

Treating HIV/AIDS



Biology of Cancer and AIDS

What Next After Testing Positive

Have you tested positive for HIV? (yes/no) ?



Get physical exam(s)
Women: Gyn & Pap



**Get key tests: CD4+
cell count & viral load**



**Get other blood tests
as needed**



Maximize your health support. Consider your treatment options.

Get CD4+ cell and viral load tests done every three months.



Early stage

CD4+ cell counts: above 500
Viral load: below 5,000

Get tests done every three months.

Consider ways to support your nutrition and immune system.

Middle stage

CD4+ cell counts: 200–500
Viral load: 5,000–100,000

Consider anti-HIV therapy.

Consider ways to support your nutrition and immune system.

Advanced stage

CD4+ cell counts: below 200
Viral load: above 100,000

Get tests done every three months.

Consider ways to prevent opportunistic infections.

Interventions Against HIV

1 General health maintenance

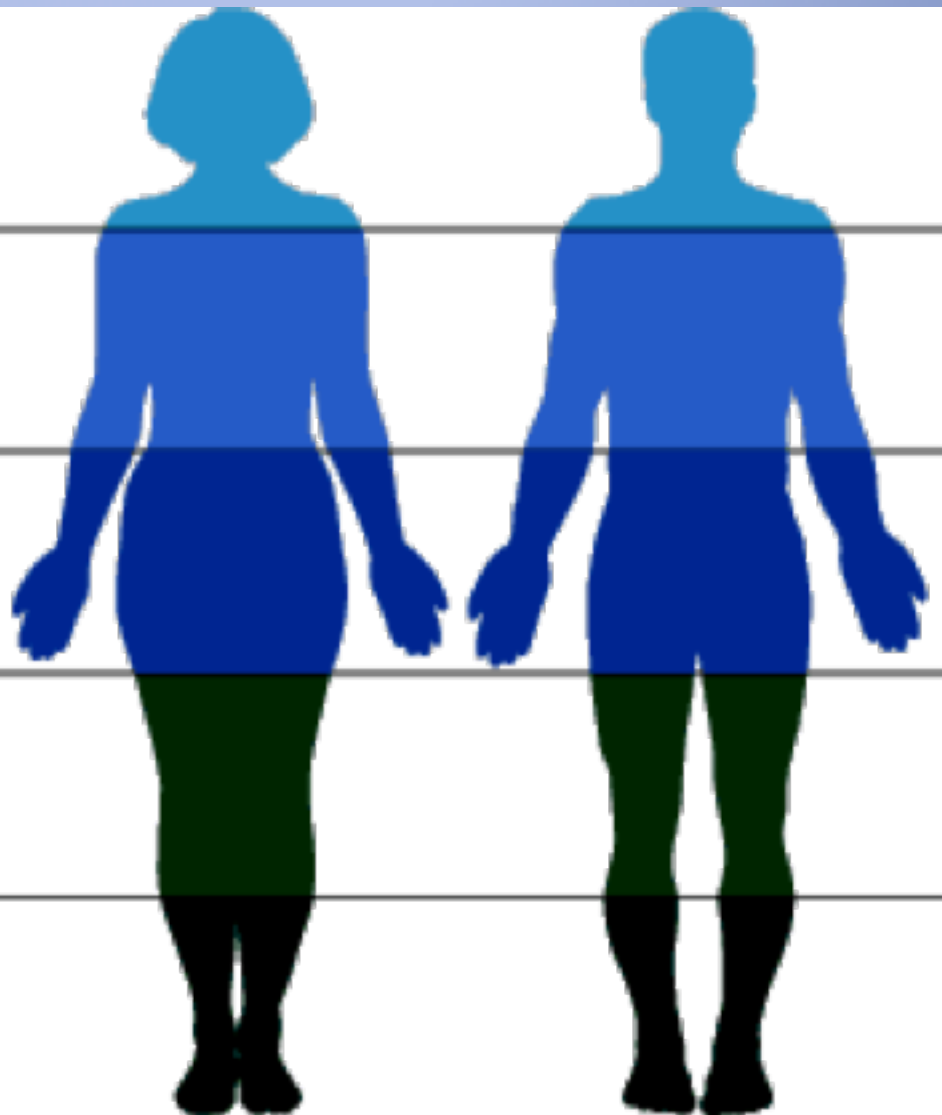


2 Supportive therapies

3 Anti-HIV treatment strategy

4 Immune therapies

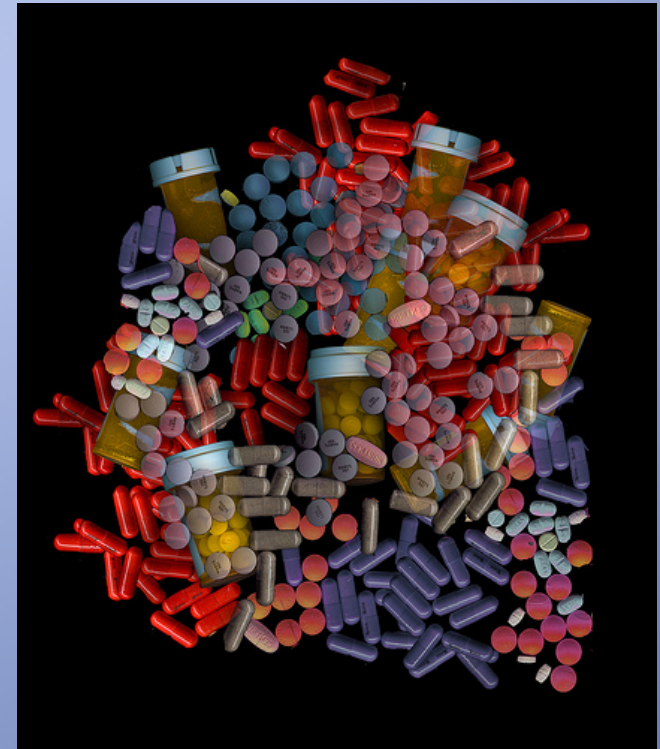
5 Opportunistic infection strategy



When to start antiretroviral therapy

Target population	2010 ART guideline
HIV+ asymptomatic ARV-naïve individuals	CD4 ≤ 350 cells/mm ³
HIV+ symptomatic ARV-naïve individuals	WHO clinical stage 2 if CD4 ≤ 350 cells/mm ³ OR WHO clinical stage 3 or 4 irrespective of CD4 cell count
HIV+ pregnant women	CD4 ≤ 350 cells/mm ³ irrespective of clinical symptoms OR WHO clinical stage 3 or 4 irrespective of CD4 cell count
HIV/TB coinfection ARV-naïve individuals	Presence of active TB disease, irrespective of CD4 cell count
HIV/HBV coinfection ARV-naïve individuals	Individuals who require treatment for their HBV infection*, irrespective of CD4 cell count

