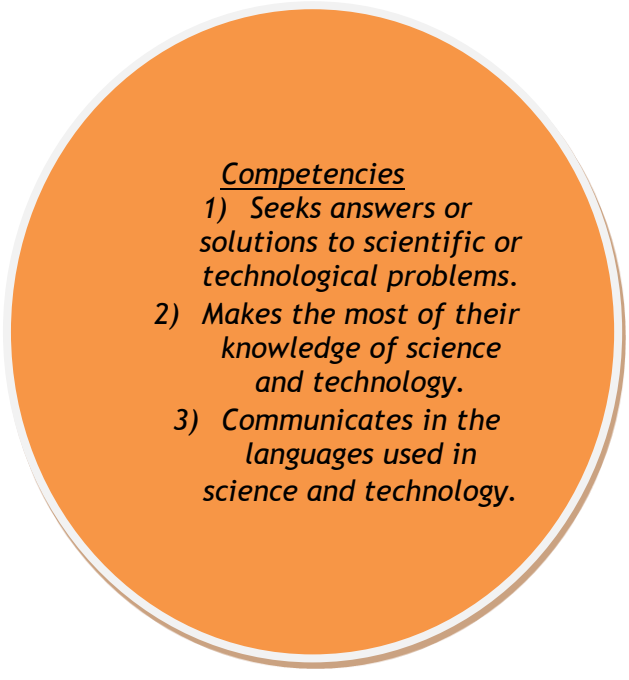
Science & Technology 3: HIV 101

Aim/Rationale

Students are provided with an application of retroviral replication, which clearly demonstrates the difference between lytic and lysogenic viral cycles, and how that distinction affects treatment and/or maintenance of an illness. In addition, students will be introduced to certain aspects of the human immune response and the effects a virus like HIV has on the human body.



Hook

Brainstorm based on guiding question: What comes to mind when you hear the term HIV?

Development/Teaching Methods

Introduction (10 minutes)

Ask students the following questions:

- *What does HIV stand for?*
  - Human Immunodeficiency Virus
  - Means that it affects humans, is transmitted *to* humans *by* humans, and affects *ALL* humans regardless of age, gender?, race, socio-economic status or sexual orientation.
  - The virus attacks the immune system (which is the body's natural defence against foreign substances).

- *What does AIDS stand for?*
  - Acquired Immunodeficiency Syndrome
  - "Acquired" because The virus must be acquired from another organism/body
  - "Syndrome" because AIDS is a collection of symptoms.
- *What's the difference?*
  - HIV is the name of the virus which infects the body. You can "get" HIV. A person with HIV is said to be HIV-positive or sero-positive.
  - AIDS is the name of the symptoms that arise years after "getting" HIV if a person is not treated. A sign of this stage is when the immune system is so compromised that a person gets **opportunistic infections**. These are illnesses that people with intact immune systems would naturally be able to fight off. These infections "see" opportunity to live in the body of someone with an already lowered immune system that cannot fight them off.

HIV Transmission (15 minutes)

- The HIV virus is transmitted through 5 bodily fluids:
  - Blood
  - Semen/Pre-ejaculate (Pre-cum)
  - Vaginal Secretions/fluids
  - Rectal fluids
  - Breast milk (from parent to baby if they do not have access to proper healthcare or treatment)
- The following three conditions must be present to transmit the virus:
  1. One of the five bodily fluids that can transmit HIV must be present: blood, semen, vaginal secretions, rectal fluids and breast milk.
  2. HIV must be present in the fluid. This means that HIV cannot be transmitted by someone who does not have the virus! Additionally, people living with HIV who take antiretroviral medications often have what is known as an undetectable viral load. This means that the amount of virus in their blood is so small that it cannot be detected on a test. People living with HIV who have an undetectable viral load **do not** transmit HIV through sex.
     Note: HIV cannot be transmitted through saliva. Saliva has a natural anti-viral enzyme, and therefore has an extremely low concentration of virus particles. Kissing is considered a "no real risk" activity. Any saliva that enters the mouth is swallowed and any virus particles would be destroyed by stomach acid.
  3. The fluid needs an entry point.
- Points of Entry:
  - Often points of entry for HIV are **mucous membranes**, which are areas of exchange with the external environment. These include: mouth, nose, tonsils, eye, vagina, tip of penis, anus.
  - Some of these areas are more susceptible to HIV transmission than others.
  - **Epithelial cells** line mucous membranes and the virus enters the body across these epithelial membranes. Some epithelial membranes are made of only ONE layer of epithelial cells—these are the areas which are most susceptible to HIV transmission.
  - The **anus**, regardless of gender, has only one layer of epithelial cells and a large surface area, making this area very susceptible to HIV transmission.
  - **People with vaginas:** The **cervix** has only one layer of epithelial cells. This thin membrane can easily be damaged by age, some STIs or vaginal infections, and rough vaginal sex. The **vaginal canal** has a thicker layer of epithelial cells, but is

