

# HIV and AIDS: What Every Optometrist Needs to Know

Joseph Sowka, OD, AAO,  
Diplomate

US EYE | CENTER FOR SIGHT

## Disclosures

- Alcon Novartis, B&L, Zeiss, Allergan, Ocular Therapeutix, Aerie, Sun Pharma
- Co-owner of Optometric Education Consultants  
[www.optometricedu.com](http://www.optometricedu.com)
- Nothing pertinent to this lecture



## Stages of Our Understanding

## AIDS in the Dark Ages

Holland GN et al. Ocular disorders associated with a new severe acquired cellular immunodeficiency syndrome. Am J Ophthalmol. 1982 Apr;93(4):393-402

Among the prominent features of a newly described acquired cellular immunodeficiency syndrome that affects previously healthy male homosexuals are multiple opportunistic infections and Kaposi's sarcoma.

***"Immunosuppression induced by cytomegalovirus infection may play a major role in the pathogenesis of this disorder"***

## AIDS as the Ebola Virus



## AIDS as Diabetes

- Chronic disease
- Medications and lifestyle alterations increase longevity
- Some ocular complications
- Can live a normal lifespan
- May contribute to death

## Acquired Immune Deficiency Syndrome (AIDS)

- ❑ Not a specific disease; rather, a complex assortment of secondary disorders
- ❑ Results from infection by the human immunodeficiency virus (HIV)
- ❑ Virus selectively attacks T-helper (CD4-T) lymphocytes and ultimately destroys the cell
- ❑ Transmitted via contaminated bodily secretions

## World Epidemiology

- è According to estimates from the UNAIDS/WHO AIDS Epidemic Update, around 36.9 million people worldwide were living with HIV at the end of 2017.
- è AIDS deaths back in 2007 were estimated at 2.1 million/yr
  - u 4 deaths per minute
- è AIDS deaths in **2017** are estimated at 940,000/yr
  - u 1.8 deaths per minute

## Global HIV epidemic – people living with HIV

2017  
Globally  
**36.9 million**  
People living with HIV

+14%  
Relative to 2010



Source: UNAIDS/WHO estimates

## Global HIV epidemic – incidence and mortality since 2010

2017  
Globally  
**36.9 million**  
People living with HIV

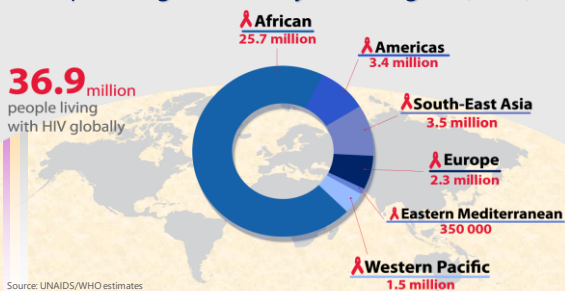
-18%  
New infections annually  
relative to 2010

-34%  
Deaths annually  
relative to 2010

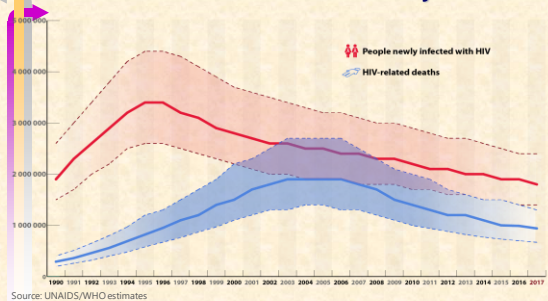


Source: UNAIDS/WHO estimates

## People living with HIV by WHO region (2017)



## Decline in HIV incidence and mortality over time

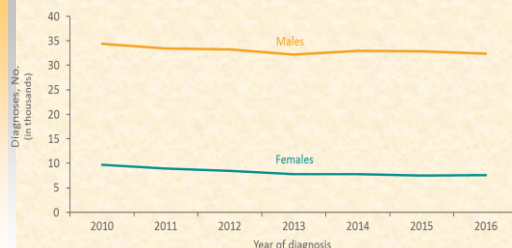


## US Surveillance Epidemiology

- From 2010 through 2016, in the United States and 6 dependent areas, the number of diagnoses of HIV infection among female and male adults and adolescents decreased.
- From 2010 through 2016, blacks/African Americans accounted for the largest percentage of diagnoses of HIV infections each year in the United States and 6 dependent areas.
- In 2016, 40,012 adults and adolescents received a diagnosis of HIV infection; of these, 81% of diagnoses were among males and 19% were among females.