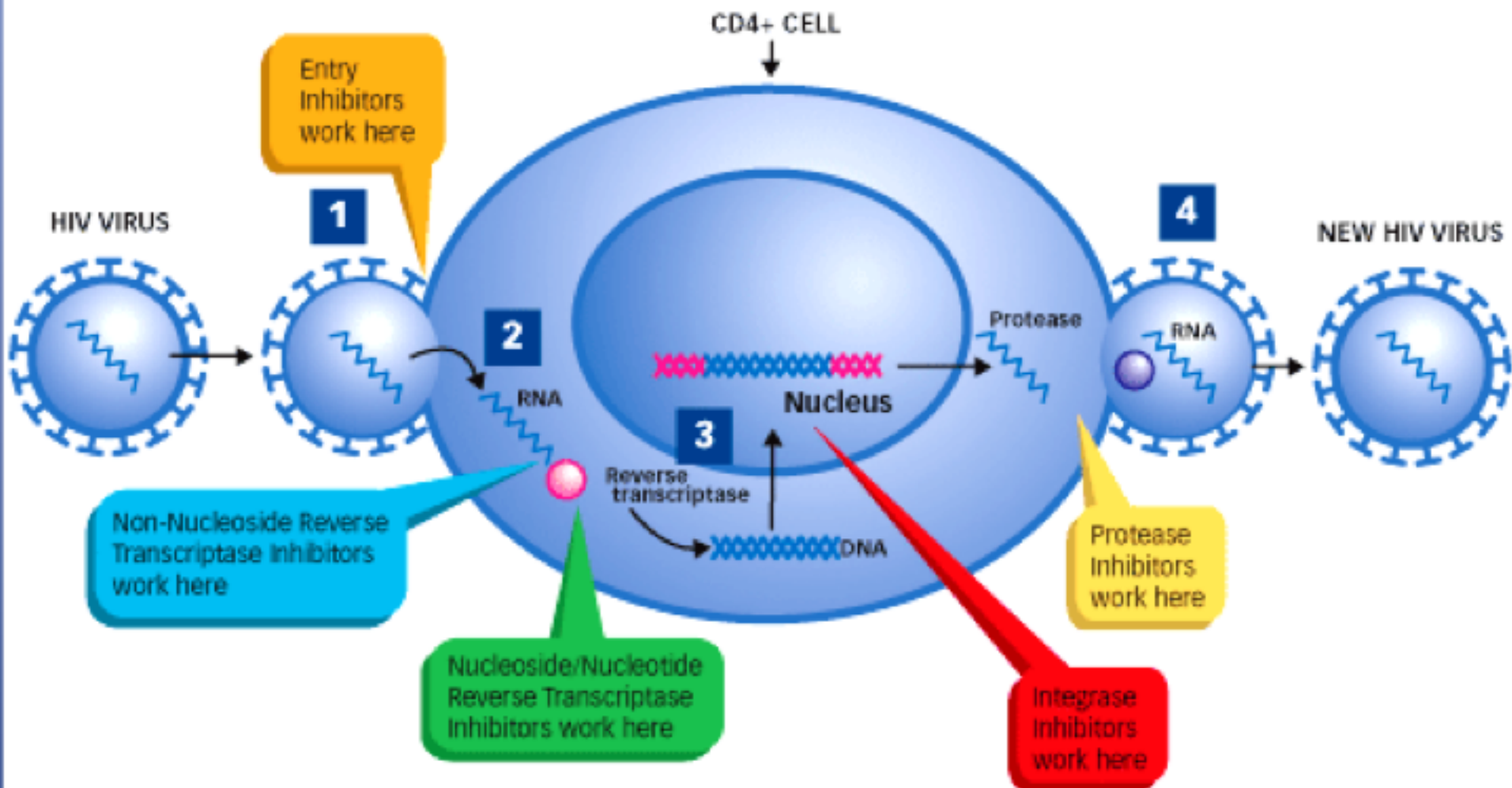
Goals of HIV Treatment



HIV therapy should:

- ❑ **Prolong** life and improve quality of life;
- ❑ **Suppress** HIV levels (viral load) below the limit of detection (<50 copies HIV RNA), or as low as possible for as long as possible;
- ❑ **Optimize** and extend the use of current therapy; and
- ❑ **Minimize** drug toxicity, and manage side effects and drug interactions.

