HIV Drugs and the HIV Lifecycle [1]

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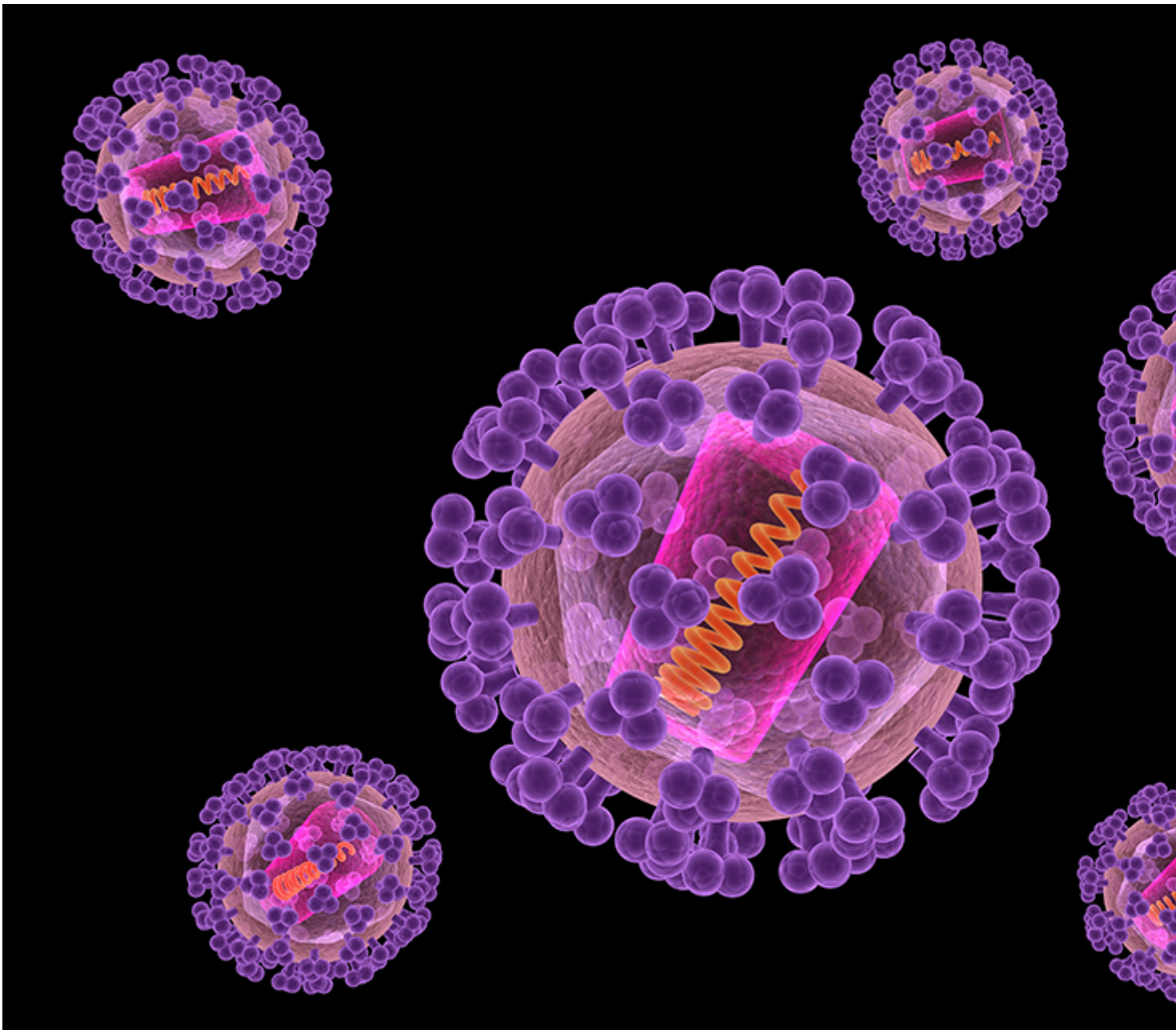

