

WVU Occupational Medicine Program for evaluation and treatment of persons exposed to Lentivirus Vectors

Hazard Description:

- Lentivirus vector systems are derived from HIV and similar viruses because of being very effective at inserting genetic material into the genome of target cells. While most researchers are working with replication-incompetent vector systems, these systems retain the ability to deliver their genetic material to human cells they contact. The goal of this program is to decrease the risk of integration of the experimental DNA into the genome of researchers who experience an accidental exposure.

Considerations in program design

- Some lentiviral systems are “targeted” and will only infect one cell type (this is called tropism). However this “targeting” is often imprecise and other cell types can also be infected, especially in other species. For example, a particular virus system targeted at mouse kidney cells might infect other cell types in a human. It is unclear if a statement from a vendor that their viral system did not infect a specific human cell line means that it cannot infect all human cells.
- Some viral systems use bits of genetic material from other viruses (like CMV and arboviruses) which may alter tropism in humans.
- The lentiviral vector systems used in the laboratory are generally “replication incompetent”, meaning that they cannot cause an “infection” that will become self-perpetuating in the host and produce more virus. There are several “generations” of replication incompetence, with the goal of making it ever more difficult for reversion to wild type (replication competent) virus to occur.
- Replication incompetent vectors DO possess the ability to insert their genetic material into human cells, with the potential of infecting 1 human cell per viral particle (usually millions or more per ml).
- Generic constructs used in the lab are typically designed to alter the function of their target cells. The long-term impact of these specific alterations on animal cells often unknown.
- While the impact of experimental genetic material on human cells is usually unknown, there is presumed to be some level of risk from all inserted genetic material.
- There is likely a greater risk for genetic constructs that include oncogenes, proto-oncogenes, cancer promoters, and toxins. It is hoped that future refinement of this program will include risk assessment tools to better classify the human health risk from different vector systems and genetic constructs. At present this program will treat all viral constructs as hazardous, and implement measures to decrease immediate risk.
- The impact of exposure to a lentiviral vector in a person who is already HIV positive is unclear. There is a concern that the “wild type” HIV will supply the viral attributes necessary to produce replication-competent virus propagating the research DNA in the infected person. WVU does not screen researchers for HIV. This program is designed to decrease the risks for persons who are both HIV positive and HIV negative. Thus there is one post-exposure protocol for all persons.

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- The average viral load of an untreated HIV patient is 100,000 viral copies/ml of serum. Most lab viral constructs are at least this concentrated and would have at least the same risk of infection as a similar route of blood exposure from a “high viral load” HIV patient.

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- Table 1 (below) is from the current (2015) New York City Health Department recommendations for assessment of post-exposure HIV risk. Please see the original document for references. It is assumed that the risk from lentiviral vector systems, based upon the “route” of exposure, is similar to the risk from exposure to blood from an HIV patient via the same route.

Table 1: Estimated Per-Act Probability of Acquiring HIV From a Known HIV-Infected Source by Exposure Act (See ^a)

Type of Exposure	Risk per 10,000 Exposures
Parenteral	
Blood Transfusion	9,000
Percutaneous (needlestick)	30
Other^b	
Biting	Negligible
Spitting	Negligible
Throwing body fluids (including semen or saliva)	Negligible
Mucous Membrane Exposure	9

Modified from the Centers for Disease Control and Prevention. HIV Transmission Risk, fact sheet; July 2012. Available at <http://www.cdc.gov/hiv/law/transmission.htm>.

^a Factors that increase the risk of HIV transmission include early and late-stage HIV infection and a high level of HIV in the blood. Factors that reduce the risk of HIV transmission include low level of HIV in the blood and the use of ART.

^b HIV transmission through these exposure routes is technically possible but extremely unlikely and cases are not well documented.

