

HIV 101 & Pharmacology

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No Disclosures

-
- **HIV Lifestyle**
 - **Mechanism of action**
 - **Principles of Treatment**
 - **First Line Naïve Regimens & Considerations**

***HIV should be* a Chronic Disease**

Normal Life Expectancy with 1 pill/day

Highly Active Antiretroviral Therapy (ART):

- Decreases morbidity by 57-91%
- Promotes a normal life expectancy
- The expected age at death was **78·0 years** (77·7–78·3) for a 20 yo patient starting ART during 2008–10 with a CD4 count >350 cells/μL 1 year after starting ART

Survival of HIV-positive patients starting antiretroviral therapy between 1996 and 2013: a collaborative analysis of cohort studies

The Antiretroviral Therapy Cohort Collaboration [†] • [Show footnotes](#)

[Open Access](#) • Published: May 10, 2017 • DOI: [https://doi.org/10.1016/S2352-3018\(17\)30066-8](https://doi.org/10.1016/S2352-3018(17)30066-8) •

 Check for updates

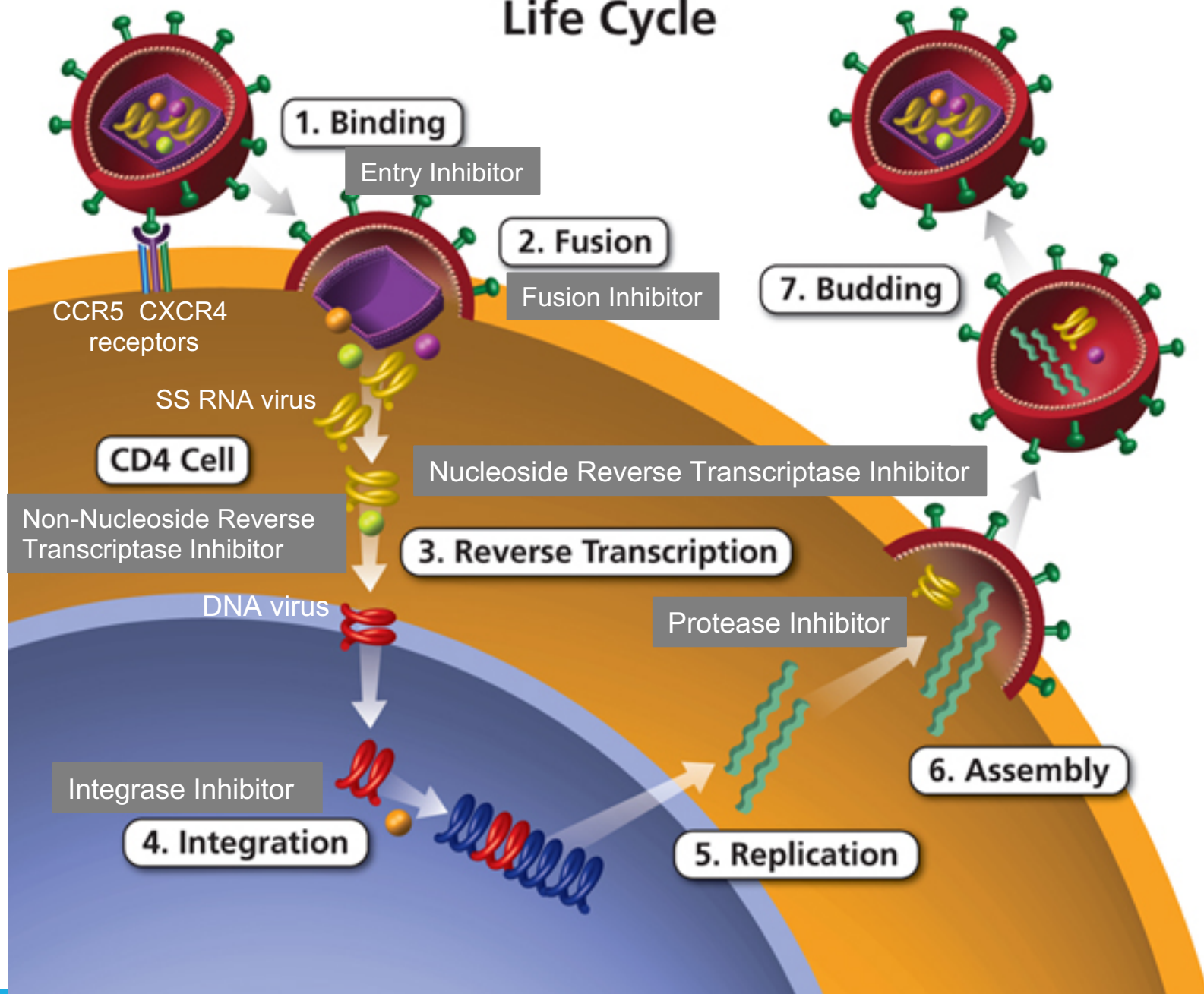


Antiretroviral Therapy Reduces HIV Transmission by 100%

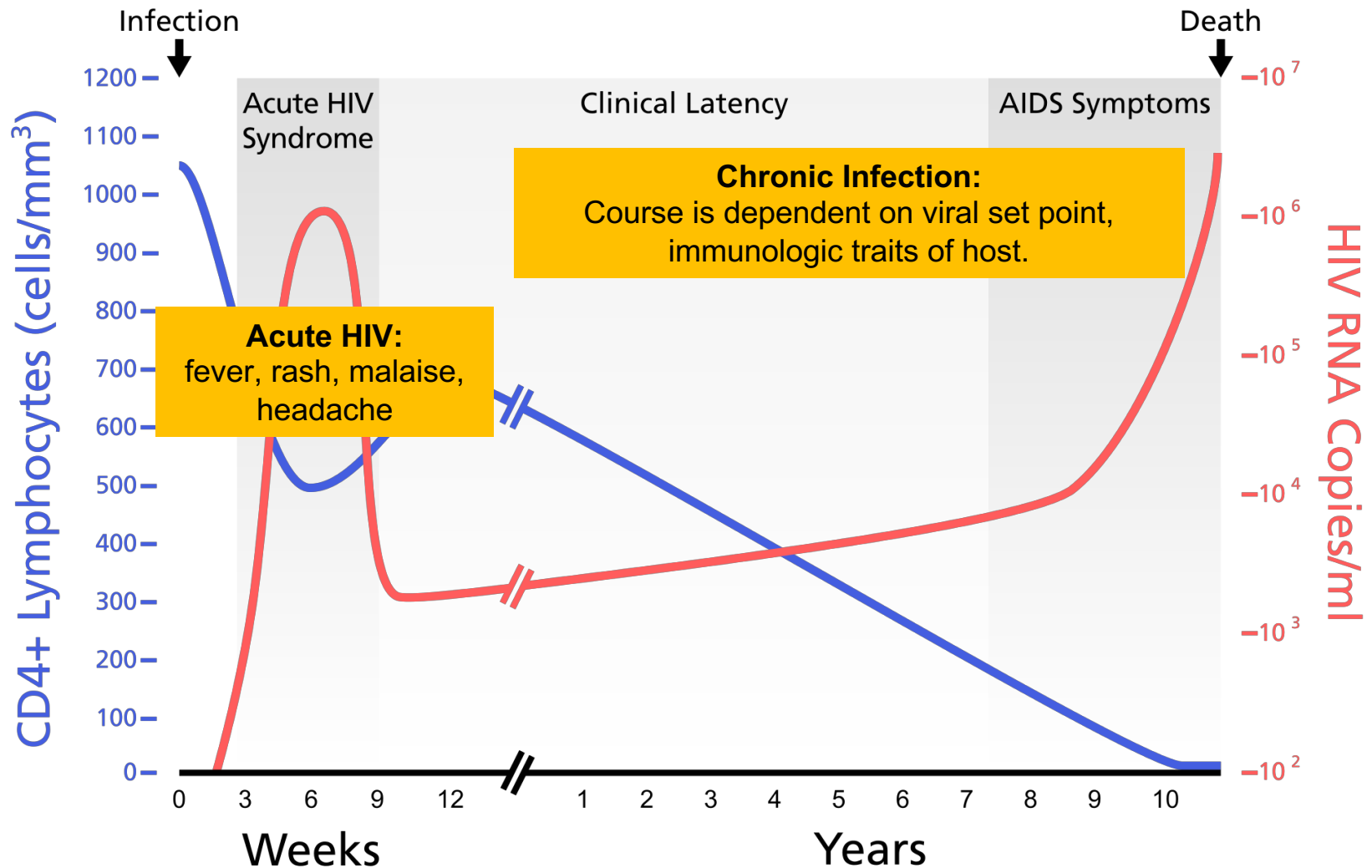


UNDETECTABLE = UNTRANSMITTABLE