nonetheless still a potential point of HIV transmission.

- **People with penises:** The **inner side of the foreskin** has more **dendritic cells** than other surfaces. When an uncircumcised penis is erect, the inner foreskin is exposed. These cells use pseudopods (like arms) to reach the outer cell layer of the mucous membrane, bind to virus particles and carry them to the lymph nodes (immune system centres throughout the body). Circumcision has been shown to reduce the risk of HIV transmission but it is NOT a method of protection against the virus.

HIV infection (15 minutes)

- Distribute the HIV Replication Handout (See Appendix)
- Label the parts of the diagram:
  - T-lymphocyte and its nucleus (A type of white blood cell that detects and fights foreign invaders of the body.)
  - HIV virus
  - Single stranded RNA inside the HIV virus
  - Double-stranded DNA in the T-lymphocyte nucleus
  - CD4 receptor (A protein present on the outside of infection- fighting white blood cells. CD4 receptors allow HIV to bind to and enter cells.)
  - Note that the CD4 co-receptor is not shown on the surface of the T-lymphocyte.
  - (In addition to binding a CD4 receptor, HIV must also bind either a CCR5 or CXCR4 co-receptor protein to get into a cell.)
- Describe the HIV Life Cycle (marked 1 to 5 on the handout) and encourage students to write in the steps on their own sheets.
  - ENTRY
    - **Binding and Fusion:** HIV begins its life cycle when it binds to a **CD4 receptor** and one of two **co-receptors** on the surface of a CD4+ **T- lymphocyte**. The virus then fuses with the host cell. After fusion, the virus releases RNA, its genetic material, into the host cell.
  - REVERSE TRANSCRIPTION
    - **Reverse Transcription:** An HIV enzyme called **reverse transcriptase** converts the single- stranded HIV RNA to double-stranded HIV DNA.
  - INTEGRATION INTO HOST DNA
    - **Integration:** The newly formed HIV DNA enters the host cell's nucleus, where an HIV enzyme called **integrase** "hides" the HIV DNA within the host cell's own DNA. The integrated HIV DNA is called provirus. The provirus may remain inactive for several years, producing few or no new copies of HIV.
  - TRANSCRIPTION AND ASSEMBLY
    - **Transcription:** When the host cell receives a signal to become active, the provirus uses a host enzyme called **RNA polymerase** to create copies of the HIV genomic material, as well as shorter strands of RNA called messenger RNA (mRNA). The mRNA is used as a blueprint to make long chains of HIV proteins.
    - **Assembly:** An HIV enzyme called **protease** cuts the long chains of HIV proteins into smaller individual proteins. As the smaller HIV proteins come together with copies of HIV's RNA genetic material, a new virus particle is assembled.
  - MATURATION AND BUDDING
    - **Budding:** The newly assembled virus pushes out ("buds") from the host cell. During budding, the new virus steals part of the cell's outer envelope. This envelope, which acts as a covering, is studded with protein/sugar combinations called HIV glycoproteins. These HIV glycoproteins are necessary for the virus to bind CD4 and co- receptors. The new copies of HIV can now move on to infect other cells.