Fifty-eight cases of documented seroconversion following occupational HIV exposure were reported to the CDC through 2013.⁸ The most recent confirmed case of occupationally acquired HIV that was reported occurred in 2008; however, no other cases have been reported to the CDC since 1999.⁸ The mean risk following an occupational percutaneous exposure is roughly 1 in 300 (0.3%). However, the mean risk may be significantly higher in cases in which more than one risk factor is present (e.g., in persons who incur a deep injury with a hollow-bore needle from an HIV-infected patient with a high viral load). Although the effect of viral load level has not been studied in the setting of occupational exposures, studies have shown that the probability of sexually transmitting HIV is correlated with HIV viral load.⁹⁻¹¹ The risk of transmission can be expected to be increased in the setting of high HIV viral load levels in the source patient.

After a mucous membrane exposure, the average risk of seroconversion is approximately 9 in 10,000 (0.09%). In this analysis, the use of ZDV PEP by HCWs in the CDC study was shown to reduce the risk of HIV acquisition by 81%.³

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MEDICAL RESPONSE TO LENTIVIRUS EXPOSURE – Basic Steps

1. Wash contact site with soap and water
2. Assess magnitude of risk
3. Initiate anti-retroviral prophylaxis, timing goal: within 2 hours
4. Schedule for followup in Occupational Medicine Clinic
5. In the Occ Med clinic a protocol-specific risk assessment (with the assistance of the Biosafety officer and appropriate scientists) will be completed and a decision made to continue or suspend the antiretroviral treatment. Information to be considered includes:
 - a. The viral vector system (generation) being used
 - b. The specific genes coded for
 - c. The tropism of the vector system (what types of cells it is known to infect)
 - d. The HIV status of the exposed person
6. Based upon the outcome of step 5. A decision will be made to suspend, or continue Antiretroviral therapy out to 2 weeks or 4 weeks (in cases involving oncogenes or genes for toxins)

The final page of this program shall be printed on colored paper and distributed to researchers who are working with lentiviral vector systems in their labs. These papers should be hung on the inside of lab doors where lentiviral systems are being used, manipulated, or stored. Following an exposure the researcher shall take this sheet to the Emergency Room or Occupational Medicine clinic to initiate care

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TREATMENT RECOMMENDATIONS

TO THE EXPOSED PERSON:

1. Cleanse the exposed area with soap and water (or eye wash) for 15 minutes
2. Seek IMMEDIATE Medical Care **(Take this sheet with you)**
 - a. Monday-Friday, 8-4:30: Call WVU Occ Med - 304-293-3693
 - b. WVU/Ruby Memorial Emergency Room
3. Schedule an appointment for ongoing care
 - a. WVU Occupational Medicine 304-293-3693

TO THE EMERGENCY PHYSICIAN:

1. Verify exposure area has been washed/irrigated
2. Assess the risk of the exposure. For percutaneous exposure (needlestick) or exposure that includes mucosal surfaces of the eyes, please initiate post-exposure prophylaxis as outlined below:
3. Please draw the following screening labs: HIV 1 & 2 screening antibody
4. Obtain medication from the supply used for hospital needlesticks and Dispense Antiviral medication –
Truvada 200/300 Daily
Raltegravir 400mg BID
Please have the patient take the **initial dose immediately**
5. Give an Rx for the balance of 1 week of therapy. (6 doses Truvada & 12 doses Raltegravir)
6. Refer the patient for follow-up in the occupational medicine clinic (304-293-3693), leave a message during off hours and we will call the worker the next business day to schedule their appointment.)
 - a. Required message contents:
 - i. Patient's name & Chart Number
 - ii. Injury type (i.e. needlestick with Lentiviral vector)
 - iii. Best daytime contact **PHONE NUMBER** for patient
7. Notify the worker that this medication can be expensive, however it is very important that they start taking the medication. They will likely need to pay for the initial fill of the medication, however they will be reimbursed either by worker's compensation or the University. We will assist the worker with completing their WC-1 form and getting reimbursed at the office visit.

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Date