Overview

- Epidemiology
- Science of HIV
- How HIV treatment and management have changed over the years
- New medicines and regimens that are currently available
- Issues that affect the aging HIV population
- Ongoing research trials that look at possible cures and vaccines
Case study

• 35-year-old man with no past medical history is recently diagnosed with HIV after routine STI testing.

• What regimens do we use for him? How is this different from 20 years ago?
Epidemiology

• Prevalence (number of people living with a disease)
  – Worldwide: 36.9 million
  – US: 1.1 million

• Incidence (new cases of a disease)
  – Worldwide: 1.8 million in 2017
  – US: 38,500 in 2015
Incidence in 2015 by transmission category

- 26,200 (68%) among gay and bisexual men
- 8,800 (23%) among heterosexuals
- 3,400 (9%) among people who inject drugs*

CDC HIV/AIDS Statistics Center, Estimated HIV incidence and prevalence in the US 2010-2015
Populations with high incidence

CDC HIV/AIDS Statistics Center, Estimated HIV incidence and prevalence in the US 2010-2015
Incidence by age, 2016

CDC HIV/AIDS Statistics Center, Estimated HIV incidence and prevalence in the US 2010-2015
Classes of therapy

• Nucleoside and nucleotide reverse-transcriptase inhibitors (NRTIs)
• Non-nucleoside reverse-transcriptase inhibitors (NNRTIs)
• Protease inhibitors
• Integrase inhibitors
• Entry inhibition (CCR5)
• Monoclonal antibody
Mechanism

Gandhi, M and RT Gandhi. NEJM 2014; 371: 248-259
Treatment principles

• Generally use 3 drugs
• At least 2 classes
• Usually NRTI + INSTI or PI
• Goal: undetectable viral load
Examples of commonly used drugs/regimens

• **NRTIs**
  - Tenofovir (TDF or TAF) – “Viread”
  - Abacavir (ABC) – “Ziagen”
  - Emtricitabine (FTC) – “Emtriva”
  - Lamivudine (3TC) – “Epivir”
  - Zidovudine (AZT) – “Retrovir”
  - Tenofovir + emtricitabine (TDF or TAF + FTC) – “Truvada” or “Descovy”
Examples of commonly used drugs/regimens continued

• NNRTIs
  – Efavirenz (EFV) – “Sustiva”
  – Rilpivirine (RPV) – “Edurant”
Examples of commonly used drugs/regimens continued

• Protease inhibitors
  – Ritonavir (r) – “Norvir”
  – Lopinavir + ritonavir (LPV/r) – “Kaletra”
  – Atazanavir (ATV) – “Reyataz”
  – Darunavir (DRV) – “Prezista”
Examples of commonly used drugs/regimens continued

• Entry Inhibitors
  – Enfuvirtide – “Fuzeon”
  – Maraviroc – “Selzentry” or “Celsentri”
Examples of commonly used drugs/regimens continued

- Integrase inhibitors
  - Raltegravir (RTG) – “Isentress”
  - Dolutegravir (DTG) – “Tivicay”
  - Elvitegravir/cobicistat – part of fixed dose regimens
  - Bictegravir (BIC) – part of fixed dose regimen called “Biktarvy”
First-line regimens for newly diagnosed HIV

- Recommended by Panel on Antiretroviral Guidelines for Adults and Adolescents
  - BIC/TAF/FTC – “Biktarvy”
  - TAF/FTC + DTG – “Truvada” or “Descovy” + “Tivicay”
  - DTG/ABC/3TC – “Triumeq”
When do we start treatment?

- Previously used to treat only patients with CD4 count < 500
- After the START study (Strategic Timing of AntiRetroviral Treatment), paradigm shifted
  - Decreased AIDS related events
  - Decreased cancer rates
  - Decreased TB rates
- Now we start ART for all HIV+ patients
Time to first primary event

The INSIGHT START Study Group. NEJM 2015; 373: 795-807
Time to other events

The INSIGHT START Study Group. NEJM 2015; 373: 795-807
Why do we use integrase inhibitors?

• Highly effective
• Drop viral load quickly
• Well-tolerated
• Less resistance
Timeline of HIV drugs

- 1987 – FDA approves AZT
- 1995 – HAART
- 1996 – triple drug therapy
- 2006 – 1 pill regimen
- 2007 – FDA approves first integrase inhibitor
How far we have come

• 1 pill once a day
• Few side effects
• Gets viral load to undetectable
Preventing HIV

- “PrEP” – pre-exposure prophylaxis
- Truvada (only FDA approved pill)
- FDA approved in 2012

![Truvada Pills](image)
How do we use PrEP?

