An HIV Update - 2019

Jan Clark, PharmD
Specialty Practice Pharmacist

THE OHIO STATE UNIVERSITY
COLLEGE OF MEDICINE
The goal of this program is to provide a review and update of HIV care and to provide a forum for discussing the current local and national trends around the management of HIV.
In English, please!
What does HIV stand for?

**Human**

Only *humans can get this.*

**Immunodeficiency**

Your immune system, which helps the body fight disease isn’t working the way it should

**Virus**

A tiny particle that causes infections by entering a cell and making copies of itself.
What does AIDS stand for?

**Acquired Immunodeficiency Syndrome**

You got this from someone else.

Your immune system, which helps the body fight disease isn’t working the way it should. It is deficient.

Cluster of signs and symptoms, may be specific to certain illnesses.
Definitions

CD4 Cells aka T-Helper Cells – a subgroup of white blood cells that play role in maximizing capabilities of immune system

- Target of HIV

Normal CD4 values between 500 and 1500

- > 500 normal risk for infections
- 200 – 500 increased risk for infections
- < 200 = severe compromise (AIDS diagnosis), at risk for potentially fatal infections
Definitions

Viral Load
- Amount of virus in the body, copies/ml blood
- “High” vs “Low”

ART – Antiretroviral Therapy
- HIV medications
- ARV – Antiretrovirals
- HAART vs ART
HIV Transmission

- HIV infection occurs through contact with infected blood and body fluids via occupational and non-occupational exposures.

YOU CAN GET HIV VIA...

- Sex without a condom
- Passed from mother to baby
- Sharing injecting equipment
- Contaminated blood transfusions & organ transplants
HIV IS **NOT** TRANSMITTED BY...

- Insect bites
- Toilet seats
- Kissing
- Sharing cutlery
- Touching
HIV Transmission

- **Sexual Transmission**
  - Receptive anal intercourse is the highest risk
  - Vaginal sex less risky than anal sex

- **Injection Drug Use/Exposure to Contaminated Blood**
  - > 16 million injectors worldwide
  - US blood supply considered safe
  - Body piercing, acupuncture and tattooing via contaminated needles are rare causes

- **Mother to child, *including* through breastfeeding**
  - In utero, around delivery or after birth during breastfeeding
  - Prophylaxis or treatment with ART drastically reduced vertical transmission rate
HIV Prevention

- Male circumcision reduced HIV infection by as much as 60% (female to male)
- Vaccine development has been disappointing
- Reduce risky behaviors
  - “Safer sex” practices should be encouraged
  - Condoms - Latex condoms protect against HIV and STDs (having an STD risk of acquiring and transmitting HIV)
  - PrEP (pre-exposure prophylaxis) programs
  - Needle exchange programs
HIV Treatment as Prevention

- HIV-positive persons with an undetectable HIV VL > 6 months on ART are unlikely to transmit HIV to their sexual partners

- HPTN 052
  - Sero-discordant couples where one partner is positive and other is negative
  - 5 year HIV transmission rate was virtually nil if an undetectable HIV viral load was achieved
#UequalsU

Science Not Stigma
PrEVENTION in a pill.

Taking a once-daily pill can reduce your risk of contracting HIV by more than 90%.
Pre-exposure Prophylaxis (PrEP)

- Approved since July 2012
  - MSM
  - Discordant adults
  - Injection drug users
  - Heterosexually active adults

- PrEP is most effective as part of a comprehensive prevention package including safer sex with condoms and behavior modification to reduce risky behavior.
The Global HIV/AIDS Epidemic

36.7 MILLION people worldwide are currently living with HIV/AIDS.

2.1 MILLION CHILDREN worldwide are living with HIV. Most of these children were infected by their HIV-positive mothers during pregnancy, childbirth or breastfeeding.
The Global HIV/AIDS Epidemic

- 95% of new infections occurs in low- and middle-income countries, particularly sub-Saharan Africa

- Affects most productive years of life, half of new infections are in those under 25 years of age

- Most new infections are heterosexually transmitted
  - Varies by country - some countries most cases are by MSM or injection drug users
  - Women represent about half of people living with HIV
HIV in the United States
USA

New HIV diagnoses for the most-affected sub-populations, 2016

- Black male to male sexual contact: 10,233
- Hispanic / Latino male to male sexual contact: 7,425
- White male to male sexual contact: 7,390
- Black women, heterosexual contact: 4,189
- Black men, heterosexual contact: 1,926
- White women, heterosexual contact: 1,032
- Hispanic, Latina women, heterosexual contact: 1,025

Source: CDC, HIV Surveillance Report 2017
New HIV Diagnoses in the United States by Age, 2016

