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HIV Drugs and the HIV Lifecycle

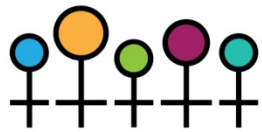
Last updated: November 7, 2019

Together, we can change the course of the HIV epidemic...one woman at a time.

#onewomanatatime

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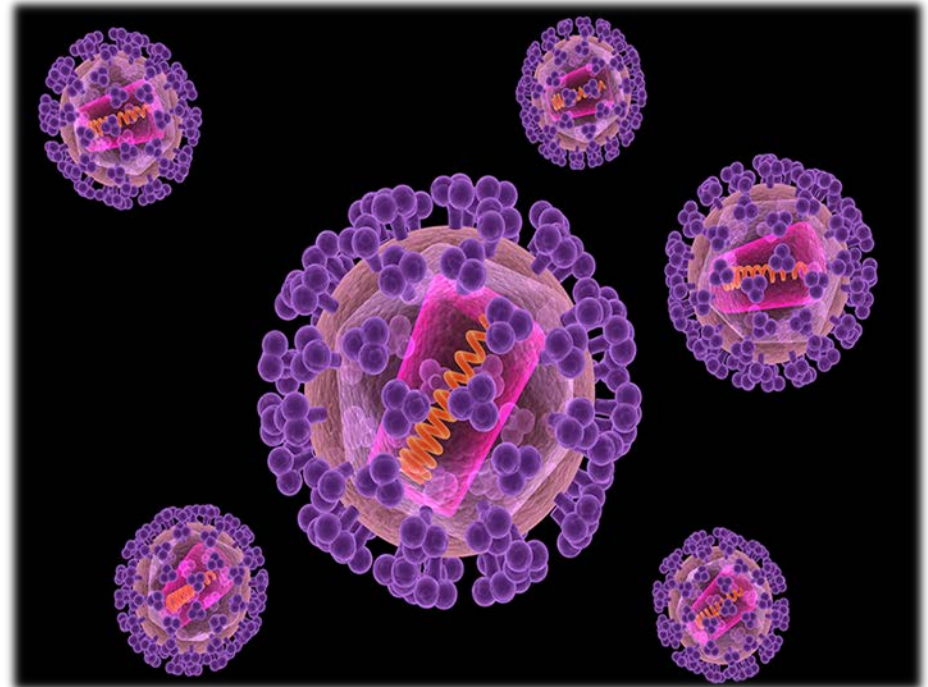


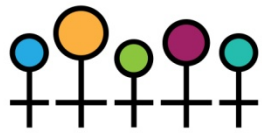
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HIV Drugs and the HIV Lifecycle

HIV must go through a number of steps to make copies of itself; these steps are called the ***HIV lifecycle***

- **All HIV drugs work by interrupting different steps in HIV's lifecycle**
- HIV drugs can't cure HIV, but can help you stay healthy by preventing HIV from reproducing
- Once HIV is in the body, it infects CD4 cells (a type of white blood cell) and other cells
- HIV turns CD4 cells into factories, producing thousands of copies of HIV