- Review important enzymes involved and their functions:
  - Reverse Transcriptase (in step 2)
  - Integrase (in step 3)
  - Protease (in step 4)

Basics of HIV Treatment (10 minutes)

- Go over basic facts about the treatment
  - HIV is incurable, and no vaccine has been discovered.
  - Antiretroviral drugs are the most effective drugs for slowing down the progress of the disease.
- Explain the classes of drugs (connect where they affect the HIV replication cycle):
  - **Entry Inhibitors**: Drugs known as *entry inhibitors* are being developed to prevent HIV from getting inside cells. Some of these drugs are designed to block the co-receptors while others prevent the virus from fusing with the cell.
  - **Reverse Transcriptase Inhibitors**: Drugs called *reverse transcriptase inhibitors* slow down or stop the action of the RT enzyme.
  - **Integrase Inhibitors**: Drugs called *integrase inhibitors* interfere with the action of integrase. This class of drug was developed fairly recently.
  - **Protease Inhibitors**: *Protease inhibitors* (PIs) are drugs that interfere with the action of protease. They prevent the protease enzyme from cutting the long chains of new viral protein. Although new virus can be formed, it is defective and cannot infect new cells. Protease inhibitors have a very powerful ability to suppress the virus and are an important part of many drug combinations.
  - **The "drug cocktail"**: A term commonly used to describe combinations of medications (i.e. multitherapy).
  - **HAART**: Highly Active Antiretroviral Treatment = Tritherapy (3 drugs from 2 different classes are used simultaneously)
- Why is it necessary to use tritherapy over monotherapy?
  - It is necessary to use **two classes of drugs simultaneously** in treatment.
  - By stopping only one point of the replication cycle, a mutant virus that was not stopped by the single drug could reproduce. The second drug would then stop the mutant virus from proliferating.
- Stages of HIV Infection:
  - **Primary or Acute Infection**: During acute HIV infection, the virus makes its way to the lymph nodes, a process which probably takes three to five days. In the lymph nodes, HIV reproduces or replicates very quickly and releases new virus into the bloodstream. This burst of rapid HIV replication usually lasts for two or three months.
  - During primary infection, the amount of HIV in the body is very high and there is often a sharp drop in the number of CD4+ cells. People with acute infection usually do not test HIV positive because the body has not yet had time to produce antibodies against the virus. And it is this antibody that is detected in the standard tests to see if someone is HIV positive.
  - **Asymptomatic Period**: Many people with HIV may have few or no signs or symptoms of the disease for up to 10 years. However, some people may progress much faster, seeing their CD4+ cells decline within a few years and experiencing symptoms in the first few years after infection.
  - Although the immune system is able to fight HIV, it cannot get rid of the virus

completely. Gradually, in most people the virus will be able to damage the immune system and they will progress to *symptomatic* infection.

- **Symptomatic Infection:** As time passes, the damage to the immune system increases and the body's defences weaken. At this stage, HIV may cause symptoms of long-term infection, such as chronic fatigue, weight loss, skin problems or diarrhoea. This may occur when CD4+ cells are still at reasonable levels, or only after they have dropped to the stage officially called AIDS.
- **AIDS (Acquired Immuno Deficiency Syndrome)**: An official diagnosis of AIDS in Canada is given when a person with HIV develops one or more *opportunistic infections* or certain cancers. A damaged immune system can leave HIV positive people vulnerable to infections that a healthy immune system could easily control. *These infections are called "opportunistic" because they take the opportunity to cause disease when the immune system is weakened.*
- **Treatment**: Antiretroviral drugs can slow or prevent the later stages of HIV infection. People on antiretroviral medications may never develop AIDS, and they have a life expectancy close to that of someone who does not have HIV.

Culmination

1. Conclusion (5 minutes):

Review Questions:

- What is the difference between HIV and AIDS?
- Does an HIV+ person have AIDS?
- Can you "get" AIDS from someone else?
- Do you feel differently about HIV/AIDS now that you know more about the virus and the disease? How so?
- What can be done to reduce the stigma/shame surrounding HIV/AIDS

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