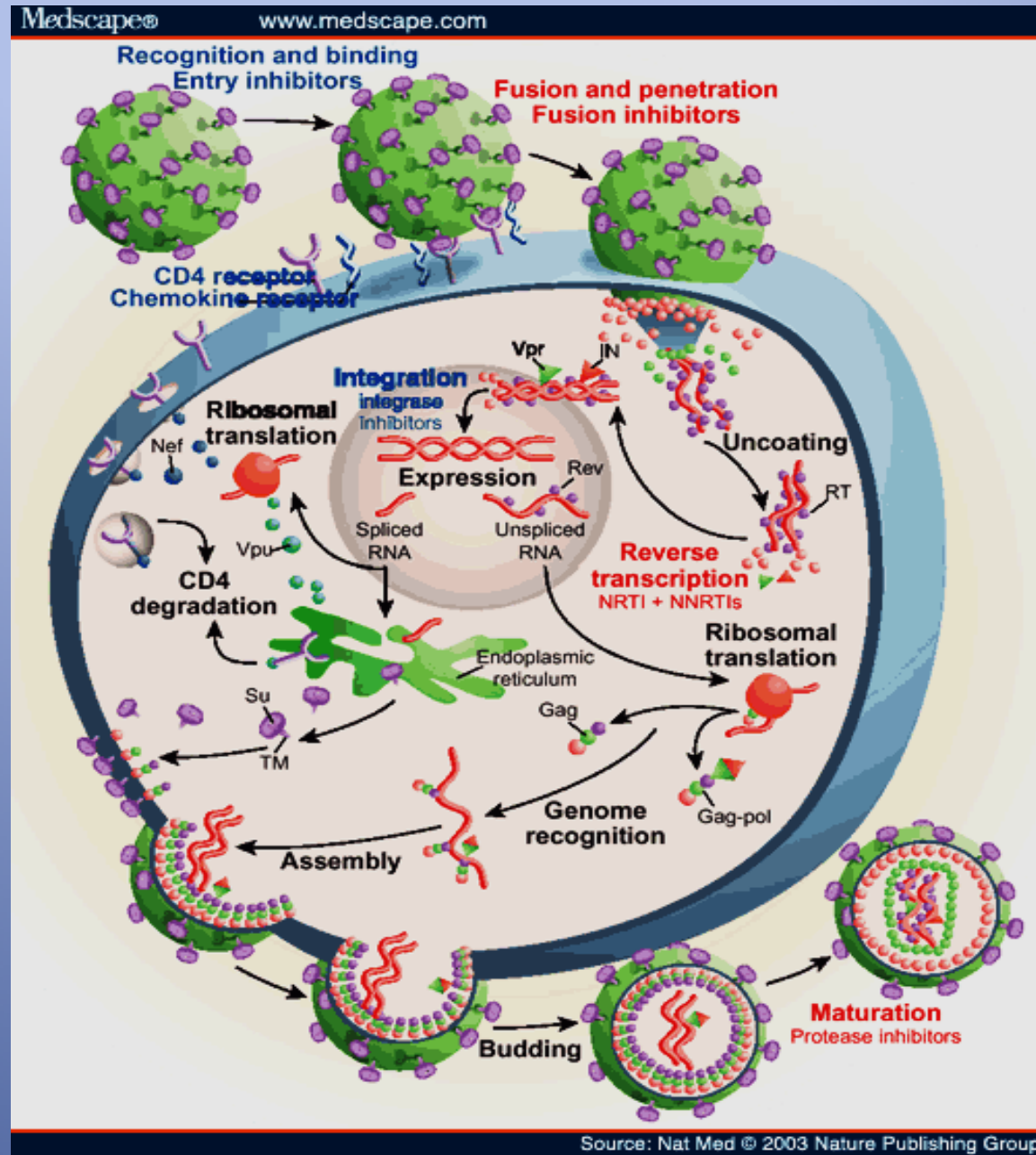
HIV and Current Drug targets



Major Classes of Anti-retroviral Drugs

- ❑ **Reverse transcriptase (RT) inhibitors** interfere with the critical step during the HIV life cycle known as reverse transcription. During this step, RT, an HIV enzyme, converts HIV RNA to HIV DNA. There are two main types of RT inhibitors.
 - **Nucleoside/nucleotide RT inhibitors or analogues (NRTIs)** are faulty DNA building blocks. When these faulty pieces are incorporated into the HIV DNA (during the process when the HIV RNA is converted to HIV DNA), the DNA chain cannot be completed, thereby blocking HIV from replicating in a cell.
 - **Non-nucleoside RT inhibitors (NNRTIs)** bind to RT, interfering with its ability to convert the HIV RNA into HIV DNA.
- ❑ **Protease inhibitors (PI)** interfere with the protease enzyme that HIV uses to produce infectious viral particles.
- ❑ **Entry and fusion inhibitors (FI)** interfere with the virus' ability to fuse with the cellular membrane, thereby blocking entry into the host cell.
- ❑ **Integrase inhibitors (II)** block integrase, the enzyme HIV uses to integrate genetic material of the virus into its target host cell.
- ❑ **Multidrug combination products** combine drugs from more than one class into a single product.

