

HIV Primary Care From Tests to Treatment

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Who Provides Care?

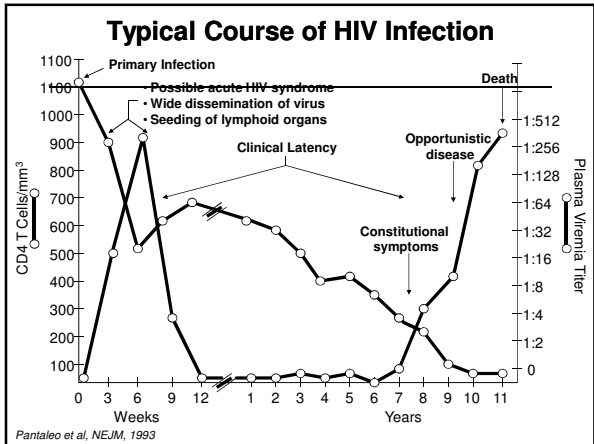
- In the US, fewer than 900 physicians write 85% of antiretroviral prescriptions
- Care is increasingly delivered in large care systems (locally, SFGH, VA etc.)
- By specialty a combination of Internal Medicine, ID, Family Medicine but also nursing, pharmacy, social work, dentistry involved in larger comprehensive clinics
- Care often involves opportunity to participate in clinical research of new drugs

HIV Therapy ARV is Only Part of the Story

- Treat the virus: Antiretroviral therapy. Often called HAART for Highly Active Antiretroviral Therapy.
- Treat infections and cancers arising from immune deficiency
- Treat complications of HIV therapy
- Treat conditions associated with patient demographics (STDs, HCV, infections from IDU etc)
- Treat conditions unrelated to HIV (HIV care is often the patient's full primary care)

Before You Start Antiretrovirals!

- Understand in as much depth as possible the patient's social network and resources
- Identify goals of therapy, plan for monitoring of therapy and plan for incomplete or transient response
- Stage disease
 - Directed history and physical exam, CD4 count, viral load (ideally test twice close to time of initiating to confirm indication and establish baseline for later comparison), HIV resistance genotype
- Identify and treat non-HIV related diseases (STDs etc)
- Support behavior of low HIV-transmission risk



Test to Stage HIV Disease and Monitor Antiretroviral Therapy

- The Big Three (CD4, Viral Load, Resistance Tests)
 - CD4 count tells how much the immune system has been damaged and whether the patient is at near term risk of serious complications
 - <50: High risk of mortality, serious complications
 - <200: Risk of many complicating "opportunistic" infections climbs
 - <350: All guidelines agree with starting ARV
 - <500: ARV guidelines moving in this direction
 - >500: "Normal" in most labs, some would still treat

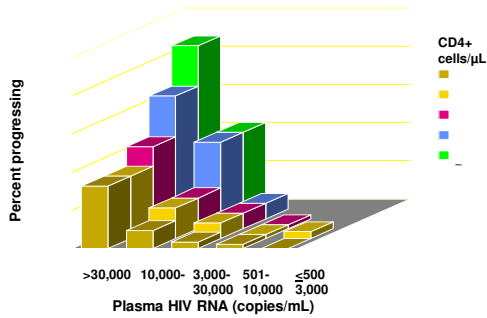
Test to Stage HIV Disease and Monitor Antiretroviral Therapy (II)

- The Big Three (CD4, Viral Load, Resistance Tests)
 - Viral Load. Quantitates number of HIV virus particles in blood. The higher the number, the faster the disease will progress. If ANY circulating HIV can be measured in a patient on ARV therapy, trouble (resistance) is brewing
 - <75 or <50 (depending on testing method used) is defined as “non-detectable and is the goal of therapy
 - >1000 generally needed to perform resistance tests
 - Choice of specific ARV drugs in regimen not based on viral load in current guidelines

Test to Stage HIV Disease and Monitor Antiretroviral Therapy (II)

- The Big Three (CD4, Viral Load, Resistance Tests)
 - Antiretroviral resistance tests come in two flavors
 - Genotype: Cheaper and quicker. Tells which mutations are present. Use before initial ARV regimen to make sure patient not infected with transmitted resistant virus. Use after therapy started if viremia (breakthrough) occurs to guide choice of next regimen.
 - Phenotype: More expensive and slower. Similar to an antibiotic sensitivity test in bacterial infections. Use in patient with very complex resistant genotype to identify drugs that still have activity.