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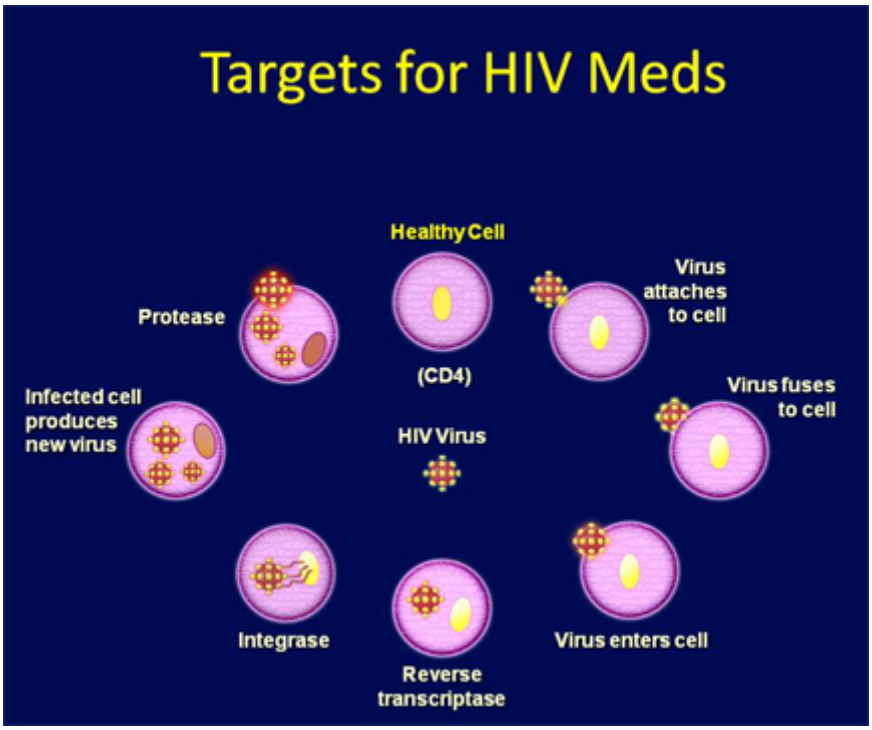
The Basics

HIV drugs cannot cure HIV [2], but they can help you stay healthy by preventing the virus from reproducing (making copies of itself). When HIV cannot reproduce, it cannot infect new cells in your body and your viral load [3] remains low.

HIV must go through a number of different steps in order to make copies of itself. This is called the HIV lifecycle. All HIV drugs work by interrupting a step in HIV's lifecycle, thereby stopping HIV "in its tracks."



The HIV Lifecycle

Once HIV is in the body, it targets and infects a certain type of white blood cell called a CD4 cell [4]. HIV then takes over or "hijacks" these cells and turns them into factories that produce thousands of copies of the virus. The steps HIV goes through to complete this process are as follows:

1. **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 co-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 (genetic material) and enzymes (proteins that cause chemical reactions) into the CD4 cell.
2. **Reverse Transcription:** HIV's genetic material is called RNA, which contains the "instructions" that will reprogram the CD4 cell so that it produces more viruses. 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.
3. **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.
4. **Transcription:** Once the virus has become part of (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.
5. **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).
6. **Budding:** The newly assembled virus pushes ("buds") out of the original CD4 cell. This new virus is now able to target and infect other CD4 cells.

Approved HIV Drugs

Different classes or groups of HIV drugs block different steps of HIV's lifecycle. There are currently five classes of HIV drugs approved by the US Food and Drug Administration (FDA):

- **Entry Inhibitors:** These drugs stop (inhibit) HIV from entering a CD4 cell. There are different types of entry inhibitors: fusion inhibitors and CCR5 antagonists. One of each type is approved:
    - Fusion inhibitor: Fuzeon (enfuvirtide or T-20)
    - CCR5 antagonist: Selzentry (maraviroc)
- **Integrase Inhibitors:** These drugs interfere with HIV's integrase enzyme. There are three approved integrase inhibitors:
    - Isentress (raltegravir)
    - Tivicay (dolutegravir)
    - Elvitegravir, which can only be taken as part of the 4-drug combination pill Stribild
- **Nucleoside and Nucleotide Reverse Transcriptase Inhibitors (NRTIs or "nukes"):** These drugs interfere with HIV's reverse transcriptase enzyme. There are many approved NRTIs:
    - Emtriva (emtricitabine or FTC)
    - Epivir (lamivudine or 3TC)
    - Retrovir (zidovudine or AZT)
    - Videx (didanosine or ddI)
    - Viread (tenofovir)
    - Zerit (stavudine or d4T)
    - Ziagen (abacavir)
- **Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs or "non-nukes"):** Like NRTIs, these drugs interfere with HIV's reverse transcriptase enzyme. There are a number of approved NNRTIs:
    - Edurant (rilpivirine or RPV)
    - Intelence (etravirine or ETR)
    - Rescriptor (delavirdine)
    - Sustiva (efavirenz)