- 13 - 19: 1,675
- 20 - 29: 14,740
- 30 - 39: 9,943
- 40 - 49: 6,490
- 50 - 59: 4,882
- 60+: 1,930
Estimated New HIV Infections in the United States by Transmission Category, 2015

- 26,200 (68%) among gay and bisexual men
- 8,800 (23%) among heterosexuals
- 3,400 (9%) among people who inject drugs*
Rates of HIV Diagnoses Among Adults and Adolescents in the US by State, 2016

The map illustrates the rates of HIV diagnoses per 100,000 people by state in the US. Colors represent different rate ranges:
- Light blue: <10.0
- Lighter blue: 10.0–19.9
- Medium blue: 20.0–29.9
- Dark blue: ≥30.0

States with the highest rates of HIV diagnoses include LA (29.7), GA (31.8), and FL (28.0). Conversely, states with the lowest rates include MA (3.6 NH), CT (1.5), and WI (4.6).
HIV Fast Facts

- ~1.2 million people in the US; 1 in 7 are unaware
- MSM, esp. young, black MSM, most affected by HIV
- African Americans face the most severe HIV burden
- The annual # of new HIV diagnoses has remained stable in recent years.
- If taking antiretroviral therapy (ART)
  - Survival is improved on ART
  - Life expectancy is still lower; accelerated aging?
  - HIV infection can be managed as chronic disease
- Pre-and post-exposure ART prophylaxis
  - Can reduce HIV transmission
  - False sense of security about becoming infected?
Untreated HIV

- Primary Infection
  - CD4+ T Lymphocyte Count (cells/mm³)
  - HIV RNA Copies per ml Plasma

- Acute HIV syndrome
  - Wide dissemination of virus
  - Seeding of lymphoid organs

- Clinical Latency

- Opportunistic Diseases

- Constitutional Symptoms

- Death

Weeks

0 3 6 9 12 1 2 3 4 5 6 7 8 9 10 11

Years

0 100 200 300 400 500 600 700 800 900 1000 1100 1200

0 10² 10³ 10⁴ 10⁵ 10⁶ 10⁷
Treatment Goals

- Reduce HIV-related diseases; prolong duration and quality of survival
- Restore and/or preserve immunologic function (as indicated by CD4 count)
- Maximally and durably suppress HIV viral load
- Prevention of HIV transmission
Based on RESEARCH, the recommendation is:

- ART for all HIV-1 infections regardless of CD4 cell count

This will:

- Reduce morbidity and mortality associated with HIV
- Prevent HIV transmission

Consider case-by-case deferral

- Significant barriers to adherence
- Co-morbidities that complicate or prohibit ART
- “Elite controllers” and long-term non-progressors
Immediate ART upon HIV Diagnosis?

- Randomized trials in SA and Haiti
  - More likely to be suppressed at 10 mo than “standard of care”
  - Improvements in both proportion retained in care and in viral suppression at 1 year
  - Underlying HIV and TB epidemics limit generalizability of findings to US
- Same-day ART may be feasible and could potentially improve clinical outcomes
- Same day – RESOURCE INTENSIVE

As these resources may not be available in all settings and the long-term clinical benefits of same-day ART initiation have yet to be proven in the United States, this approach remains investigational.
Reverse Transcriptase Inhibitors

(Includes AZT, Truvada, Descovy and Epzicom)
HIV-Associated Lipoatrophy
HIV-Associated Lipoatrophy
NRTIs

Combinations Frequently used

Epzicom (abacavir/lamivudine)
Truvada (tenofovir DF/emtricitabine)
Descovy (tenofovir AF/emtricitabine)
Non-Nucleoside Reverse Transcriptase Inhibitors
1 NNRTI + 2 NRTIs are a Complete HIV regimen

Atripla®
Complera®
Odefsey®
Delstrigo®

1. Nevirapine *(Viramune®)*
2. Efavirenz *(Sustiva®, also in Atripla)*
3. Delavirdine *(Rescriptor®)*
4. Rilpivirine *(Edurant®, also in Complera and Odefsey)*
5. Etravirine *(Intelence®)*
6. Doravirine *(Pifeltro®)*
   - NEW for 2018
   - In combination with Truvada as Delstrigo
Rilpiverine (Edurant, Stribild and Genvoya) is contraindicated with proton pump inhibitors (Prilosec, Nexium, Prevacid).

Caution in initial therapy for patients with high viral loads and low CD4 counts.
Protease Enzyme and Inhibitors

Ribbon diagram of HIV PR
Protease Inhibitors Fast Facts

- Credited with making HIV a “chronic” disease rather than a “fatal” disease.