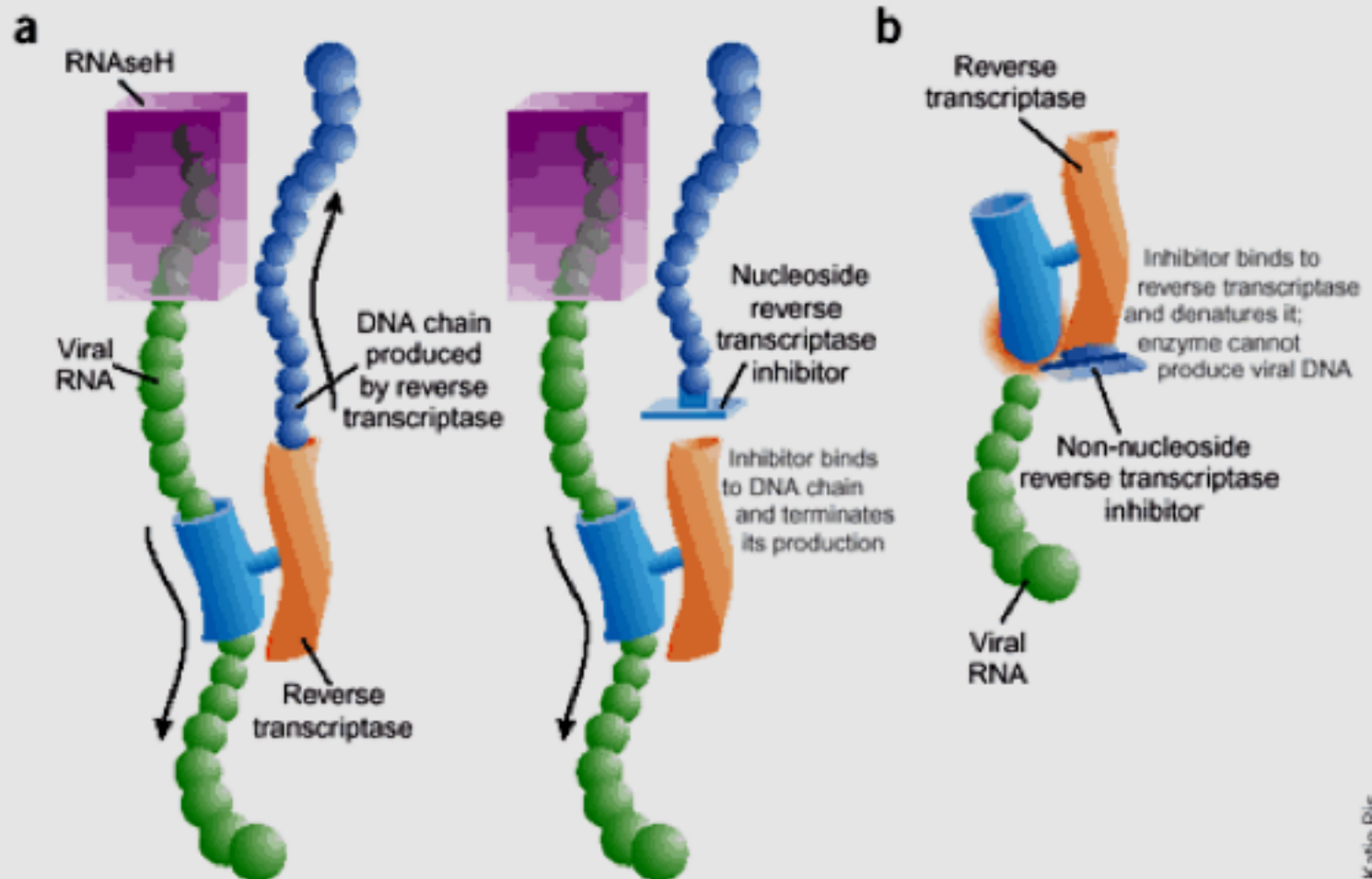
HIV-1 life cycle & Current Drug targets



NRTIs and NNRTIs: mechanisms of action

Medscape®

www.medscape.com



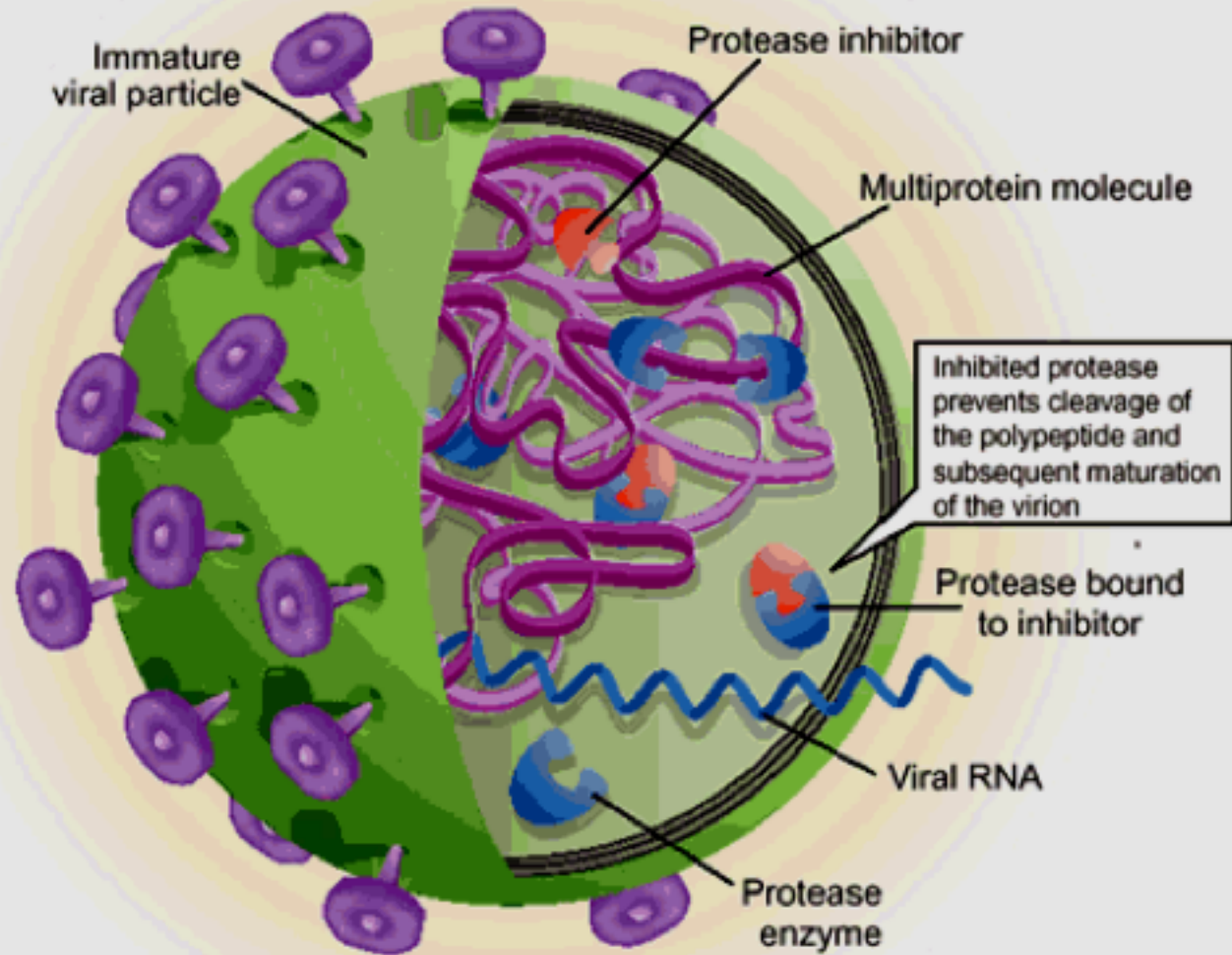
Katie Riis

Source: Nat Med © 2003 Nature Publishing Group

Protease Inhibitors: Mechanisms of Action

Medscape®

www.medscape.com

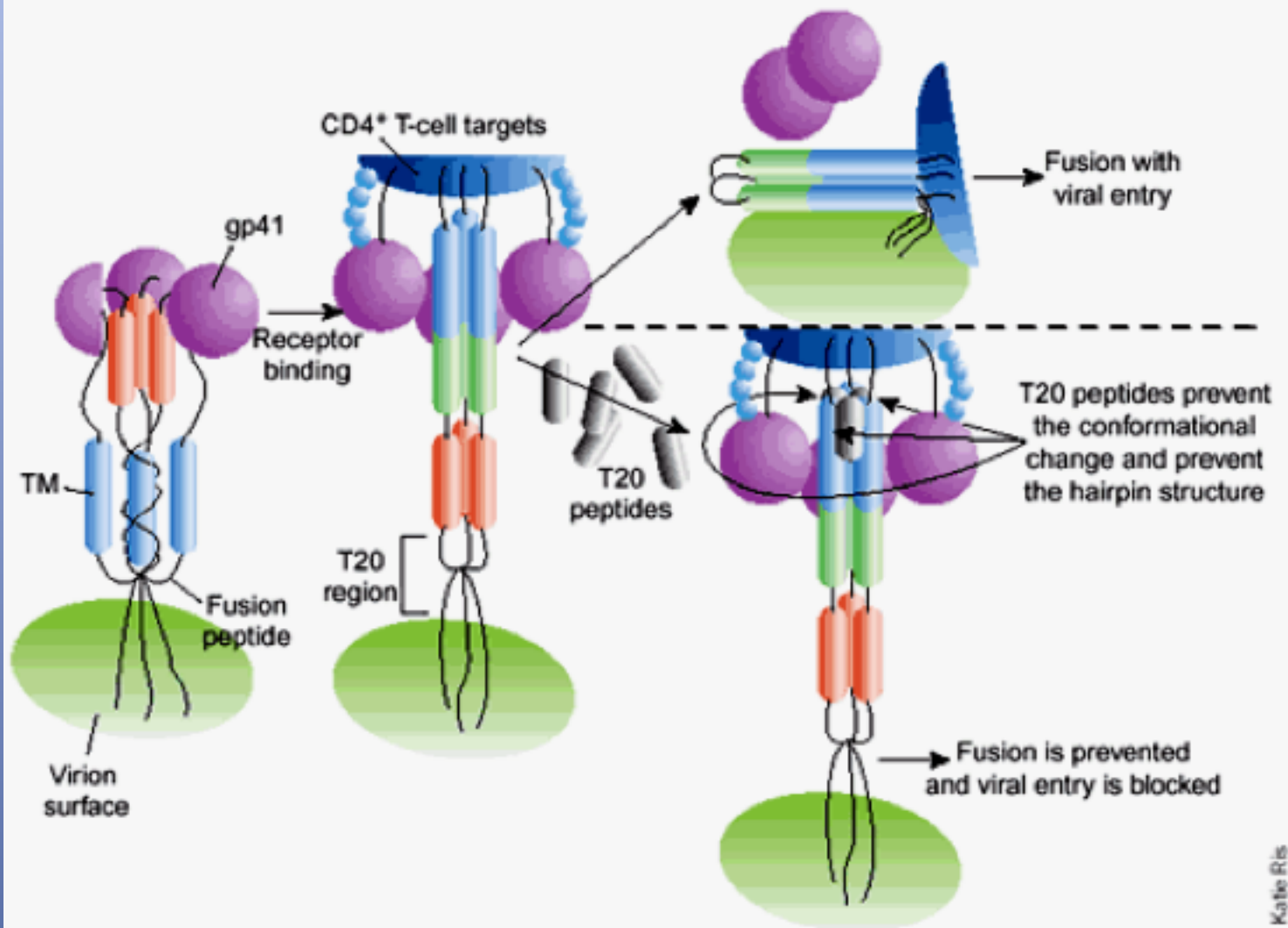


Katie R. Is

Fusion inhibitors: Mechanisms of Action

Medscape®

www.medscape.com



Katie Reis

Source: Nat Med © 2003 Nature Publishing Group

Fusion or Entry Inhibitors

Brand Name	Generic Name	Mode of Action	Experimental Code	Pharmaceutical Company