Likelihood of Developing AIDS in 3 Years

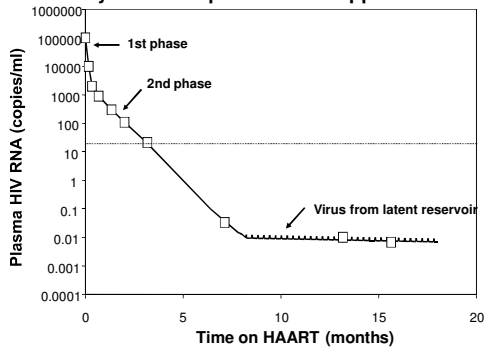


Adapted from: Mellors J et al. *Ann Intern Med.* 1997.

What are the Goals of HIV Therapy?

- Begin therapy at the optimal point for each patient
- Choose best drug regimen that:
 - Is potent enough to achieve maximal suppression of replication
 - Is well tolerated both in short and long term use
 - Is compatible with patients other medical conditions and prescriptions

The Goal of Ideal First Line HIV Therapy: Viral Decay and “Complete” Virus Suppression



Issues in the Timing of HIV Therapy The “Old” Paradigm

- Start before immune deficiency fixed, before HIV becomes more virulent
- Start as late as possible to avoid
 - Toxicity of unnecessarily long term drug exposure
 - Eventual selection of drug resistant mutations
 - Cost
 - Treatment burnout

Issues in the Timing of HIV Therapy The "New" Paradigm

- Start before immune deficiency fixed, before HIV becomes more virulent
- Start to decrease chance of viral replication causing serious "non-AIDS" problems (heart disease, cancer, kidney failure)
- Start to decrease chance of HIV transmission
- Look for any reason not to treat instead of looking for a reason to treat!

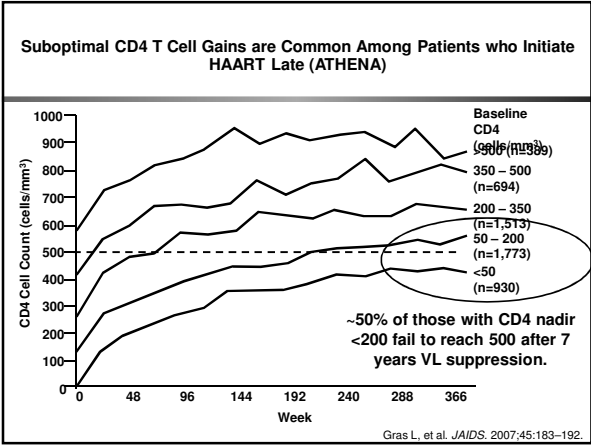
Immune Recovery With Potent Antiretroviral Therapy

Immune Competence

Normal

Safe

Dangerous



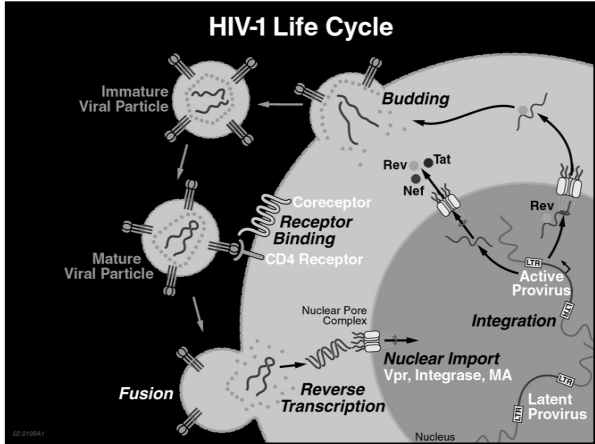
When to Start Therapy: Balance Tipping in Favor of Earlier Initiation

- Drug toxicity
- Preservation of limited Rx options
- Potency, durability, simplicity and safety of current regimens
- Improved formulations and PK
- Enhanced adherence
- Diminished emergence of resistance
- More treatment options
- Recognition of deleterious effect of uncontrolled viremia at all CD4 levels

