From exposure to infection: The biology of HIV transmission

By James Wilton

One way HIV is transmitted is through sex—but how does the virus infect someone after they have been exposed to HIV during sex?

In this article, we will follow the journey that HIV takes from the time someone is first exposed to the virus through to infection. Along the way, we will identify various factors that increase or decrease the chances that the virus will cause an infection.

It begins with an exposure...

The journey begins with an exposure. For an HIV exposure to pose a risk of infection, specific bodily fluids from an HIV-positive person need to come into contact with specific body parts of an HIV-negative person. This happens most often through anal or vaginal sex.

We know that if a person is HIV-positive, only some of their bodily fluids contain enough virus to transmit HIV sexually—these include semen, pre-cum, vaginal fluid and rectal fluid. Blood also contains enough virus to transmit HIV, but it is not commonly involved in the sexual transmission of HIV.

The HIV in these fluids may cause infection if it enters the body of a sex partner. Most of the body's surfaces are “dry” skin (for example, on the arms and legs)—these surfaces don’t allow HIV to enter the body unless a cut or sore is present. However, other parts of the body are covered by “wet” skin, also known as mucous membranes, which are more vulnerable to HIV. The mucous membranes most commonly involved in the sexual transmission of HIV include the:

- foreskin and urethra on the penis
- cervix and vagina
- anus and rectum

A closer look at the mucous membranes

Let’s take a closer look at the mucous membranes and find out why they are so vulnerable to HIV infection.

Whereas most of the skin on the body is covered with a protective layer of fibers that makes the skin “dry” and that HIV cannot cross unless there is a cut or sore, the mucous membranes are not covered with this protective layer of fibers because it would hinder their function. Without this protective layer, mucous membranes are more vulnerable and often the main “routes” that germs use to enter the body.
Vulnerable but not defenseless!

Infection isn’t automatic if an exposure to HIV occurs. After a fluid containing HIV comes into contact with a mucous membrane, HIV still needs to complete a difficult journey before it can cause an infection. In some cases, HIV is not able to complete this journey and infection does not occur.

The mucous membranes are vulnerable but not defenseless. These membranes are covered with a layer of cells (called epithelial cells) that are tightly joined together. This helps to prevent germs from entering the body and causing an infection. Some mucous membranes (such as the rectum) have a single layer of cells while others (such as the foreskin, urethra and vagina) have multiple layers. The more layers, the more protection there is. The mucous itself also contains chemicals and antibodies that can kill germs.

Even if HIV manages to pass through the mucous and the layer of cells, there are still ways the body can prevent an HIV infection. Under the cell layer, a large concentration of immune cells is responsible for attacking and killing germs that manage to find their way past the cell layer.

To cause an infection after an exposure, HIV first needs to cross the cell layer and then avoid being destroyed by the immune cells below. If the virus overcomes these defenses, it can then spread past the site of infection to other parts of the body, by entering the blood and lymphatic vessels in the mucous membrane tissue. Once HIV has spread throughout the body, the virus can establish infections in different organs and tissues. At this point, the HIV infection becomes permanent (see Figure). In some cases, HIV may not be able either to cross the mucosal cell layer or win its battle against the immune cells in the mucosal tissue below. Also, if HIV spreads beyond the mucous membranes, immune cells in the blood and lymphatic vessels and organs and tissues may be able to clear the virus before a permanent infection is established. This explains why some exposures to HIV do not lead to infection.

Crossing the cell layer

HIV can travel across the cell layer and enter the body on its own, but damage to the cell layer can make it easier for HIV to get across. Things that damage an intact cell layer and have the potential to increase the risk of infection include:

- Some sexually transmitted infections (STIs), such as herpes and syphilis, which can cause sores or ulcers (“holes”) on the mucous membranes.
- Tiny tears that can occur during sex due to friction. These “microtears” in the epithelial layer, which commonly occur during sex, can increase the risk of HIV infection. Some mucous membranes are more vulnerable to tearing, either because they are covered by a thinner cell layer or because they do not produce lubrication to reduce friction during sex. This partly explains why receptive anal sex (receiving the penis into the anus, also known as “bottoming” among gay men) with someone who is HIV-positive is generally the riskiest type of sex. The rectum’s cell layer is thin and does not produce extra lubrication during sex.
- The mucous membranes can also be damaged in other ways, such as enemas, dental work, surgery, douching, brushing teeth and flossing.
- Although lubricants are often promoted to reduce the risk of tearing during sex, preliminary research suggests that some types of sexual lubricants may cause damage to the epithelial cell layer. More research is needed before we can change our recommendations regarding the use of lubricants.
Other factors that increase or decrease the risk of HIV crossing the cell layer

Surface area of cell layer

The larger the surface of the cell layer exposed to HIV, the more likely it is that HIV will be able to find a way to cross it.