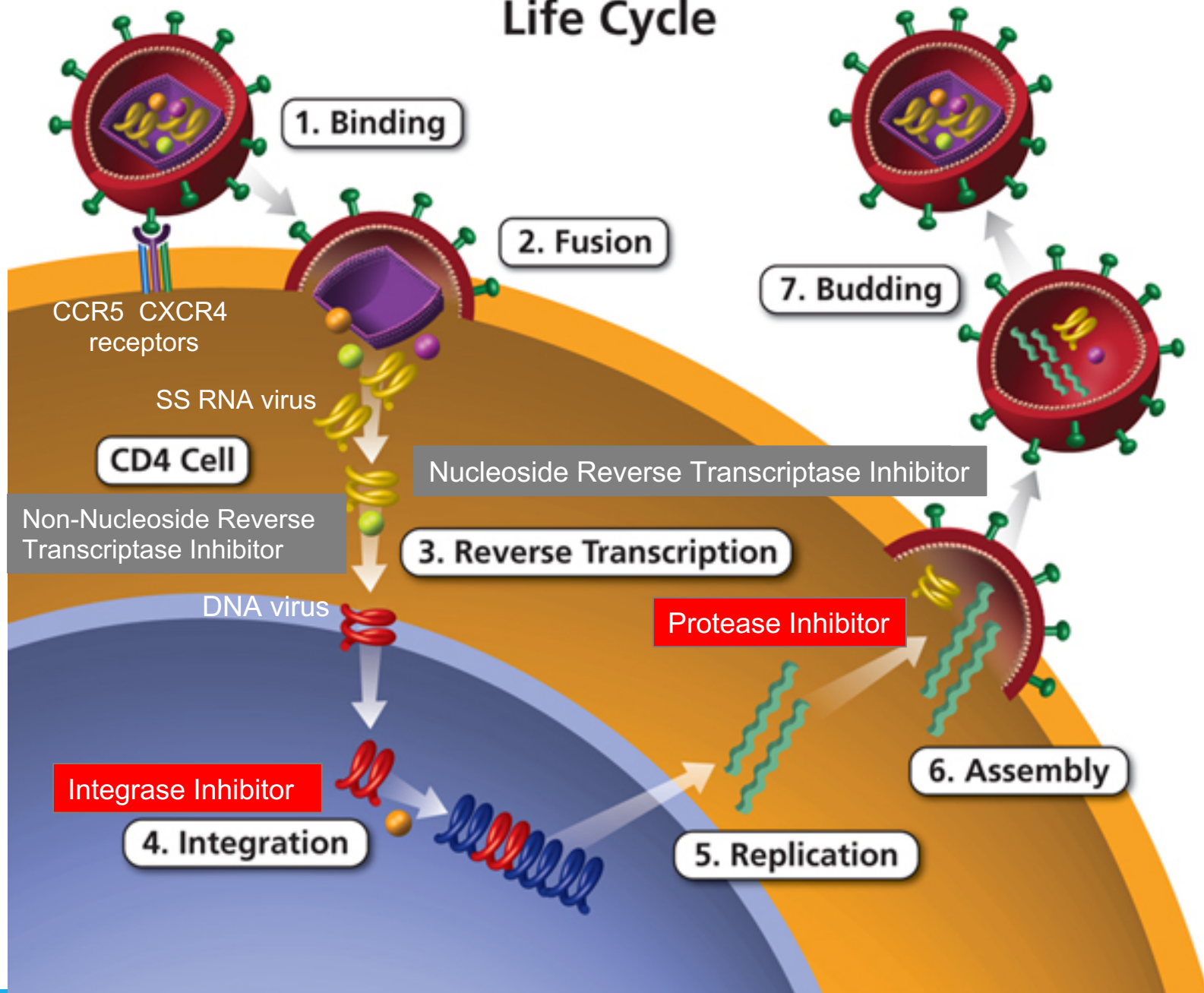
Life Cycle



The natural history of HIV



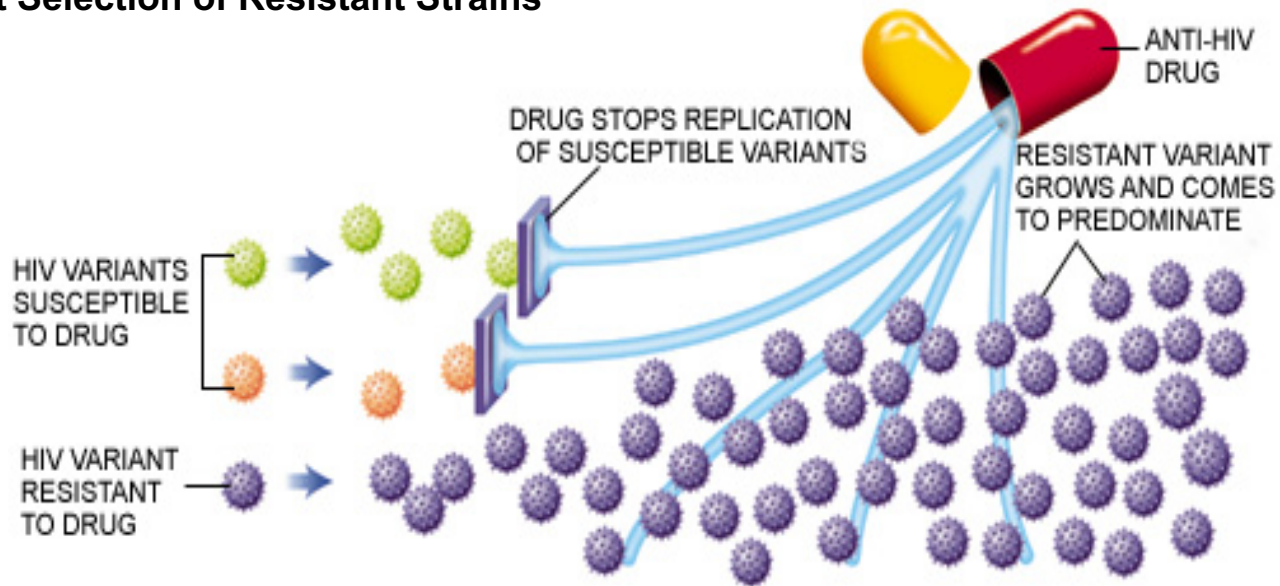
Life Cycle



3 ACTIVE DRUGS from 2 CLASSES: “NUC” BACKBONE + Integrase or PI

Why 3 drugs?

Prevent Selection of Resistant Strains



How drug resistance arises. Richman, DD. Scientific American , July 1998

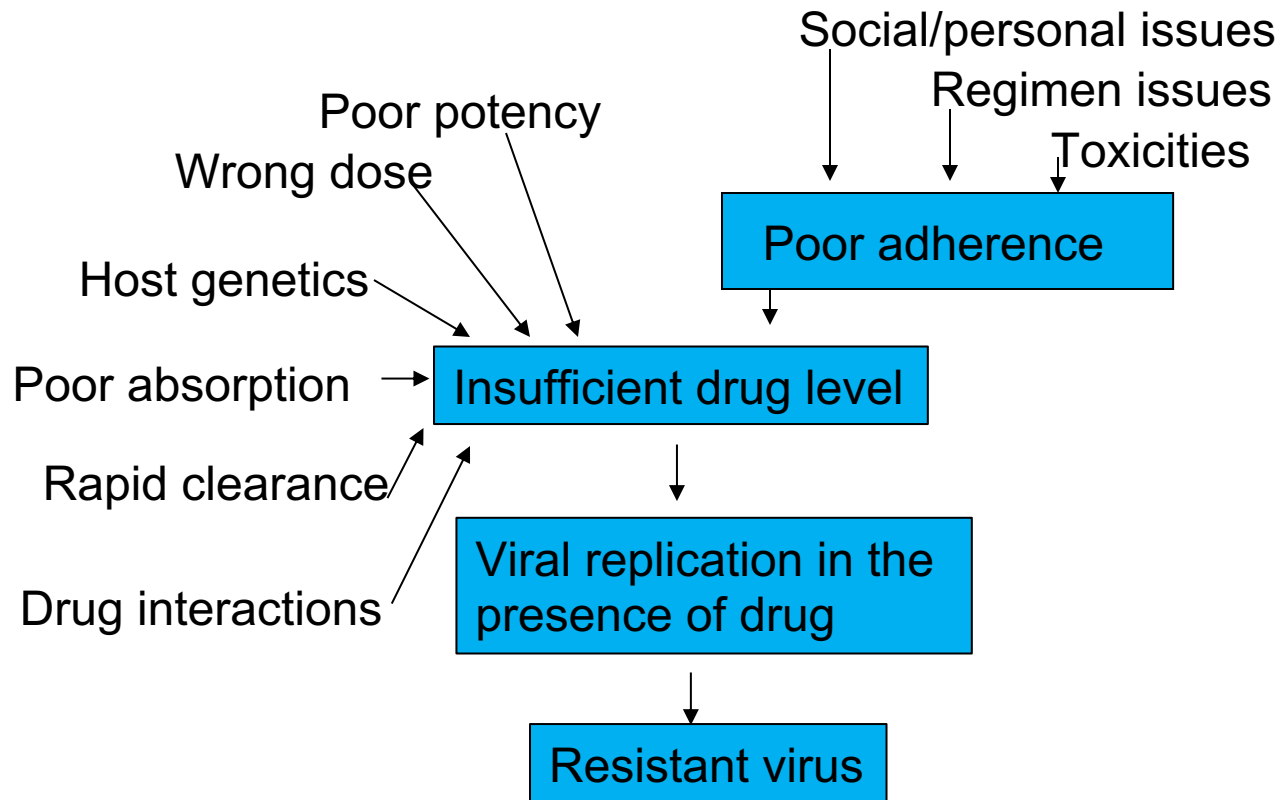
What is HIV Resistance?

