The Use of Postexposure Prophylaxis For Occupational HIV Exposure

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"Will I lose my dignity
Will someone care
Will I wake tomorrow
From this nightmare?"
- Jonathan Larson, Rent

Occupational health is usually conceptualized in terms of safe work practices and educating workers about potential hazards. However, in the field of healthcare, there are additional occupational risks associated with exposure to disease-causing agents. One such risk is exposure to the human immunodeficiency virus, HIV.

As of 2001, the U.S. Centre for Disease Control (CDC) has reported 56 cases of HIV known to be transmitted through occupational exposure, with an additional 138 cases suspected to be caused by occupational exposure (CDC, 2001a). Health Care Workers (HCW) who are exposed to HIV may avoid infection with the use of immediate chemoprophylaxis treatment. This is called Post-Exposure Prophylaxis (PEP) and although little epidemiological evidence exists for its efficacy, many physicians agree that it could potentially prevent HIV infection if used appropriately.

Occupational Exposure to HIV

Unlike most cases of sexually-transmitted HIV, contact with mucosal surfaces during occupational exposure has been identified as the transmission route in only a minority of cases (CDC, 2001b). Usually, exposure is by percutaneous injury, which has a calculated risk of infection of 0.3% per episode

	Infection Status of Source Patient		
Exposure Risk	HIV+ class 1 • Asymptomatic or low known viral load	HIV+ class 2 • Symptomatic or high known viral load, or • Patient has AIDS, or • Acute seroconversion	HIV Status Unknown • No sample available for HIV testing • Ex. Deceased source patient
Less-Severe • Superficial injury • Injury with solid device • No visible blood on device	Basic 2-drug PEP regimen recommended	Extended 3+ drug regimen recommended	Generally no PEP warranted; consider basic 2-drug regimen for source or setting with HIV risk factors
More-Severe • Injury with large hollow-bore instrument • Deep puncture • Visible blood on device • Device previously in source patient's artery or vein	Extended 3-drug PEP regimen recommended	Extended 3+ drug PEP regimen recommenced	Generally no PEP warranted; consider basic 2-drug regimen for source or setting with HIV risk factors

Table 1: Recommended PEP regimens based on occupational exposure risk and infection status of source patient. Modified from CDC. Updated U.S. public health service guidelines for the management of occupational exposures to HBV, HCV and HIV and recommendations for postexposure prophylaxis (CDC, 2001a).

(95% CI=0.2%-0.5%) (Henderson, Saah, Zak et al., 1986; Bell, 1997). Hollow-bore needlestick injuries have been responsible for most HIV infections among HCWs, likely the result of the larger inoculum of source-patient blood compared with that found on solid surgical instruments (Henderson & Gerberding, 2003). The CDC formulates occupational PEP guidelines based on the likelihood that the source-patient is infected with HIV and whether a sufficient amount of blood or bodily fluid was transmitted to result in infection, given the specific transmission route.

Basic versus Expanded PEP

An important consideration with occupational HIV exposure is that PEP is prescribed based not on clinical measures, but on the risk profile associated with the exposure. This is to avoid delay in onset of treatment, which has a theoretically preventative effect that limits the proliferation of HIV during the short time the virus is localized to dendritic cells and regional lymph nodes (Henderson & Gerberding, 2003). The CDC has issued guidelines indicating which exposure events are considered "less-severe" and "more-severe." Based on the risk associated with exposure and any other relevant risk factors, the guidelines recommend no PEP, a basic two-drug regimen of PEP, or an expanded multi-drug regimen of PEP (CDC, 2001a). Table 1 shows a simplified version of the CDC's guidelines. The duration of PEP has been set by the CDC at 28 days, with the understanding that it is more beneficial to adjust the number or type of drugs to accommodate side effects rather than stop PEP prematurely (CDC, 2001a).

Antiretrovirals (ARVs) Used For PEP

The main drugs used in PEP target either reverse transcriptase function or protease activity. Nucleoside/tide Reverse Transcription Inhibitors (NRTI/NtRTI) block reverse transcription of viral RNA into complementary DNA (cDNA). NRTI and NtRTIs work by substituting faulty nucleotides into the elongating cDNA during reverse transcription. This results in dysfunctional cDNA or cDNA chain termination. The first antiretroviral agent approved for HIV treatment was the NRTI zidovudine (AZT) (Fischl, 2003). In both basic and extended regimens of PEP, zidovudine is one of the drugs preferentially recommended. The basic PEP regimen uses zidovudine with another NRTI called lamivudine (CDC, 2001a).

Almost all expanded PEP regimens include one Protease Inhibitor (PI) in combination with two NRTI/NtRTIs. After mRNA translation, viral protease is required to cleave primary structure polypeptides for subsequent folding and assembly into viral proteins. PIs inhibit viral proteases, resulting in dysfunctional HIV proteins that assemble into immature, non-infectious HIV virons. Ritonavir (RTV) and lopinavir (LPV) are two PIs suggested for use in combination with zidovudine and lamivudine in the preferred expanded PEP regimen (CDC, 2001a). Ritonavir has low affinity for human aspartic proteases such as renin and pepsin, meaning cytotoxicity is low in concentrations used for ARV therapy and PEP (Danner, 2003). In addition to protease inhibition, ritonavir is used to boost the efficacy of other PIs by inhibiting enzymes that metabolize them. For this reason, it is often combined with other PIs in a single capsule, such as the ritonavir/lopinavir combination recommended in expanded PEP. Lopinavir is a potent, highly-specific "second generation" PI that is active against ritonavir-resistant HIV-1 isolates (Johnson & Kuritzkes, 2003).