The surface area of the mucous membranes on the penis (the urethra and foreskin) is much smaller than the surface area of the rectum or vagina. This partly explains why insertive (anal or vaginal) sex generally carries a lower risk of getting HIV compared to receptive sex. For example, insertive anal sex (inserting the penis into the anus, also known as “topping” among gay men) is less risky than receptive anal sex (receiving the penis into the anus). Similarly, insertive vaginal sex is less risky than receptive vaginal sex. Although potentially less risky than its receptive counterpart, insertive sex (both vaginal and anal) still carries a high risk for the transmission of HIV.

This also explains why male circumcision reduces the risk of HIV infection for men who participate in vaginal sex. Removal of the foreskin can decrease the risk of HIV infection because it reduces the surface area of the mucous membrane cell layer that HIV can use to enter the body. Similarly, circumcision may also reduce the risk of HIV infection for men who participate in insertive anal sex. Therefore, male circumcision may be beneficial for gay men who only top, but not for gay men who top and bottom.

Amount of virus in the fluid (viral load)

The more HIV that the cell layer is exposed to, the greater the chance that one or more virus particles will be able to find a way past the layer, enter the tissue below and cause infection. Therefore, factors that lower the amount of virus (the viral load) in the fluids of someone who is HIV positive can greatly reduce their risk of transmitting HIV. HIV treatment can reduce a person’s viral load to levels that are undetectable by routinely used tests. If a person on treatment is engaged in care and maintains an undetectable viral load, they do not pass HIV sexually.

When an HIV-positive person is not on treatment, factors that increase viral load may increase their risk of transmitting HIV. STIs, such as gonorrhea, chlamydia, herpes and syphilis, can increase the viral load in the bodily fluid at the site of the STI. The stage of HIV infection can also affect the amount of virus in an HIV-positive person’s body. The viral load of a person who is not on treatment is very high during the first 10 to 12 weeks after a person becomes infected and also when a person has advanced HIV disease.

Winning the battle against the immune cells

Once HIV has successfully crossed the cell layer, the virus faces a battle against the immune cells waiting in the tissue below. This battle lasts from one to three days. There are many types of immune cells in the mucous membranes and each plays a role in mounting an attack against HIV. Although some of these cells can kill the virus quite well, HIV is able to infect one type of immune cell (CD4 cells), make copies of itself and release more virus. If HIV is able to replicate faster than the immune cells are able to kill copies, then HIV may be able to spread throughout the body. Once this happens, the mucosal immune system is defeated and the infection can become permanent. However, infection does not occur if the immune cells are able to eradicate the virus in the mucous membrane. Further, if HIV spreads beyond the mucous membranes, immune cells elsewhere in the body (that is, in the blood and lymphatic vessels and organs and tissues) may also be able to clear the virus before a permanent infection has been established.

The factors that can make it easier or more difficult for HIV to make copies of itself in the mucous membrane tissue (below the cell layer) and win its battle against the immune cells include:

- inflammation
- antiretroviral drugs
- vaccines

Inflammation

Inflammation is part of the body’s immune response to infection or tissue damage. The inflammatory response is
usually protective: It brings more immune cells to an infected or damaged area to help clear germs or repair damaged tissue. However, HIV likes to infect some of these immune cells, the CD4 cells. A higher number of these immune cells in the mucous membranes can allow HIV to make copies of itself more quickly and help the virus win its battle against the immune cells.

Therefore, anything that causes inflammation of the mucous membranes may increase the risk of HIV infection if the inflamed area is exposed to HIV. Inflammation of the mucous membranes can be caused by STIs and other infections, such as bacterial vaginosis and gum disease, or tearing/damage (including that caused by sex, douching, enemas, brushing teeth, flossing, etc).

**Antiretroviral drugs or vaccines**

Interventions are available, and in development, to help the immune cells in the mucous membrane destroy HIV before the virus spreads throughout the body. These interventions need to act quickly because HIV needs to replicate for only one to three days before it is able to spread beyond the mucous membrane and cause a permanent infection. Interventions that act during this brief “window of opportunity” include antiretrovirals or, potentially, a vaccine.

Antiretroviral drugs prevent HIV from creating copies of itself in immune cells. If an HIV-negative person takes antiretrovirals, this greatly reduces the ability of HIV to create more copies of itself and help the immune cells clear the virus from the body. Post-exposure prophylaxis (PEP) and pre-exposure prophylaxis (PrEP) are two prevention methods that involve HIV-negative people taking antiretrovirals. They are highly effective at reducing a person’s risk of infection when taken consistently and correctly.

An HIV/AIDS vaccine is not yet available but its goal would be to prepare the immune cells in the mucous membrane to respond more quickly to HIV if an exposure were to occur. If the immune cells can react more quickly and with greater strength, this may give them a better chance of clearing the virus before it spreads throughout the body.

**Conclusion**

The sexual transmission of HIV is a complex process that begins with a person being exposed to the virus and ends with infection. However, as we have learned from this article, this is a journey that HIV is not always able to complete.

It is important to note that if an exposure occurs, there is no way of reducing the risk of infection to zero. This means that avoiding an exposure in the first place—by using condoms and knowing your partner’s HIV status—is the most effective method of preventing infection.

*Revised June 2018.*

**References**


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Production of this content has been made possible through a financial contribution from the Public Health Agency of Canada.

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