

‘A Case Scenario cutting across different HIV Prevention issues’

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Abstract

Background Most new HIV infections are acquired from stable, long-term partners. HIV serodiscordant relationships are among the most vulnerable to acquiring???? It is not uncommon getting exposed to body fluids of an HIV infected partner in a serodiscordant (magnetic couples) set ups. This is an interesting case scenario cutting across many issues about the transmissibility of HIV infection in. There may be queries from apprehensive people – seeking advice reg?? HIV’s probability of acquisition under some very uncommon conditions which may be helpful for training/teaching purposes

Objectives The scenario (A non-HIV Patient getting exposed to semen of a HIV positive man with an undetectable viral load –VL at the hand having an open cut) is an interesting, educative and unique case scenario as it involves almost all issues related to HIV prevention i.e. scanty information --withholding his/her name and gender possibly due to stigma/discrimination issues forwarded by the questioner and issues involving responses to various situations in serodiscordant couples (‘magnetic couples’) exposure in **an unique non-occupational yet non-sexual mode**, counseling& testing issues, initiating nPEP (Non-occupational Post Exposure Prophylaxis) and PrEP (Pre-Exposure Prophylaxis), TasP (Treatment as Prevention) and HTPN 052 Study. The importance of answering this kind of scenarios lies in the fact that it would help many--including the questioner itself.

Methods Descriptive study discussing the different aspects of HIV Prevention.

Results The questioner’s HIV-acquisition risks are extremely low (theoretically) & unwarranted still we will try to put his/her fears to rest by examining the issues involved in this case critically and coming up with scientifically based explanations and accordingly advice him/her taking into the considerations of HIV Testing and Treatment policies and Guidelines of the land available.

Conclusions This scenario is a very interesting one, requiring many basic concepts of prevention of HIV/AIDS for answering and may be used for teaching/training even medical professionals. The questioner’s HIV-acquisition risks are extremely low (theoretically) & unwarranted and we will try to put his/her fears to rest by examining the issues involved in this case critically and coming up with scientifically based explanations and accordingly advice him/her taking into the considerations of HIV Testing and Treatment Policies and Guidelines of the land available. The importance of answering this kind of scenarios lies in the fact that it would help other health professionals and questioners alike and may be useful in teaching/training settings.

Keywords: nPEP, PrEP, Discordant couple TasP

CASE SCENARIO IN QUESTION (this question was asked to me in a site for reply)

‘I am in a relationship with a positive undetectable man. I am neg. We refrain from oral and anal sex. Last night while masturbating some of his semen got on my hand and I had an open cut. I have not been able to sleep. I do have a question. Since we are in a monogamous relationship and he is undetectable????, should I get tested on same frequency. Going for testing freaks me out. I have not been tested since 3 months after his diagnosis which was three years ago’

Introduction

It is a case of providing inadequate information (about his/her gender, the HIV infected partner being on ART or not, age of cut in his /her hand, which part of the hand –palm or dorsum and has asked question about his/her going for testing of HIV at the frequency specified as per country Guidelines. With whatever little information we have from this person's history, it is to be advised to him/he that though probability of transmission is extremely low, but due to paucity of information provided and just to be very sure, about non-transmission of the virus, notwithstanding the negligibility of spread he /she should go for testing as per the country guidelines Considering all issues involved, It is suggested that HIV-antibody tests are to be done for the questioner as per the country's testing guidelines. This will enable the questioner not only to gain psychological peace of mind but also by knowing the status --whether negative or positive help him/her to lead healthy life. Though we expect the result to be negative, considering low risk, but, it is to be **remembered that decreased risk is not no risk**. Effective cART that drives the viral load to undetectable levels significantly decreases any chance of HIV transmission; however, it does not eliminate the risk completely, so one should always adopt 'safest sexual practices '.That's the critical point in a discordant scenario. **Strategies Based on Action by Uninfected Individual to Prevent Infection are:** Education/behavior change, Condoms. Male circumcision, Microbicides, PrEP(Pre-Exposure Prophylaxis). Vaccines and possibly 'PEP(Post Exposure Prophylaxis)