• Daily
  – iPrEx study for MSM
    • 44% reduction in incidence of HIV when on TDF/FTC
  – Partners PrEP study in serodiscordant couples in East Africa
    • 75% reduction in incidence of HIV on TDF/FTC
  – TDF2 study in heterosexuals
    • 62% effective in preventing HIV
How do we use PrEP? continued

• On-demand (not FDA approved)
• Take 2 pills 2-24 hours before, 3rd pill 24 hours after, 4th pill 24 hours thereafter
  – IPERGAY – double blind RCT looking at MSM
    • 86% reduction in HIV
    • On average taking 15 pills a month
  – Prevenir – cohort study looking at daily vs. on-demand PrEP in MSM, ongoing
    • 0 cases of HIV infection
Future of PrEP

- Can we use Descovy (TAF/FTC)?
- DISCOVER trial ongoing
- Will know by February 2019
- Will it work? (lower drug levels in tissues)
Trend in mortality

Trends in Age-Adjusted* Rate of Death due to HIV Infection, USA, 1987-2000

Deaths per 100,000 Population

87 88 89 90 91 92 93 94 95 96 97 98 99 ‘00+

*Using the year 2000 US standard population.
†Preliminary mortality data for 2000

Note: For comparison with data for 1999-2000, data for 1987-1998 were modified to account for ICD-10 rules instead of ICD-9 rules.
Mortality of HIV compared to other causes


- Unintentional injury
- Cancer
- Heart disease
- Suicide
- HIV infection
- Homicide
- Chronic liver disease
- Stroke
- Diabetes

Note: For comparison with data for 1999-2000, data for 1987-1998 were modified to account for ICD-10 rules instead of ICD-9 rules.

*Preliminary mortality data for 2000.*
Sexual transmission of HIV

- U=U – undetectable = untransmissible
- HPTN 052 – studied serodiscordant couples
  - Early ART at enrollment led to 93% lower risk of linked partner infection
  - No cases of HIV transmission when HIV VL was suppressed
HPTN 052

A. All Partner Infections

<table>
<thead>
<tr>
<th>No. at Risk</th>
<th>Years since Randomization</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early ART</td>
<td>903 808 746 697 645 569 263 95 28 26 1</td>
</tr>
<tr>
<td>Delayed ART</td>
<td>890 792 715 663 611 536 269 99 21 19 2</td>
</tr>
</tbody>
</table>

Sexual transmission of HIV

- U=U – undetectable = untransmissible
- PARTNER study – examined condomless sexual activity in serodiscordant couples (MSM and heterosexual)
  - 0 case of transmission over median of 2 years
Sexual transmission of HIV

- U=U – undetectable = untransmissible
- Opposites Attract study – studied serodiscordant MSM couples
  - 0 cases of linked HIV
HIV and aging

• Patients living into their 60s and 70s with HIV
• Dealing with issues of aging
Issues affecting older HIV patients

- Increased risk of CV disease
- Osteoporosis
- Neuropathy
- Cognitive decline
Cardiovascular health and HIV

• Higher rates of MI (heart attacks) in HIV patients
• Why does this happen?
• No published evidence for prevention
REPRIEVE trial

- RCT ongoing
- Started March 2015
- Sites include MGH
- Evaluating pitavastatin to reduce CVD risk in HIV+ adults
- Enrollment: HIV+ on ART for 6 months, with low-moderate ASCVD risk
- Randomized to placebo or pitavastatin
Can there be a cure?

• Antibodies
  – ACTG trial: RC 607/ACTG A5378: A Phase I, Single-Dose Study of the Safety and Virologic Effect of an HIV-1-Specific Broadly Neutralizing Human Monoclonal Antibody, VRC-HIVMAB080-00-AB (VRC01LS) or VRC-HIVMAB075-00-AB (VRC07-523LS), Administered Intravenously to HIV-Infected Adults
  – Aim: looking at a human monoclonal antibody that neutralizes the HIV virus
  – Enrolling patients who are HIV+ not on ART, with VL between 500 and 100K, and CD4 >350
Can there be a cure? continued

• Vaccines
  – Barrouch, et al. Evaluation of a mosaic HIV-1 vaccine in a multicentre, randomised, double-blind, placebo-controlled, phase 1/2a clinical trial (APPROACH) and in rhesus monkeys (NHP 13-19).
  – Multicenter RCT with humans and monkeys
  – Elicited antibody responses and T-cell response
  – 67% protection of SHIV (HIV in monkeys) in monkeys
References


5. Clinicaltrials.gov