- Ability of HIV to mutate and replicate in the presence of antiretrovirals
- Results in treatment failure and possible further transmission of resistance virus
- Can be acquired or transmitted.

How does HIV Resistance Develop?

- HIV reverse transcriptase is a low-fidelity enzyme
- Mistakes (mutations) lead to mutant strains of HIV
- Most are inconsequential or result in incompetent strains of HIV
- A small number confer resistance to currently available antiretroviral drugs
- Insufficiently potent antiretrovirals exert reproductive pressure that selects for resistance-bearing strains

How does HIV Resistance Develop?

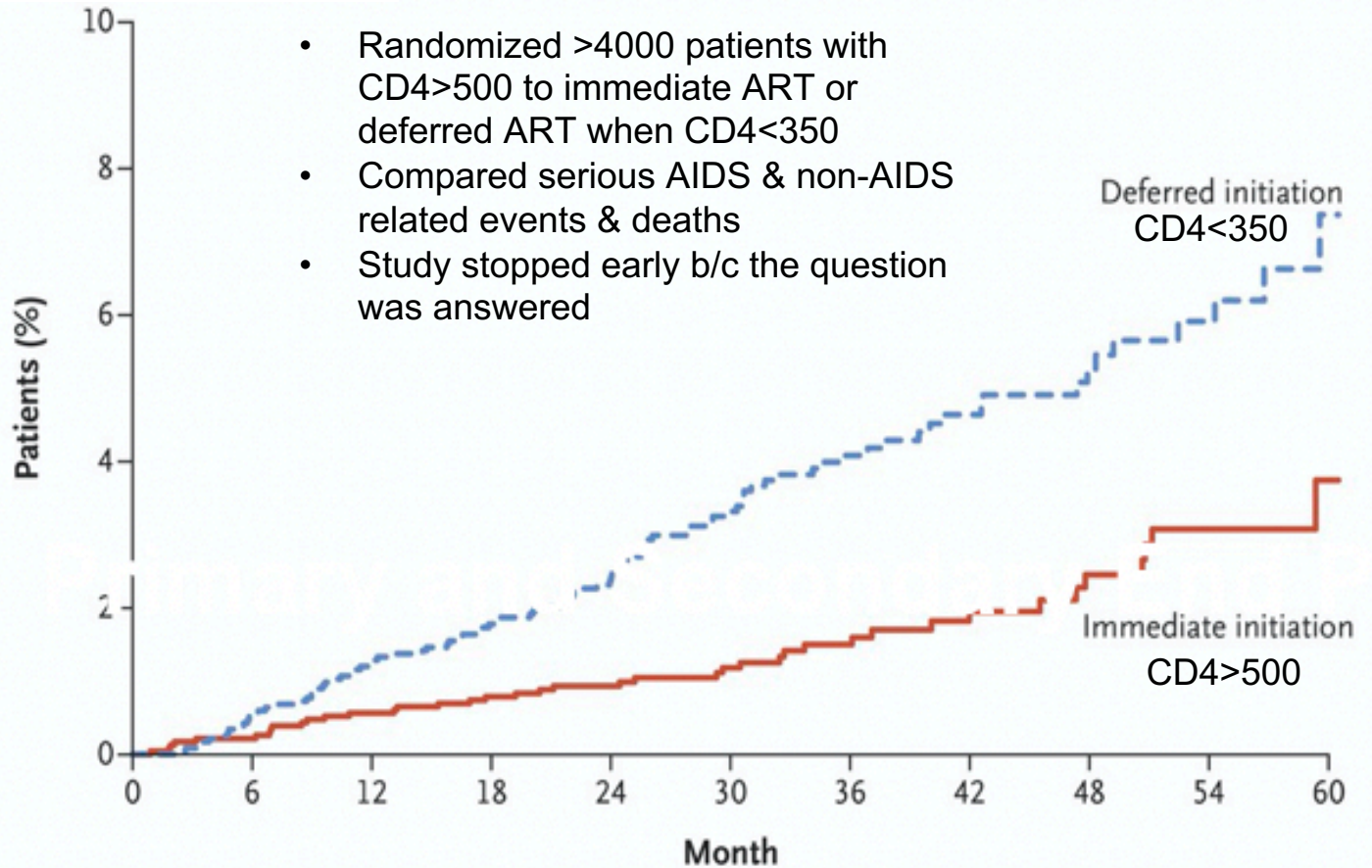


Who do we treat? Everyone

Years	Eligible population
2004 – 2010	<ul style="list-style-type: none">• CD4 <200 cells/μl or• WHO stage 4
2010 – 2013	<ul style="list-style-type: none">• CD4 \leq200 cells/μl or• WHO stage 4 or• CD4 \leq350 cells/μl (TB/HIV or pregnant women only) or• MDR/XDR-TB