Strategies to Block Transmission Based on Action by Infected Individual to Reduce Infectiousness /Prevent Virus Release are: Prevention of mother-to-child transmission, Treatment of positive partner in discordant couples, Treatment as prevention (TasP) --TasP for all, TasP for higher VL, TasP for higher CD4, More rapid clinical linkage to ART Out of the above mentioned, there could be various options available in this scenario for prevention of further transmission (**Tas P,PrEP, nPEP**—Non-Occupational Post-Exposure Prophylaxis). We presume, the positive partner is on ART, as that person is undetectable, so his (positive partner) taking ART, will be acting as Treatment as Prevention(TasP) in this scenario. If this questioner decides to take ART for his /her benefit, to reduce the chances of transmission, subject to fulfilling certain conditions, then this will be called ' PrEP (Pre Exposure Prophylaxis). Of course in both the set ups (PrEP, nPEP), the questioner has to go for 'Tests at base line and subsequent times, more so when the questioner decides to start ART as PrEP, because the moment he/she becomes positive after initiating PrEP, then he/she has to stop two drug regimen used as PrEP and further initiate ART as per the Guidelines for HIV infected persons. This is a question involving many issues about the transmissibility of HIV infection under serodiscordant scenarios. The questioner's HIV-acquisition risks are extremely low (theoretically) & unwarranted and we will try to put his/her fears to rest by examining the issues involved in this case critically and coming up with scientifically based explanations

Results and discussion

Issues involved

We will critically examine the issues involved in this scenario as follows:

The first issue: Basic science tells us that HIV/AIDS is not readily contracted and hence the word 'Acquired' we find in the acronym 'AIDS'! One has to put in extra labor to 'acquire' it.

In order for infection to occur, three things must happen:

- One must be exposed to pre-cum semen, vaginal secretions, blood or breast milk, AND

- The virus must get directly into one's bloodstream through some fresh cut, open sore, abrasion etc., AND
- Transmission must occur, directly from one person to the other, very quickly (the virus does not survive more than a few minutes outside the body).

No matter what the circumstances are, if one thinks about these three criteria for transmission, he/she should be able to determine whether he/she is at risk for HIV or not.

The second issue: The questioner has not mentioned that '**how old the cut was and where (palmer/dorsal side)**, It may be presumed, the cut was in the process of healing when the questioner asked this question, which means that even though the cut was still visible, there was probably not direct access to the blood stream. There would have to be "open, active sores and then "enough fluids entering for there even to be a remote chance. As we know that chances of transmission in intact skin is zero but through mucous membrane is not zero. So the palmer side do has more risk than dorsal side even it is intact. Blood contains the highest concentration of the virus, followed by semen, followed by vaginal fluids. Breast milk can also contain a high concentration of the virus, but transmissibility depends on '**Who' and How'**?

It is not enough to be in contact with an infected fluid to become infected instead will require prolonged and sustained contact. Healthy, unbroken skin does not allow HIV to get into the body. HIV can only enter through an open cut or sore, or through contact with the mucous membranes in the anus and rectum, the genitals, the mouth, and the eyes. The vulnerability of the mucous membrane can be increased by inflammation, rough sex, the location and thickness of the mucous membrane and STIs. It's important to note though, **unless** there is something unusual and undeniable as an open sore on the skin, there is **no risk** from semen on the skin. There is **no risk** from casual contact either. Also, Mutual masturbation and frottage are not considered HIV transmission risks (a **no risk** activity –not a very low risk activity !) as long as there are no active bleeding cuts on one's person. We can have look at the individual risks and calculate the probability

Risk of HIV transmission following an exposure from a known HIV-positive individual

Type of exposure Estimated risk of HIV transmission per exposure (%)

Blood transfusion (one unit)	90–100
Receptive anal intercourse	0.1–3.0
Receptive vaginal intercourse	0.1–0.2
Insertive vaginal intercourse	0.03–0.09
Insertive anal intercourse	0.06
Receptive oral sex (fellatio)	0–0.04
Needle stick injury	0.3 (95% CI 0.2–0.5)
Sharing injecting equipment	0.67
Mucous membrane exposure	0.09 (95% CI 0.006–0.5)