IAS USA 2008

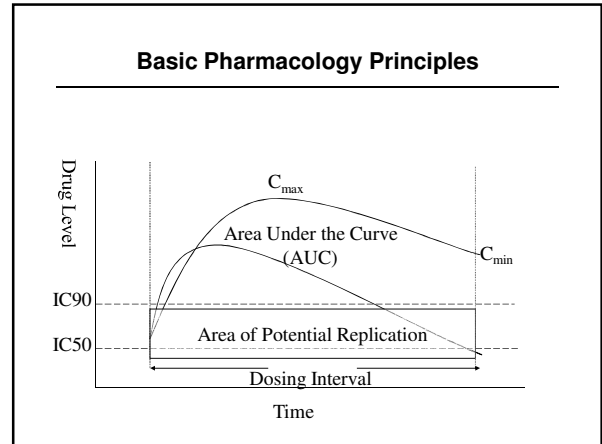
HIV Drugs

- Three main enzymatic targets: reverse transcriptase, protease, integrase
- Five drug classes
 - Reverse Transcriptase Inhibitors (RTIs)
 - Nucleoside analogs (and nucleotide analogs) often termed nRTIs
 - Non-nucleoside analogs often termed nnRTIs
 - Protease Inhibitors often termed PIs
 - Integrase Inhibitors
 - Attachment inhibitors
 - Fusion inhibitors



Current ARV Medications

<p>NRTI</p> <ul style="list-style-type: none"> • Abacavir (ABC) • Didanosine (ddI) • Emtricitabine (FTC) • Lamivudine (3TC) • Stavudine (d4T) • Tenofovir (TDF) • Zidovudine (ZDV) <p>NNRTI</p> <ul style="list-style-type: none"> • Efavirenz (EFV) • Etravirine (ETR) • Nevirapine (NVP) 	<p>PI</p> <ul style="list-style-type: none"> • Atazanavir (ATV) • Darunavir (DRV) • Fosamprenavir (FPV) • Indinavir (IDV) • Lopinavir (LPV) • Nelfinavir (NFV) • Ritonavir (RTV) • Saquinavir (SQV) • Tipranavir (TPV) 	<p>Fusion Inhibitor</p> <ul style="list-style-type: none"> • Enfuvirtide (ENF, T-20) <p>CCR5 Antagonist</p> <ul style="list-style-type: none"> • Maraviroc (MVC) <p>Integrase Inhibitor</p> <ul style="list-style-type: none"> • Raltegravir (RAL)
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- ### Is There A Single Best Initial Regimen?
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- Potency comparable in various regimens
 - Achieving non-detectability in naïve patient almost routine
 - Regimen choice individualized
 - Convenience [pill number and size, frequency, food restrictions etc.]
 - Tolerability [short term side effects, metabolic side effects]
 - Durability of benefit [probability of breakthrough if non-compliant]
 - “Strategic considerations” [does first regimen limit salvage options?]

- ### HIV Drug Regimens
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- Always combine multiple agents
 - Usually 2 nRTIs along with:
 - A PI enhanced with a low dose of a second PI, RTV
 - An nnRTI
 - An integrase inhibitor
 - An attachment inhibitor

- ### Adherence in HIV Care
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- Best virologic and immunologic outcome if viral load in blood below limits of detection
 - This requires nearly perfect and continuous adherence
 - If virus remains detectable on therapy, degree of adherence correlates with degree of drug resistance
 - One factor in increasing prevalence of drug resistance in population

- ### Why Should You Care?
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- No matter what you do in healthcare, wherever you plan to live and work, you will encounter this epidemic (and the next one)
 - The response to HIV in the past and now is perhaps the best example of medical professionalism and should make us proud of our career choices
 - Working with HIV involves us in confronting the challenges of healthcare in the US and globally

Where Can You Get More Information?

- Books:
 - Global HIV/AIDS Medicine (mine!)
 - VA Primary Care manual
- Web Sites:
 - HIV InSite (mine!)
 - VA HIV and HCV sites
 - AIDSinfo (DHHS guidelines: ARV,OI, Pediatric)
 - IAS-USA (IAS-USA guidelines: ARV, HIV resistance)

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Thanks!

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