<u>Fuzeon</u>	enfuvirtide	Targets gp41	T-20	<u>Genentech</u>
<u>Selzentry or Celsentri</u>	<u>maraviroc</u>	Targets CCR5	UK-427,857	<u>ViiV Healthcare</u>
	<u>vicriviroc</u>	Targets CCR5	SCH-D; SCH-417690	<u>Schering-Plough Corporation</u>
	<u>ibalizumab</u>	Targets CD4	<u>TNX-355</u>	<u>TaiMed Biologics</u>
		Targets CCR5	<u>PRO 140</u>	<u>Progenics Pharmaceuticals</u>

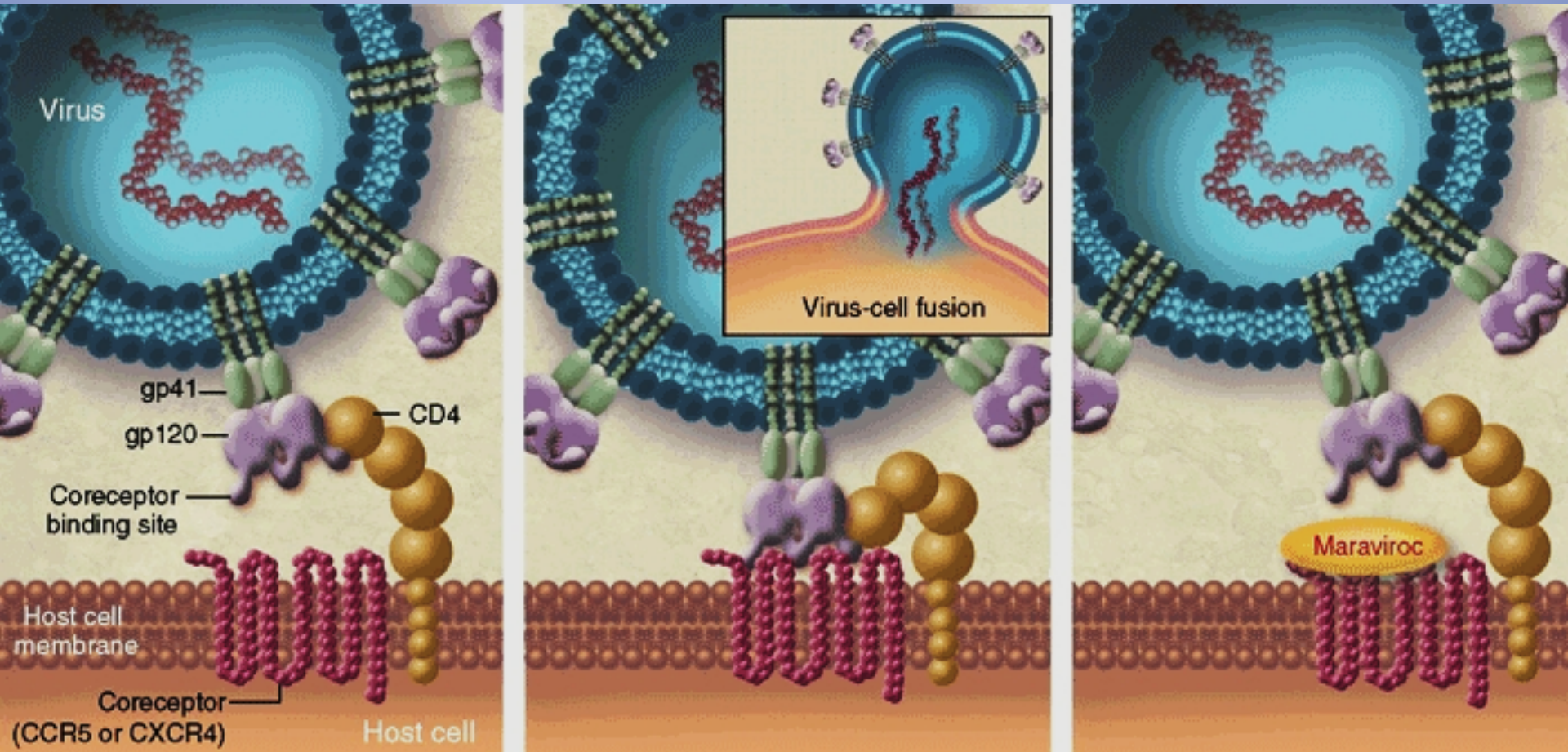
❑ **Fuzeon**: peptide that binds to gp41 preventing HIV from binding to surface of T-cells (FDA approved 2003) **MIMICS CD4 CONTACT MULTIFAILURE**