Although the only known epidemiological study on PEP had a small sample size and was retrospective in nature, its findings infer that the prognosis does look good for most occupational exposures. Zidovudine alone appears to provide an 80% protective effect (Henderson & Gerberding, 2003), and the combination of other ARVs administered within hours of exposure and maintained for the full course of the PEP regimen suggest that seroconversion can be avoided in many cases.

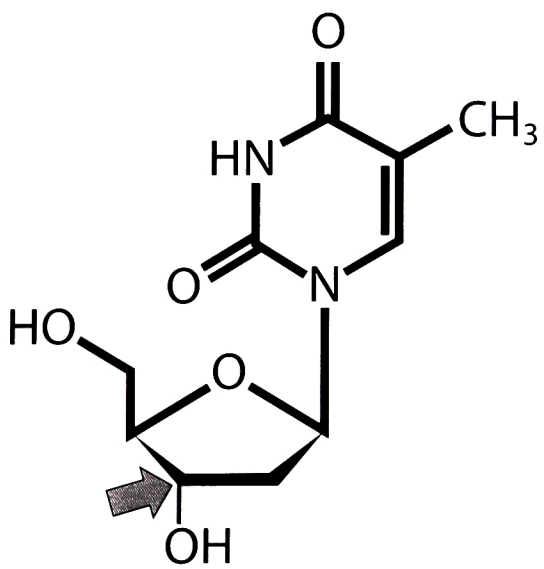

Figure 1: Thymidine nucleoside with 3' hydroxyl group. The arrow points to the 3' carbon.

Toxicity, Drug Interactions and Side Effects of PEP

A substantial number of HCWs are unable to complete the four-week regimen of PEP due to ARV side effects (Wang, Panlilio, Doi et al., 2003). Side effects range from non-life-threatening adverse events to more severe cases of hyperglycemia, hepatic steatosis and hyperlipidemia (CDC, 2001a). In a study of 449 HCWs who took PEP, 76% identified at least one adverse event, in addition to common side effects that include nausea (57%), malaise (38%), headache (18%), vomiting (16%), diarrhea (14%) and myalgia (6%) (Wang, Panlilio, Doi et al., 2003). Serious or life-threatening drug interactions are also of concern, particularly with PI usage. Ritonavir/lopinavir has been associated with accelerated clearance of certain drugs, increased serum cholesterol and triglycerides and severe events such as cardiac arrhythmia, respiratory depression and ischemia of tissues (Johnson & Kuritzkes, 2003). For this reason, several over-the-counter and prescription drugs are contraindicated when PIs are included in the PEP regimen.

Patient monitoring is essential during PEP for early drug toxicity detection. When drug toxicity is detected, a modified PEP regimen is suggested along with expert consultation.

Sociopolitical Considerations

Part of the discourse surrounding HIV legal and ethical issues is framed as a balancing act between protecting the rights of the individual and the rights of society (OLRC, 1992). Some HCWs are fortunate enough to know their source-patient's HIV status, however, it is not unreasonable that an exposure could occur without this knowledge. Attaining HIV status information is often seen as a privacy issue, whereas not attaining this information may have deleterious consequences for the exposed HCW. People with HIV infection remain stigmatized in society, making the acquisition of HIV status information without consent a difficult prospect.

Economic constraints are another important consideration with respect to any form of ARV therapy, including PEP. For people living in Ontario who are infected with HIV, ARV drugs are partially covered under the Ontario Drugs Benefit Plan. However, individuals who are not yet diagnosed as HIV-positive but have been prescribed PEP generally must cover the costs associated with the drug regimen or apply for occupational compensation (Ontario Health Coalition, 2002).

Another consideration worth mentioning is the impact PEP could have on a person's life. It is possible that family life, job productivity and self-efficacy could be negatively affected if side effects persist, which is often the case. This highlights the need for proper counselling and monitoring of side effects and regimen adherence. Indeed, the high rate of PEP discontinuation among occupational exposure cases has been attributed to lack of HCW counselling regarding potential side effects and the importance of regimen completion (Wang, Panlilio, Doi et al., 2003).

Conclusion

Occupational exposure among healthcare workers has not been identified as a substantial transmission route for HIV. However potential exposure justifies careful consideration of the postexposure treatment options available. The use of postexposure prophylaxis can prevent the onset of HIV infection if ARV drugs are administered correctly and within a short timeframe. The drug regimen prescribed must take into consideration the severity of the exposure, the HIV status of the source patient—whether known or unknown—and potential drug interactions or debilitating side effects. Non-medical consequences of PEP must also be addressed and sufficient counselling is necessary to accompany medical treatment. M

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