2013 – 2015	<ul style="list-style-type: none">• CD4 \leq350 cells/μl or• WHO stage 3 or 4 or• All TB/HIV co-infected
2015 - 2016	<ul style="list-style-type: none">• CD4 \leq500 cells/μl or• WHO stage 3 or 4 or• All TB/HIV co-infected or• Hepatitis B co-infected or• Pregnant/breastfeeding women
2016 – present	“Treat all” (test-and-treat)

Reduced AIDS Related Events/Death with Early ART

Time to Serious AIDS-related event or death



Goals of Treatment

- Reduce HIV-associated morbidity and prolong the duration and quality of survival
- Restore and preserve immunologic function
- Maximally and durably suppress plasma HIV viral load (VL <50 copies/ml)
- Prevent HIV transmission

Adherence

>95% adherence to achieve therapeutic goals

10% reduction in adherence = doubling of VL

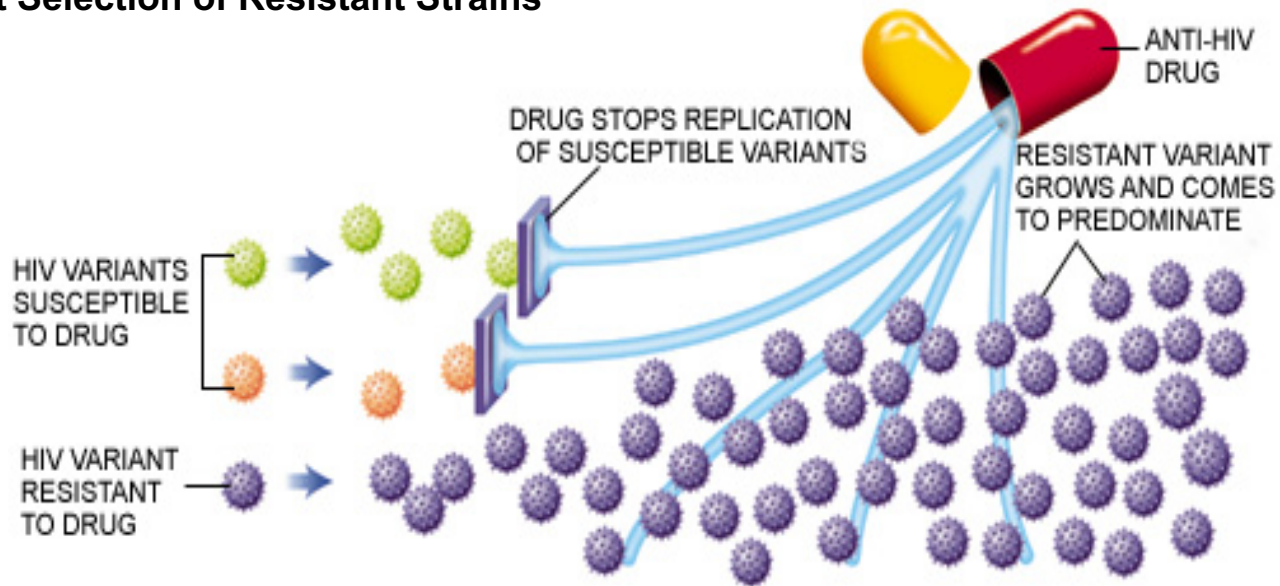
Result of non-adherence- RESISTANCE

Many reasons for poor adherence

Knowledge/Understanding	Side Effects
Irregular schedules	Pill Fatigue
Memory	Access to meds/\$\$
Mental Health Issues	Illicit Drug Abuse
Issues swallowing	Stigma

Why 3 drugs?