(CI, confidence interval)

The third issue: The **gender** of the questioner has not been mentioned, and the questioner is in relationship with a positively charged male (positive), making them a 'magnetic couple' (sero-discordant) which certainly puts one at additional risk of transmission (howsoever small-if the questioner is a female and having 'vaginal sex' with HIV + male without protection)

Here are certain facts about —Sexual transmission of HIV in discordant situations:

- Stage of Illness the HIV --the pt is in to (HIV levels in blood are almost 10-times higher during the acute phase of infection, as many as 50% of new infections may occur through sex or sharing needles with someone who has just recently been infected.)

- During inflammation, immune cells are brought to the area to fight infection. These immune cells include dendritic cells, which may transport HIV to the lymph nodes, and CD4+ cells (the cells that HIV infects).
- In an HIV-positive person, inflammation of the genital tract or rectum increases the viral load in the genital or anal fluids, even though it does not increase the blood viral load. This is because inflammation at a site usually brings more infected immune cells to the area. When these cells become active to fight the infection they unwittingly make more copies of HIV.
- If an HIV-negative person has inflammation, a larger number of immune cells will arrive at the site to fight off the cause of the inflammation. This means there is a greater chance that HIV, (if in this period he/she has sex with an infected partner) which will come into contact with these cells and infect them.
- Fidelity(faithfulness)/ monogamous in relationship/marriage also affects the transmission as one could never be able to figure out the person's HIV status, one is going to have sex with as HIV(and not AIDS ! -there is difference between HIV& AIDS) is not visible and recognizable by one's physical appearance

These things may not apply in this case as it is a kind of a non-sexual exposure in non-occupational setup in serodiscordant couple.

The fourth issue: The probability of HIV Transmission with nearly any type of exposure is directly correlated with viral load. Recently there have been studies released that show that in magnetic partners (one being HIV positive and the other negative) if the positive partner is on antiretroviral medications has an undetectable viral load and no other STI's (Sexually Transmitted Infections) present, then the likelihood of HIV transmission is small. (the famous **Swiss Federal Commission Report & HTPN 052 Trial**) *HTPN 052 Trial --A GAME CHANGER*, showed 96% reduction in HIV transmission between serodiscordant partners when HIV infected partner began ART immediately. Even CDC in its campaign for 'Act against AIDS Campaign' says that at VL 50,000 or more copies/ml, it is projected 26 new infections related to sexual intercourse. In contrast at VL, 3500 copies/ml, the projected no of new infections drops to 2.

Shedding of virus in the male genital tract is not uncommon, even in men with consistently undetectable plasma HIV RNA., and the timing and frequency of this shedding appear to be unpredictable. Furthermore, previous studies have shown no clear association between the presumed penetration of specific antiretroviral into the genital tract and the likelihood of detectable virus in semen.

Three studies all with small number of subjects, have demonstrated that effective ART can reduce VL in serum, to undetectable level, however reductions in HIV in serum do not always lead to reductions of HIV in genital secretion to undetectable levels.

Politch *et al* in 2012 reported in their research among men having sex with men (MSM) that appropriate treatment of STDs can further reduce their seminal HIV shedding for men on ART. This research confirms that lower VL (Plasma) are also associated with lower genital viral loads. Transmission risks are less but exists.

The threshold level of genital-tract HIV necessary for transmission is not known, HIV transmission can be "very likely", between **magnetic couples**, even when the positively charged person is on effective combination antiretroviral therapy (cART-combined ART) that has driven his HIV plasma to viral load undetectable levels,, are overestimating the risk considerably.

The fifth issue: While we are on the topic of "**undetectable**" viral loads (VL), Here some basic things need to be discussed to clear common misunderstandings about this

term’.