- Most must be boosted with a second agent to achieve effective drug levels.
  - Ritonavir
  - Cobicistat

- PIs are generally associated with inhibition of CYP enzyme system causing multiple drug interactions
HIV-Associated Lipodystrophy
Meet the PIs

1. Saquinavir (Invirase®, Fortovase®)
2. Ritonavir (Norvir®)
3. Indinavir (Crixivan®)
4. Nelfinavir (Viracept®)
5. Amprenavir (Agenerase®)
6. Fosamprenavir (Lexiva®)
7. Atazanavir (Reyataz®, Evotaz®)
8. Darunavir (Prezista, Prezcobix®)
9. Lopinavir/rtv (Kaletra®)
10. Tipranavir (Aptivus®)

Co-formulated with a booster: Kaletra (with ritonavir) and Prezcobix and Evotaz (with cobicistat)
Most commonly used Protease Inhibitors are atazanavir (Reyataz) and darunavir (Prezista).

**Darunavir** (DRV, Prezista®, Prezcobix ®)
- Less food effect, OK with PPIs
- Requires boosting always
- Useful for PI-resistant viruses *(dosed BID)*
- *Caution* if **severe** sulfa allergy
Integrase Inhibitors (INSTIs)

HIV integrase enzyme has no equivalent in the host cell.

Integrase inhibitors are considered safe because they do not interfere with normal cellular processes.

Provide rapid drop in viral load.
1. Raltegravir (Isentress®)
2. Dolutegravir (Tivicay®,
also in Triumeq®)
3. Elvitegravir (in Stribild®
and Genvoya®)
4. Bictegravir (in Biktarvy®)

1 INSTI + 2 NRTIs = Complete HIV regimen

Triumeq®
Stribild®
Genvoya®
Biktarvy®
There’s help!

- Treatment guidelines available to provide information about recommended regimens ([aidsinfo.nih.gov](https://aidsinfo.nih.gov))

- Individualize for the patient
Initial antiretroviral therapy generally consists of two NRTIs (termed a nucleoside backbone) plus one active drug from another class:

- Integrase Inhibitor
- Protease Inhibitor
- Non-NRTI
- CCR5 antagonist (entry inhibitor)

Regimens for experienced patients is complex, expert advise is critical.
- Consider past regimens
- Consider resistance
Recommended Initial Regimens for Most People with HIV

- Bictegravir/tenofovir alafenamide/emtricitabine
  - Biktarvy
- Dolutegravir/abacavir/lamivudine (only for patients who are HLA-B*5701-negative)
  - Triumeq
- Dolutegravir plus tenofovir/emtricitabine
  - Tivicay plus Truvada or Tivicay plus Descovy
- Raltegravir plus tenofovir/emtricitabine
  - Isentress plus Truvada or Isentress plus Descovy

**NOTICE THESE ARE ALL INTEGRASE BASED REGIMENS** (with a 2-NRTI backbone)
Recommended Initial Regimens In Certain Clinical Situations

**INSTI + 2 NRTIs:**
- EVG/c tenofovir/emtricitabine (Stribild or Genvoya)
- RAL + abacavir/lamivudine (if HIV RNA < 100,000 copies/mL)

**Boosted PI + 2 NRTIs:**
- DRV/c or DRV/r + tenofovir/emtricitabine
- ATV/c or ATV/r + tenofovir/emtricitabine
- DRV/c or DRV/r + abacavir/lamivudine

**NNRTI + 2 NRTIs:**
- EFV + tenofovir/emtricitabine (Atripla)
- RPV + tenofovir/emtricitabine (if HIV RNA <100,000 copies/mL and CD4 >200 cells/mm) (Complera)
- DOR + tenofovir/emtricitabine or tenofovir/lamivudine
SIDE EFFECTS
Treatment-Experienced Patients

- In clinical studies of ART, most patients maintained virologic suppression for at least 3-7 years
  - Appropriate initial ARV regimens should suppress HIV indefinitely, assuming adequate adherence

- In patients with undetectable viral load:
  - Assess adherence frequently
  - Simplify ARV regimen as much as possible
    - **Reduce pill burden**
      - Are there combination tablets now available? Would this reduce co-pays?
    - **Reduce dosing frequency**
      - Are there now once daily regimens that would be appropriate?
    - **Enhance tolerability**
      - Ask about side effects
    - **Decrease food and fluid requirements**
      - Review specific food requirements
Treatment-Experienced - Failing Patients

- Assess and address aggressively
  - This is complex – expert advice is critical
  - Drug resistance testing should be done - expert review
  - New regimens should include at least 2 and preferably three fully active agents
  - In some patients with multidrug resistant HIV, being undetectable may not be possible
    - ART should be continued with regimens designed to minimize toxicity, preserve CD4 count and delay clinical progression
“There were some complications. It looked way easier on YouTube.”
If you have any questions, write to me...

Jan.Clark@osumc.edu