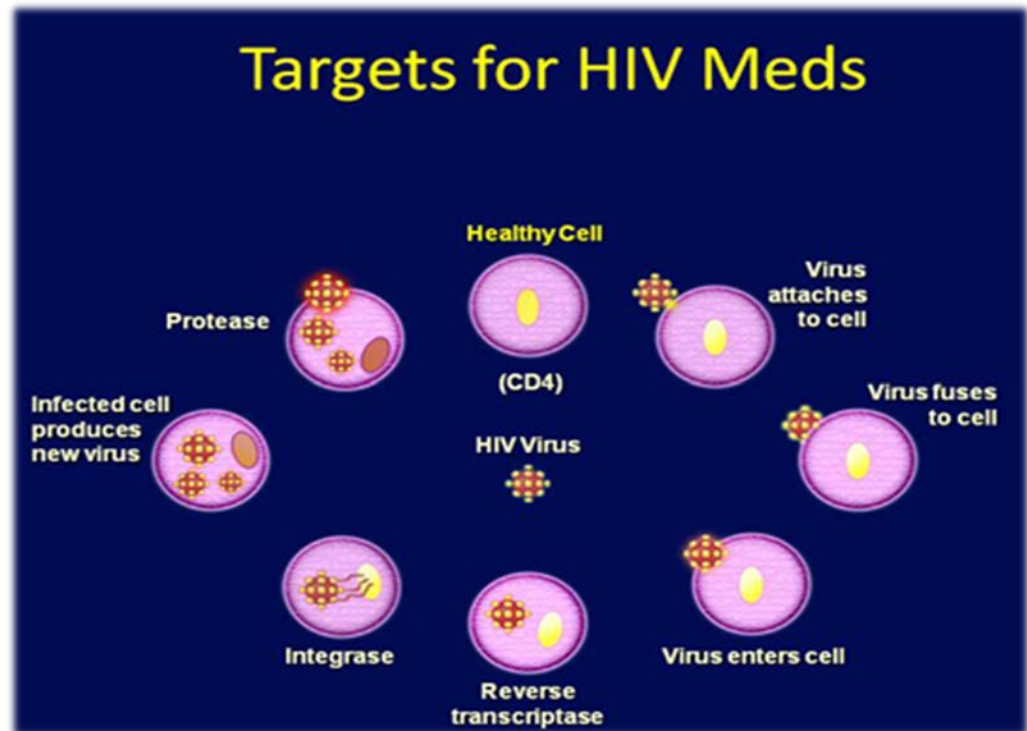


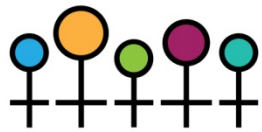
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The HIV Lifecycle

The steps HIV goes through to complete the process of reproducing itself are:

- Binding and fusion
- Reverse transcription
- Integration
- Transcription
- Assembly
- Budding



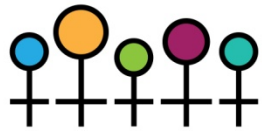


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The HIV Lifecycle

Binding and Fusion: HIV begins to enter a CD4 cell by binding, or attaching itself, to a specific point, called a **CD4 receptor**, on the cell's surface

- HIV must then bind to a second **receptor**, either the CCR5 co-receptor or the CXCR4 co-receptor
- This allows the virus to join, or merge, with the CD4 cell in a process called **fusion**
- After fusion, HIV releases its **RNA** (HIV's genetic material) and **enzymes** (proteins causing chemical reactions) into the CD4 cell



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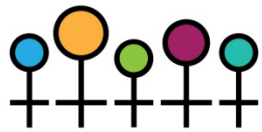
The HIV Lifecycle

Reverse Transcription: HIV's RNA contains the "instructions" that will reprogram the CD4 cell to produce more virus

- In order to be effective, HIV's RNA must be changed into DNA
- An HIV enzyme called **reverse transcriptase** changes the HIV RNA into HIV DNA

Integration: Next, the newly formed HIV DNA enters the nucleus (command center) of the CD4 cell

- Another HIV enzyme called **integrase** combines or “integrates” HIV's DNA with the CD4 cell's DNA



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The HIV Lifecycle

Transcription: Once the virus is integrated into the CD4 cell, it commands the CD4 cell to start making new HIV proteins

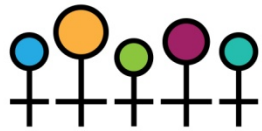
- The proteins are the building blocks for new HIV viruses
- They are produced in long chains

Assembly: An HIV enzyme called **protease** cuts the long chains of HIV proteins into smaller pieces

- As the smaller protein pieces come together with copies of HIV's RNA, a new virus is put together (assembled)

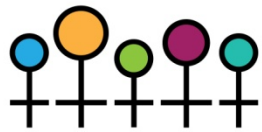
Budding: The newly assembled virus pushes ("buds") out of the original CD4 cell

- This new virus can now target and infect other CD4 cells



HIV Drugs

- Different **classes or groups** of HIV drugs block different steps in HIV's lifecycle
- U.S. Food and Drug Administration (FDA) has approved **six classes of HIV drugs**:
 - Entry Inhibitors
 - Integrase Inhibitors
 - Nucleoside and Nucleotide Reverse Transcriptase Inhibitors (NRTIs or "nukes")
 - Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs or "non-nukes")
 - Protease Inhibitors (PIs)
 - Boosting Agents



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Entry and Integrase Inhibitors

Entry Inhibitors:

Stop HIV from entering CD4 cell

Different types of entry inhibitors

- **Fusion inhibitor:** Fuzeon (enfuvirtide)
- **CCR5 antagonist:** Selzentry (maraviroc)
- **Post-attachment inhibitor:** Trogarzo (ibalizumab)



Integrase Inhibitors:

Interfere with HIV's integrase enzyme

There are 4 integrase inhibitors for HIV treatment:

- Isentress (raltegravir)
- Tivicay (dolutegravir)
- Vitekta (elvitegravir)
- bictegravir (in the combination pill Biktarvy)



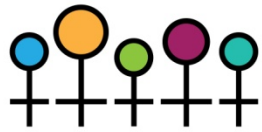


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NRTIs (“Nukes”)

Nucleoside and Nucleotide Reverse Transcriptase Inhibitors (NRTIs or “nukes”):

- Interfere with HIV's **reverse transcriptase** enzyme
 - Emtriva (emtricitabine or FTC)
 - Epivir (lamivudine or 3TC)
 - Retrovir (zidovudine or AZT)
 - tenofovir alafenamide fumarate (TAF) (in several combination pills, also sold separately as Vemlidy for treatment of hepatitis B)
 - Videx (didanosine or ddi) (no longer used in the US)
 - Viread (tenofovir disoproxil fumarate or TDF)
 - Zerit (stavudine or d4T) (no longer used in the US)
 - Ziagen (abacavir)