    - Viramune (nevirapine)
- **Protease Inhibitors (PIs):** These drugs interfere with HIV's protease enzyme. There are many approved PIs:
    - Aptivus (tipranivir)
    - Crixivan (indinavir)
    - Invirase (saquinavir)
    - Kaletra (lopinavir plus ritonavir)
    - Lexiva (fosamprenavir)
    - Norvir (ritonavir)
    - Prezista (darunavir)
    - Reyataz (atazanavir)
    - Viracept (nelfinavir)
- **Fixed-Dose Combinations:** Although not a separate class, there are fixed-dose drugs that combine two or more HIV drugs from one or more classes in just one pill. This can make dosing easier. There are seven combination pills approved:
    - Atripla (Sustiva plus Emtriva plus Viread)
    - Combivir (Retrovir plus Epivir)
    - Complera (Emtriva plus Viread plus Edurant)
    - Epzicom (Epivir plus Ziagen)
    - Stribild (Emtriva plus Viread plus elvitegravir plus cobicistat)
    - Trizivir (Retrovir plus Epivir plus Ziagen)
    - Truvada (Emtriva plus Viread)

For more information on any of these HIV drugs, see The Well Project's HIV Drug Chart [5].

Combining HIV Drugs

Health care providers often combine drugs from different classes in order to attack HIV at more than one step in its lifecycle. This is because HIV can make changes, called mutations, when it reproduces. Certain mutations keep certain HIV drugs from working. When this happens, we say that HIV has become resistant [6] to a particular HIV drug.

If you take only one drug (monotherapy) or take a few drugs that all belong to one class, it is easy for HIV to develop mutations that make it resistant to that drug or drug class. However, if you take a combination of drugs from different classes, HIV has a much harder time changing enough to develop drug resistance.

What does this mean for you? It means that combination therapy with drugs that block HIV at different steps of its lifecycle can prevent most of the production of new HIV. Most importantly, it means slower disease progression and longer life for people living with HIV (HIV+ people).

The Bottom Line

Currently five classes of HIV drugs target four steps of HIV's lifecycle. Attacking HIV on multiple fronts by combining drugs from different classes is the best way to slow or stop HIV reproduction. It is also the best way to prevent the development of drug resistance. The approval of new classes of HIV drugs?and new drugs in the classes already available?will continue to provide more treatment options for HIV+ people in the future.

Tags:

- HIV drugs [7]
- how does HIV work [8]
- HIV Virus [9]
- lifecycle of HIV virus in women [10]
- new HIV drug [11]
- HIV drug [12]
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- lifecycle HIV [14]
- protease [15]
- integrase [16]
- NRTI [17]
- NNRTI [18]
- fusion inhibitor [19]
- women HIV [20]
- women AIDS [21]
- HIV treatment [22]

Additional Resources

Select the links below for additional material related to the HIV lifecycle.
The HIV Life Cycle (NIH) [23]
Treatments for HIV & AIDS (AIDSmeds) [24]
HIV Structure and Life Cycle (Avert) [25]
HIV Lifecycle: how drugs work in different ways (i-base) [26]
How AIDS Works (howstuffworks) [27]
HIV Lifecycle (AIDSmap) [28]
Video of HIV Lifecycle (HHMI) [29]

Source URL: http://www.thewellproject.org/hiv-information/hiv-drugs-and-hiv-lifecycle

Links:
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[3] http://www.thewellproject.org/hiv-information/women-and-viral-load
[4] http://www.thewellproject.org/hiv-information/understanding-cd4-cells-and-cd4-cell-tests
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