❑ **Selzentry**: CCR5-blocking entry inhibitor (approved by FDA August 2007)

❑ **Vicriviroc & PRO140** bind CCR5, preventing the virus from infecting healthy cells (not yet FDA approved).

❑ **TNX-355**: experimental monoclonal antibody that targets the CD4 protein on Helper T cells

Mechanism of action of Maraviroc



Once-a-day HIV drug cocktail — in one pill — wins FDA approval

Updated 7/16/2006 7:02 AM ET

E-mail | Save | Print | Reprints & Permissions | [RSS](#)

By Steve Sternberg, USA TODAY

WASHINGTON — The federal government on Wednesday approved the first HIV treatment that packs a triple-drug cocktail into a one-a-day pill.

Doctors say the salmon-colored pill will vastly simplify AIDS care and turn what a few years ago was a bothersome regimen of 20 or 30 tablets to one pill taken before bed.

To be sold as Atripla, the pill includes doses of three drugs now sold in the USA by two companies. The drugs are Bristol-Myers Squibb's Sustiva and Gilead Pharmaceutical's Truvada, a combo of Viread and Emtriva.

Taking the trio as a single pill makes it less likely that patients will miss doses, which would allow the virus to rebound and become resistant to treatment, doctors say. Keeping the virus in check also helps lower the risk that a patient will infect someone else.

"To me, it achieves the ultimate goal," says AIDS specialist John Bartlett of Johns Hopkins University. "It's a pill you can take without regard to meals, it's about as potent a regimen as we have, and it's relatively free of side effects."

The Food and Drug Administration approved the drug in three months, as part of a fast-track process introduced two years ago, after research showed the pill is equivalent to the drugs taken separately. The wholesale price of a 30-day supply of the pill will be \$1,150.88, the same as Truvada and Sustiva purchased separately, Gilead officials say. Atripla is expected to be on sale within four days.

"It's a big step forward from where we were 10 years ago," says Norbert Bischofberger, Gilead's vice president of research and development. "Even though (anti-HIV drugs) had a miraculous effect, they were impossible for anybody to take long-term."

FDA's acting commissioner, Andrew von Eschenbach, told reporters Wednesday that "compliance with therapy is as important as therapy itself."



[Enlarge](#)

By Haraz N. Ghanbari, AP

Andrew von Eschenbach, acting director of the Food and Drug Administration, announces a new fixed-dose, once-a-day pill, called Atripla, for the treatment of HIV-positive patients.



[Enlarge](#)

Atripla

- ❑ Atripla is a tablet that contains three antiretroviral drugs (ARVs) used to fight HIV
- ❑ Atripla is taken as one tablet once a day
- ❑ Atripla was approved in 2006 as an ARV for adults with HIV infection
- ❑ The drugs in Atripla are a non-nucleoside reverse transcriptase inhibitor (efavirenz) and two nucleoside analog reverse transcriptase inhibitors (emtricitabine and tenofovir)



What is Combination Therapy, (HAART)?

- ❑ Taking two or more antiretroviral drugs at the same time vastly reduces the rate at which resistance develops
- ❑ **Highly Active Antiretroviral Therapy (HAART)** is used to describe a combination of three or more anti-HIV drugs
- ❑ The most common combination of drugs used in HAART today includes 2 NRTIs with 1 NNRTI or PI
- ❑ The number of pills can range from as few as 1 to as many as 16

Combination	Brand name
ABC + 3TC	Epzicom (US) Kivexa (Europe)
ABC + AZT + 3TC	Trivizir
AZT + 3TC	Combivir
TDF + FTC	Truvada

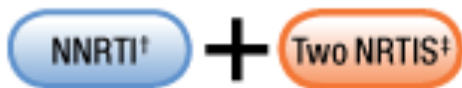
Various HAART Combinations

- ❑ AZT or **zidovudine** is a nucleoside reverse transcriptase inhibitor
- ❑ 3TC, also known as **lamivudine**, is an antiretroviral that works in the same way as AZT
- ❑ **Abacavir (ABC)** is the most powerful nucleoside analog (NRTI) used to treat HIV/AIDS

DHHS Recommended Regimens

The DHHS recommends one of 3 types of HIV regimens for patients new to therapy

NNRTI-Based Regimen



PI-Based Regimen



PIs are preferably boosted

INSTI-Based Regimen



Adapted from DHHS Guidelines, December 1, 2009. Please see the DHHS Guidelines for additional important information.