- **‘Undetectable’** means the HIV plasma viral load is below the lower limit of detection for the particular test assay that is being used. Early viral load tests could only test down to 10,000 copies. Newer tests were able to test down to 500 copies of the virus per milliliter of plasma. The even newer ultrasensitive viral load assays can test all the way down to 25 or 50 copies/ml. We now have ultra-ultrasensitive assays available in some research laboratories that can test down to a single copy per ml! However, even in HIV-positive patients with HIV plasma viral loads below 1 copy/ml, this does not mean they have zero virus in their body. HIV still exists inside cells in the blood, lymph nodes and other body compartments.
- **‘Undetectable’** does not mean cured! There is no cure for HIV/AIDS, though this has become a chronic treatable and manageable disease just like High Blood Pressure(Hypertension) and High sugar level(Diabetes), you have to ‘gulp’ medicines for life.
- **‘Undetectable’** does not mean noninfectious (that you cannot transmit the virus to others)! We have cases documenting HIV transmission from a man with an undetectable viral load to his HIV-negative wife via unprotected vaginal sex. There are also cases of mother-to-child transmission, despite the mother having an undetectable viral load, though undetectability certainly decreases the risk of transmission.
- **‘Undetectable’** does not mean the virus cannot be detected anywhere in the body. Despite having an undetectable viral load in the blood (plasma), the virus would still be readily detectable in other tissues and body compartments, but the ability to transmit decreases considerably from a HIV ptwho is undetectable.
- **‘Effective combination antiretroviral therapy does not kill the virus!’** Rather it merely suppresses viral replication. Consequently, if someone with an undetectable viral load on combination antiretroviral therapy stops taking his drugs, the virus will soon start reproducing again and the viral load will skyrocket to levels near to where the viral load was before treatment was begun. That’s why the compliance /adherence to ART regimen must be at least 95% if not total(100%)

The sixth issue: Testing is an important tool for prevention and treatment as well. One American model tells us that nearly 1.2 millions PLHAs (people living with HIV/AIDS) in US, 20% do not know they are infected. Of an estimated 9,42000 aware of their HIV infection about 77% were linked to care only 51% remained in care Among those retained in care 89% were prescribed ART of whom 77% achieved viral suppression. Following our progress on each step, we can see that only 28 % of all HIV infected person in US have a suppressed Viral load, and we know that suppressed VL is essential for non-transfer of the infection.

We see that knowing about one status is very important as 20 unaware out of 100 PLHAs are a big number which is going to have a big impact on any Prevention program as unaware PLHA can further aggravate the pool of infected persons. Unaware persons are unable to realize any of the health and prevention benefits of ART (Anti –retroviral therapy) Increased testing and engagement in care is also at the heart of National HIV/AIDS Strategy in US that has been released by White House in 2010.

Newer research have shown that Anti-retrovirals (ARVs) can be used by uninfected persons to prevent HIV before an exposure (**called PrEP**) and after a non occupational exposure (**called ‘nPEP’**). In this set up (sero-discordant), one must be aware be aware about the availability of the options—I believe the positive partner is on ART, as he is undetectable, then this ART is acting as ‘Treatment as Prevention

(**TasP/T4P**)). If it is decided that the questioner should take ART after this exposure for fixed number of days (as this exposure comes within the time period of 72 hours) then this becomes ‘**nPEP**’, that is ‘**Non Occupational Post Exposure Prophylaxis**’.

It has been found through research that fewer MSM population in US are aware of these modalities. If this questioner decides to take ART for his /her benefit, to reduce the chances of transmission, subject to fulfilling certain conditions then this will be called ‘**PrEP (Pre Exposure Prophylaxis)**’. Of course in both the set ups (PrEP, nPEP), the questioner has to go for ‘Testing’ at base line and subsequent times as per the protocol of the country, more so when the questioner decides to start ART as PrEP, because the moment he/she becomes positive after initiating PrEP, then he/she has to stop two drug regimen used as PrEP and further initiate ART as per the Guidelines for HIV infected persons

The seventh issue: “Treatment as prevention” (TasP) is the use of combination antiretroviral therapy (ART) in HIV-positive individuals to preserve their health and reduce the risk of transmitting the virus. Anti-retroviral therapy (ART) initiation has been shown to dramatically reduce HIV transmission in discordant heterosexual couples prompting revisions to treatment eligibility criteria. Responding to this, new guidelines recommend starting ART either at HIV diagnosis, or at CD4 counts of ≤ 500 cells/mm³. In June 2013, the World Health Organization updated its ARV guidelines to reflect treatment and prevention benefits—and suggests that countries offer ART to all HIV-positive individuals with CD4 cell counts of 500 or below, and to specific groups (pregnant or breastfeeding women, HIV-positive people in serodiscordant couples) regardless of CD4 cell count.