Prevent Selection of Resistant Strains



How drug resistance arises. Richman, DD. Scientific American , July 1998

7 First-Line Therapies

For Treatment-Naïve Patients

Brand Name	1st "NUC"	2nd "NUC"	Integrase	Notes
<u>Biktarvy</u> [®]	Tenofovir alafenamide (TAF)	Emtricitabine (FTC)	Bictegravir (BIC)	
<u>Triumeq</u> [®]	Abacavir* (ABC)	Lamivudine (3TC)	Dolutegravir (DTG)	ABC hypersensitivity
Truvada [®] + Tivicay [®]	Tenofovir (TDF)	Emtricitabine (FTC)	Dolutegravir (DTG)	
Descovy [®] + Tivicay [®]	Tenofovir alafenamide (TAF)	Emtricitabine (FTC)	Dolutegravir (DTG)	
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Descovy [®] + Isentress [®]	Tenofovir alafenamide (TAF)	Emtricitabine (FTC)	Raltegravir (RAL)	
<u>Dovato</u> [®]	<i>Lamivudine (3TC)</i>		<i>Dolutegravir (DTG)</i>	<i>VL > 500,000 copies/mL, no genotype Unknown HBV status</i>

Biktarvy, Triumeq, Dovato 1 pill once daily

Other Single Tablet Regimens

Brand Name	1st “NUC”	2nd “NUC”	Integrase	Booster/ Other	Notes
Genvoya®	Tenofovir alafenamide (TAF)	Emtricitabine (FTC)	Elvitegravir (DTG)		
Stribild®	Tenofovir (TDF)	Emtricitabine (FTC)	Elvitegravir (DTG)	Cobicistat (c)	
Odefsey®	Tenofovir alafenamide (TAF)	Emtricitabine (FTC)		Rilpivirine (RPV)	RPV Interactions RPV CD4>200, VL <100K
Complera®	Tenofovir (TDF)	Emtricitabine (FTC)		Rilpivirine (RPV)	RPV Interactions RPV CD4>200, VL <100K
Atripla®	Tenofovir (TDF)	Emtricitabine (FTC)		Efavirenz (EFV)	EFV CNS side effects, increased suicidality
Symtuza®	Tenofovir alafenamide (TAF)	Emtricitabine (FTC)		Darunavir (DRV) Cobicistat(c)	

Other Commonly Used Agents

Brand Name	NRTI/NNRTI	PI	Booster*	Notes
Prezista®		Darunavir (DRV)		
Prezcobix®		Darunavir (DRV)	Cobicistat (c)	
Reyataz®		Atazanavir (ATV)		
Evotaz®		Atazanavir (ATV)	Cobicistat (c)	
Norvir®			Ritonavir (r)	Used to boost ATV or DRV

Always consider drug-drug interactions for booster agents

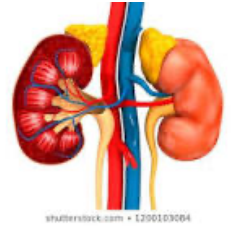
How to Choose

- Drug Resistance
- Pharmacogenetics
- Pill size (for some)
- Comorbidities
 - Chronic Kidney Disease
 - Hepatitis B Virus
 - Diabetes
 - Reflux
 - Anticoagulation
 - Antiplatelet
 - Asthma

How to Choose: Baseline Resistance

- Drug resistance can be transmitted
- Drug-resistance mutations can remain for years in
- 10-17% of patients may have baseline resistance to at least 1 drug
- Can have suboptimal response to ART if resistance is present and regimen is not adjusted
- HIV genotype to Nucleoside and Reverse Transcriptase should be obtained
- Rare transmitted integrase resistance

How to Choose: Chronic Kidney Disease (CKD)



- **Many agents need to be dose-adjusted or avoided in patients with CKD**
- Emtricitabine (FTC), Lamivudine (3TC) must be separated from fixed dose pill and redosed
- Tenofovir (TDF) can be used if Creatinine Clearance >50 mL/min
- Tenofovir Alafenamide (TAF) can be used if Creatinine Clearance >30 mL/min

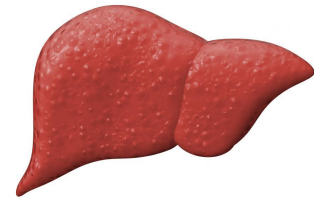
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How to Choose: Hepatitis B Virus



- HIV/HBV Coinfection
- Baseline tests should include Hepatitis B Testing
- Hepatitis B surface Antibody, Hepatitis B surface Antigen, Hepatitis B core Antibody
- Highest rates among MSM and IVDU
- HBV surface Antigen + or HBV sAb -/cAB+
 - Get HBV viral load
- **HBV needs TAF or TDF + 3TC or FTC**

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How to Choose: Diabetes

- METFORMIN levels increased with dolutegravir/bictegravir
- Don't use more than 1 gram of METFORMIN daily

Dolutegravir Considerations

- Study from Botswana suggested increased risk of neural tube defects in infants born to women taking DTG at conception
- Later studies suggested lower estimates (0.9% vs. 0.3% compared to 0.1% risk)
- Unknown whether this also applies to other integrase inhibitors (bictegravir)
- Pregnancy test for women of childbearing age
- Perinatal guidelines for women trying to conceive
- Conception for those not planning to conceive
- **Discussion of risk/benefit with women of childbearing age**

