaired humoral immunity; however, there are no data to determine a specific approach.

Routine monitoring of plasma HIV load to detect early infection should not be performed since there is a risk of false positive test results. HIV load testing should only be obtained if there is clinical evidence of acute HIV infection.

D. POST-EXPOSURE PROPHYLAXIS

Post-exposure prophylaxis (PEP) using a three-drug regimen should be offered to healthcare personnel (HCP) with a percutaneous, mucous membrane, or nonintact skin exposure to body fluids of concern (eg, blood or blood tinged fluids) if the source patient is, or is suspected to be, HIV-infected.

PEP should be discontinued if testing shows that the source patient is HIV-negative, unless there is concern that the source is acutely infected with HIV.

In all cases, the decision to administer PEP must weigh the risk of infection with HIV against the toxicity and inconvenience of PEP, although in general the newer regimens are very well tolerated with minimal side effects. The individual preferences of the exposed HCP will generally determine the decision about whether to proceed with PEP.

Timing — PEP should be initiated as soon as possible. The goal is to start within one to two hours (or earlier) after exposure, often using a "starter pack" with appropriate drugs that are immediately available. It is likely that a delay in initiating PEP can reduce efficacy

For most HCP, we do not initiate PEP if more than 72 hours have elapsed after the initial exposure; PEP is likely to be less effective when administered after that period of time However, we offer three-drug PEP after a longer interval to patients with a very high-risk exposure (eg, sharps injuries from a needle that was in an artery or vein of an HIV-infected source patient). For such HCP, The United States Public Health Services suggests that PEP can be offered up to one week after the exposure Selection of antiretroviral therapy

Preferred antiretroviral regimens for PEP We suggest a three-drug regimen for all HCP who opt for PEP. This approach is supported by the United States Public Health Service, the International Antiviral Society-USA panel, and the World Health Organization. LEAP has decided on the following PEP regimens for HCP with an occupational exposure to HIV, provided the source does not have detectable virus with known resistance to these agents. The regimen is Truvada (Tenofovir-emtricitabine 300/200mg), Prezista (darunavir 800 mg), and Norvir (ritonavir 100 mg) – for 30 days of one tab daily of each.

For individuals with significant renal disease, or if there is concern about significant risk of resistant HIV virus, please see the entire UptoDate article.

Rationale for preferred PEP regimens — Since there are no data on the most efficacious PEP regimens for persons with exposure to HIV, selected medications are chosen based upon their known efficacy for the treatment of HIV, side effect profiles, patient convenience (eg, pill burden and dosing frequencies), and completion rates.

PEP in resource-limited settings — The World Health Organization recommends PEP for HCP following an exposure to potentially infectious body fluids from a patient who is or is suspected to be HIV-PEP should not be delayed pending the source's HIV test results, especially in areas where HIV is firmly established in the general population (eg, HIV prevalence consistently exceeding 1 percent among pregnant women) In such settings, it should be presumed that sources with an unknown HIV status pose a risk of infection. The WHO guidelines suggest a three-drug regimen using tenofovir-emtricitabine as the preferred NRTI combination and a ritonavir-boosted protease inhibitor (lopinavir or atazanavir) as the third agent.

These agents are widely available in low- and middle-income countries. Where available, raltegravir, boosted darunavir, or dolutegravir can also be

used as a third agent. If a three-drug regimen is not available, a dual nucleoside regimen with tenofovir-emtricitabine can be used.

Duration of therapy - The recommended duration of PEP is four weeks because a course of zidovudine for this duration appeared protective in some studies; however, the optimal duration of PEP is unknown. It is biologically plausible that shorter durations of PEP would be as effective, especially with more potent agents. However, until further data are available, we administer PEP for four weeks. PEP should be discontinued if testing shows that the source patient is HIV-negative.

Patient monitoring — HCP should be seen in follow-up within 72 hours of the exposure and starting PEP At that visit, clinicians can evaluate if PEP should be continued and if side effects are present. *(Obviously on a LEAP trip the exposed volunteer should have ongoing discussion with the team medical advisor/ pediatrician regarding tolerance of the medication, and information which may help determine whether to continue PEP or not.)*

Exposed HCP should be seen again two weeks after the exposure and have laboratory testing to assess for drug toxicity (see 'Laboratory monitoring' below). Adherence to the PEP regimen should be emphasized at each visit since experience with HCP indicates that only about 60 percent complete the recommended course of therapy

Laboratory monitoring — Patients who receive PEP should be monitored for drug toxicity. Testing should include a complete blood count including differential, and tests of hepatic and renal function at baseline and at two and four weeks after initiation of PEP Patients treated with a protease inhibitor should also be monitored for hyperglycemia. Additional testing may be indicated depending on the PEP regimen selected. (See "Selecting antiretroviral regimens for the treatment-naïve HIV-infected patient".)