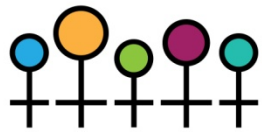
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NNRTIs (“Non-Nukes”)

Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs or “non-nukes”):

- Like NRTIs, interfere with HIV's reverse transcriptase enzyme
- There are a number of approved NNRTIs:
 - Edurant (rilpivirine or RPV)
 - Intelence (etravirine or ETR)
 - Pifeltro (doravirine or DOR)
 - Rescriptor (delavirdine) (no longer used in the US)
 - Sustiva (efavirenz)
 - Viramune (nevirapine)





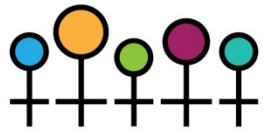
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Protease Inhibitors ("PIs")

Protease Inhibitors (PIs):

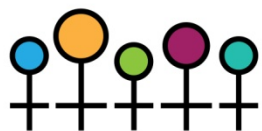
- Interfere with HIV's **protease** enzyme
 - Aptivus (tipranavir)
 - Crixivan (indinavir) (no longer used in the US)
 - Invirase (saquinavir)
 - Kaletra (lopinavir plus ritonavir)
 - Lexiva (fosamprenavir)
 - Norvir (ritonavir)
 - Prezista (darunavir)
 - Reyataz (atazanavir)
 - Viracept (nelfinavir)





Boosting Agents:

- Drugs do not affect HIV's lifecycle
- Instead, they improve, or 'boost', the level of other HIV drugs in the blood stream so they can be taken at a lower dose
- Approved boosting agents:
 - Norvir (ritonavir)
 - Tybost (cobicistat)

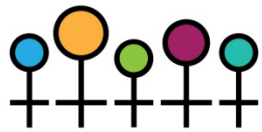


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Fixed-Dose Combinations

Fixed-dose drugs **combine 2 or more HIV drugs from 1 or more classes in just 1 pill** for easier dosing

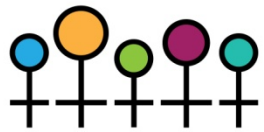
- Atripla (Sustiva plus Emtriva plus Viread)
- Biktarvy (bictegravir plus Descovy)
- Cimduo (Epidr plus Viread)
- Combivir (Retrovir plus Epidr)
- Complera (Emtriva plus Viread plus Edurant)
- Delstrigo (Pifeltro plus Epidr plus Viread)
- Descovy (Emtriva plus tenofovir alafenamide (TAF))
- Dovato (Tivicay plus Epidr)
- Epzicom (Epidr plus Ziagen)
- Evotaz (Reyataz plus Tybost)
- Genvoya (Vitekta plus Tybost plus Emtriva plus tenofovir alafenamide fumarate (TAF))
- Juluca (Tivicay plus Edurant)
- Odefsey (Emtriva plus tenofovir alafenamide (TAF) plus Edurant)
- Prezcofix (Prezista plus Tybost)
- Stribild (Emtriva plus Viread plus Vitekta plus Tybost)
- Symfi and Symfi Lo (contains less Sustiva) (Sustiva plus Epidr plus Viread)
- Symtuza (Prezista plus Tybost plus Emtriva plus tenofovir alafenamide (TAF))
- Triumeq (Ziagen plus Tivicay plus Epidr)
- Trizivir (Retrovir plus Epidr plus Ziagen)
- Truvada (Emtriva plus Viread)



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Combining HIV Drugs

- Health care providers combine drugs from different classes in order to attack HIV at more than one step in its lifecycle
 - HIV can **mutate** when it reproduces, which could stop HIV drugs from working
 - When this happens, we say that HIV has become **resistant** to that drug
- If you take only one drug (monotherapy) or a few drugs that belong to the same class, HIV can develop mutations that make it resistant to that drug or drug class
- **HIV has a much harder time changing enough to develop drug mutations and resistance when you take a combination of drugs from different classes**

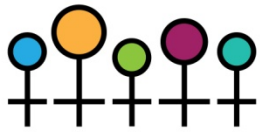


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What Does This Mean for You?

Combination therapy with drugs that block HIV at different steps of its lifecycle can prevent most of the production of new HIV.

Most important, it means **slower disease progression and longer life** for people living with HIV.



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Learn More!

- To learn more, please read the full fact sheet on this topic:
 - [HIV Drugs and the HIV Lifecycle](#)
- For more information on approved HIV drugs:
 - The Well Project's [HIV Drug Chart](#)
- For more fact sheets and to connect to our community of women living with HIV, visit:
 - www.thewellproject.org
 - www.facebook.com/thewellproject
 - www.twitter.com/thewellproject