†NNRTI = Non-nucleoside reverse transcriptase inhibitor

‡NRTI = Nucleoside reverse transcriptase inhibitor

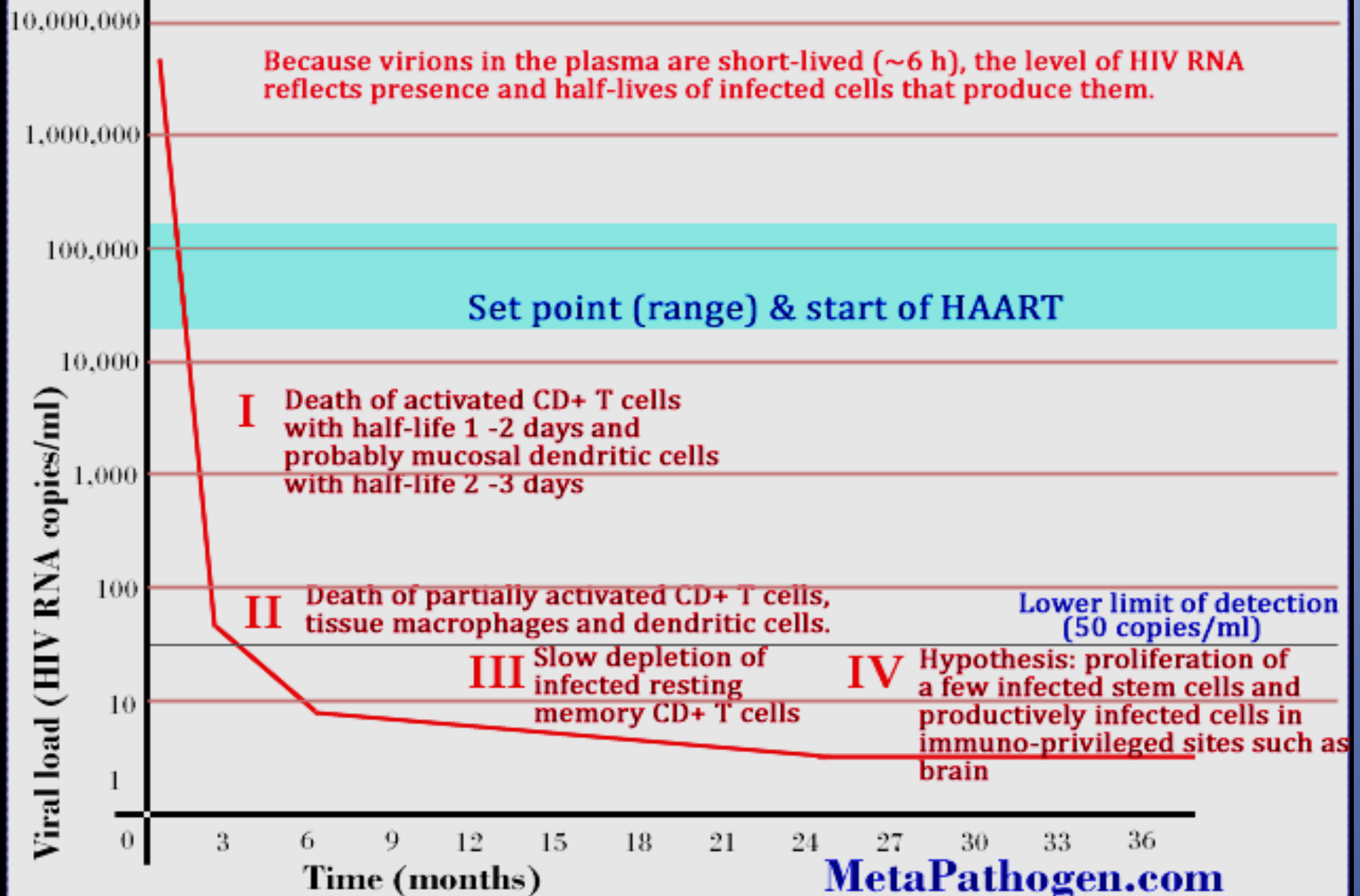
§PI = Protease inhibitor

¶INSTI = Integrase strand transfer inhibitor

HIV Set Point and HAART

Phases of viremia decay after start of HAART

Adapted from Dahl V et al., Antiviral Res. 2010



Possible side effects of HAART include:



<http://www.thebody.com/content/treat/art5044.html>

- ☐ liver problems
- ☐ diabetes
- ☐ anemia
- ☐ abnormal fat distribution (lipodystrophy syndrome)
- ☐ high cholesterol
- ☐ increased bleeding in patients with hemophilia
- ☐ decreased bone density
- ☐ skin rash
- ☐ pancreatitis (inflammation of the pancreas)
- ☐ nerve problems

Life Expectancies in Patients Taking Combination Antiretrovirals

- ❑ HIV survival is improving in wealthy countries, and a **20-year-old** starting combination antiretroviral therapy can expect to live **another 43 years**, according to an industry-funded *Lancet* study.
- ❑ Using cohorts from Canada, Europe, and the U.S., 43,600 strong, researchers found that the years of life remaining for a 20-year-old starting therapy increased from 36 in the 1996–99 period to almost 50 years in the 2003–05 period.
- ❑ However, those acquiring HIV through injection-drug use and those starting treatment at lower CD4 cell counts had much higher mortality rates.

Mother to Child Transmission (MTCT)

- ❑ In 2005, ~700,000 children under 15 became infected with HIV, mainly through MTCT
- ❑ ~ 90% of these MTCT infections occurred in Africa where AIDS is beginning to reverse decades of steady progress in child survival.
- ❑ Pregnant women who receive a course of the antiretroviral drug zidovudine (AZT) had a two-thirds lower risk of transmitting HIV than those who took a placebo.
- ❑ UNAIDS 2012 - report significant gains in reducing MTCT in several African countries
- ❑ A number of studies have shown that the protective benefit of AZT or HAART is diminished when babies continue to be exposed to HIV through breastfeeding

Goals/Quality of Life Issues

- ❑ Reducing viral load as low as possible, preferably below the level of detection, should be an important goal of therapy.
- ❑ Successful long-term use of therapies is more important than short-term gains.
- ❑ The use of treatment that is only partly effective speeds the development of viral resistance.
- ❑ Using a drug exactly as prescribed is critical to success.