How to Choose

- Comorbidities
 - **Reflux (Antacids, PPI, H2 Blockers)**
 - Atazanavir, Rilpivirine
 - No PPI, space antacids/H2 blockers
 - **Anticoagulation (Factor 10a inhibitors)**
 - Cobicistat/Ritonavir (Boosters)
 - **Antiplatelet**
 - Cobicistat/Ritonavir (Boosters)
 - **Asthma** (Inhaled corticosteroids)
 - Cobicistat/Ritonavir (Boosters)

Baseline Laboratories

HIV RNA viral load

CD4 count

HIV resistance testing (RT/Protease)

Hepatitis B Serologies

Hepatitis C Screening

BMP

Liver Function Testing

Pregnancy test

HLA B5701 (if using ABC)

Fasting lipid profile

Urinalysis

Hemoglobin A1C

STI Testing

Toxoplasma IgG

Side Effects

AIDS 1985- One Patient's Experience

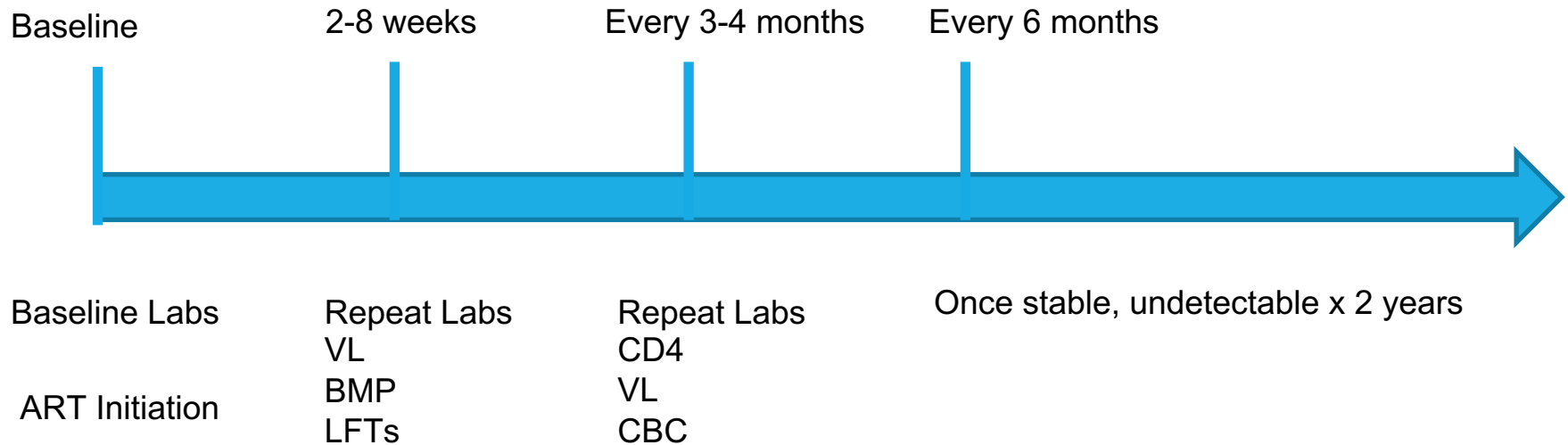
- 322 IV insertions
- 14 hospital admissions
- 11 months of hospital stay
- 60 phlebotomies
- 32 chest x-rays
- 5 CT scans of head
- 3 abdominal ct scans
- 6 bronchoscopies
- 8 intubations
- 4 lumbar punctures
- 3 bone marrows
- 5 cycles of chemo
- 2 lymph node bx

Pablo never received a medicine to treat his HIV or prevent any of the complications of AIDS.

Opportunistic Infection Prophylaxis

- Pneumocystis Pneumonia
- Toxoplasmosis
- (Mycobacterium Avium Complex)

You started ART now what?



Useful HIV Websites

www.vanderbilthealth.com/vccc

www.aidsinfonet.org

www.aidsetc.org

www.hivatis.org (DHHS, USPHS/IDSA Guidelines)

www.cdc.gov/nchstp/hiv_aids.htm

www.hiv-web.lanl.gov (Resistance mutations)

www.niaid.nih.gov

www.AIDS.medscape.com

www.hopkins-aids.edu

www.iapac.org

www.igm.gov

www.centerwatch.com

www.ucsf.edu/medical

www.virology.net

WWW.SEAETC.COM

Conclusions

HIV treatment involves using 3 fully active meds representing at least 2 class of ART

Integrase inhibitors along with a two NRTIs are currently the preferred regimen for treatment naïve

Regimens are very well tolerated

Be mindful of drug-drug interactions