A large proportion of HIV infected adults not qualifying for immediate ART at the CD4 count threshold of 350 cells/mm³ may have high viral loads. Sarishen Govender et al reported that of the ART-naïve first time testers whose CD4 count was above the CD4 threshold for ART initiation as per South African guidelines (< 350),, 34% had a VL $> 10,000$ copies/ml suggesting that CD4 count at the time of HIV diagnosis may be a poor proxy for HIV transmission risk. Consideration should be given to replacing CD4 count threshold with viral load threshold for ART initiation when planning treatment as prevention (TasP) interventions.

We presume here that, the positive partner is on ART, as he is undetectable, **so his (positive partner himself)** taking ART, is acting as **Treatment as Prevention (TasP)** in this scenario.

The eight issue: Stigma and discrimination This issue do have psych-social reasons. The patient has not come up physically to seek help (chosen to seek advice through mail) and has provided inadequate/insufficient information possibly due fear of rejection/ostracism/ fear of discrimination or stigmatization.

HIV stigma and related discrimination remain key barriers to dealing effectively with the HIV. HIV stigma can deter people at risk from being tested for HIV and deter HIV-positive people from accessing appropriate treatment and care. It also remains the key obstacle for HIV-positive people disclosing their status to friends and family, employers and work colleagues, health care providers, insurance companies, landlords, and sexual partners for fear of being treated less favorably, or being out-rightly rejected or abused. Stigmatization/discrimination often done on moral grounds culminating into to rejection, which prevents them to seek advice openly to as HIV/AIDS is often linked to be at-risk behavior resulting in people labeled as immoral, more so when there are homosexual activities involved (as we presume in this case.)

Conclusions

This is an interesting case scenario involving multiple modalities of HIV

prevention and generates many though provoking Q & A making them useful in training/teaching setups too. This review yields following learning points and take home messages which forms the base of core knowledge and skills to develop strategies to fight and prevent HIV.

Learning points /take home messages

- Most new HIV infections are acquired from stable, long-term partners.
- No one is immune from HIV.
- HIV is still stigmatized and discriminated in societal terms
- HIV serodiscordant relationships are among the most vulnerable to acquiring Discordancy is at the core of HIV sexual transmission, and diagnosing it is key to HIV prevention
- HIV negative partners in discordant couples are at very high risk of infection.
- Acquiring It is not uncommon getting exposed to body fluids of an HIV infected partner in a serodiscordant (magnetic couples/ serodivergent /mixed status couples') set ups.
- HIV discordance is not a sure sign of infidelity.
- HIV is not transmitted on every exposure.
- Viral load(VL) is important in transmission, but it changes over time
- VL is proportional to acquisition of HIV through any route.
- Undetectable VL reduces the risk of transmission of HIV. But undetectability does not mean no risk or no infection.
- Effective risk reduction options exist(PrEP, nPEP)
- HIV transmission within discordant couples can be prevented.
- A large proportion of HIV infected adults not qualifying for immediate ART at the CD4 count threshold of 350 cells/mm³ have high viral loads.
- It is possible for couples to stay HIV serodiscordant indefinitely if they consistently practice safer sex using condoms.
- Couples' testing and counseling is as cost-effective than other interventions, such as ART
- Disclosure is important for HIV prevention.
- Treatment for the HIV-positive partner also is highly effective in reducing the risk of transmission to the HIV-negative partner (called Treatment as Prevention—TasPor T4P)
- Combined, treatment and consistent condom use are likely to offer greater protection than either one alone.

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