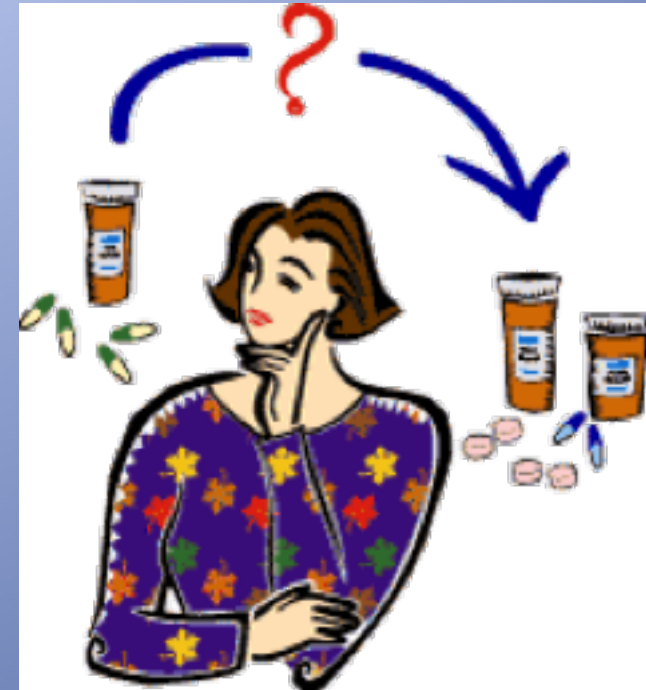
- The ability to tolerate side effects
- Drug interactions
- The demands of a particular regimen
- If you can't take a drug consistently as prescribed, its potency is irrelevant
- Not adhering to a drug regimen will quickly contribute to developing drug resistance



When is it Time to Change Therapies?

The Federal Guidelines recommend that people switch therapies when:

- ☐ **Detectable HIV levels after being undetectable**
- ☐ **HIV levels remain detectable after 4–6 months of starting anti-HIV therapy**
- ☐ **Persistent decreases in CD4+ cell counts**
- ☐ **Intolerable side effects occur**
- ☐ **Adherence is poor**
- ☐ **There is less than a 0.5–0.75 log (3- to 6-fold) reduction in HIV levels after four weeks or less than one log after eight weeks of starting anti-HIV therapy**
- ☐ **Symptoms of HIV disease occur; and/or**
- ☐ **A three-fold or greater increase in HIV levels from their lowest levels.**



Prevention and Treatment as Prevention

Randomized, Controlled Intervention Trial of Male Circumcision for Reduction of HIV Infection Risk: The ANRS 1265 Trial.

PLoS Medicine, 2005 Nov;2(11):e298.

Preexposure Chemoprophylaxis for HIV Prevention in Men Who Have Sex with Men.

N Engl J Med., 2010 Dec 30;363(27):2587-99.

Prevention of HIV-1 Infection with Early Antiretroviral Therapy

N Engl J Med., 10.1056/NEJMoa1105243

PrEP: Pre-Exposure Prophylaxis

3 Things to Know About PrEP for HIV

Posted: 04/09/2013 3:46 pm



Follow > [HIV/AIDS](#), [Health](#), [Health](#), [Personal Health](#), [HIV Prevention](#), [LGBT Health](#), [Gay Health](#), [Hiv](#), [Hiv Prevention Pill](#), [Pre-Exposure Prophylaxis](#), [Prep](#), [Prep Hiv](#), [Healthy Living News](#)

SHARE THIS STORY

Like 88 people like this. Sign Up to see what your friends like.

16

14

1

0

share tweet email +1

Submit this story

February 2012, New York, N.Y.: People on their way to the Black Party report seeing pushers on the street selling a brand new "party kit" which allegedly included ecstasy, Viagra, and a pill to prevent HIV infection.

July 16, 2012, Silver Spring, Md.: The U.S. Food and Drug Administration [approved the drug Truvada](#) from Gilead Science to reduce the risk of HIV infection in uninfected individuals who are at high risk of HIV infection.

November 30, 2012: ManhuntCares sends out an email broadcast to Manhunt users to commemorate World AIDS Day with the tag line "HIV Prevention Pill for Negative Men: A choice when condoms are in the way or not enough?" ([The tagline was later changed](#) to: "HIV Prevention Pill for Negative Men: Another choice for staying HIV free?" to avoid mischaracterization of the message).

In Wake of Latest Trial Results, CDC Stresses That Consistent Use Is Imperative When Using Pre-Exposure Prophylaxis to Prevent HIV Infection

Statement for Attribution to Jonathan Mermin, M.D., Director of CDC's Division of HIV/AIDS Prevention

The Vaginal and Oral Interventions to Control the Epidemic study, also known as the VOICE study, released today by the National Institute of Allergy and Infectious Diseases, National Institutes of Health indicates that participants provided daily oral pre-exposure prophylaxis (PrEP) did not experience any protection against HIV compared to those in the placebo arm, likely because very few were taking the study drugs as directed. Less than one-third of participants assigned to the two study arms evaluating daily oral tenofovir (TDF) and daily oral TDF/FTC had any study drug detected in their blood.

Given the low levels of adherence in the study, this result is not surprising: PrEP must be taken consistently to work effectively.

Not enough health care providers know about PrEP.

Pre-exposure prophylaxis (PrEP) is a medicine taken daily that can be used to prevent HIV infection. PrEP is for people without HIV who are at very high risk for acquiring it from sex or injection drug use.



90%

Daily PrEP can reduce the risk of sexually acquired HIV by more than 90%.



70%

Daily PrEP can reduce the risk of HIV infection among people who inject drugs by more than 70%.



1 in 3

1 in 3 primary care doctors and nurses haven't heard about PrEP.

SOURCE: CDC Vital Signs, Dec. 2015.



Scotland Recommends Making HIV Prevention Pill **Truvada** Available

Laboratory Equipment - 8 hours ago

The Scottish Medicines Consortium recommended making an HIV prevention pill called **Truvada** available to people through the United ...

Scotland says yes to **Truvada** as PrEP