17

## Diagnoses of HIV Infection among Adults and Adolescents, by Sex 2010–2016—United States and 6 Dependent Areas



18

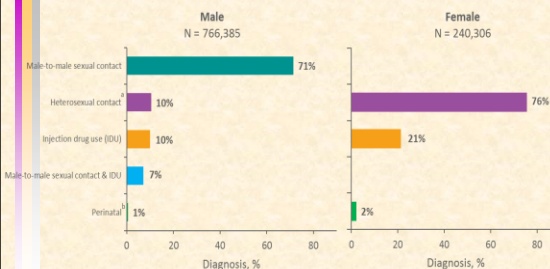
## Diagnoses of HIV Infection among Adults and Adolescents, by Transmission Category, 2010–2016—United States and 6 Dependent Areas



Note: Data have been statistically adjusted to account for missing transmission category. "Other" transmission category not displayed as it comprises less than 1% of cases.  
\*Heterosexual contact with a person known to have, or to be at high risk for, HIV infection.

20

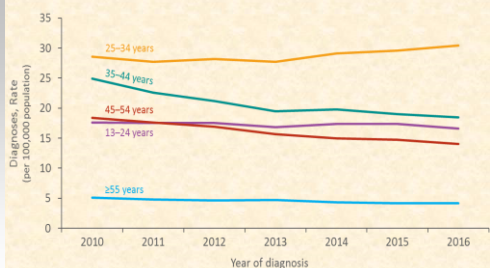
## Adults and Adolescents Living with Diagnosed HIV Infection, by Sex and Transmission Category, Year-end 2016—United States and 6 Dependent Areas



Note: Data have been statistically adjusted to account for missing transmission category. "Other" transmission category not displayed as it comprises less than 1% of cases.  
\*Heterosexual contact with a person known to have, or to be at high risk for, HIV infection.  
\*Perinatal includes persons whose infections were attributed to perinatal transmission, but were aged 13 years and older at the end of 2016.

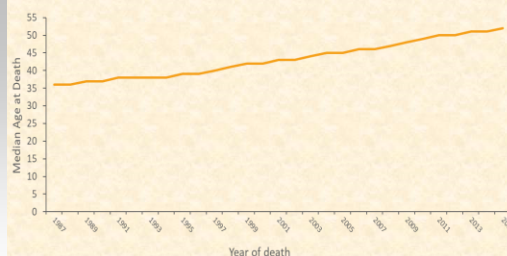
21

## Rates of Diagnoses of HIV Infection among Adults and Adolescents by Age at Diagnosis, 2010–2016—United States



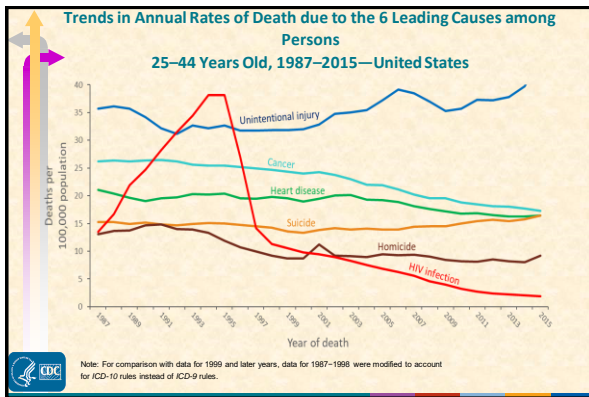
23

## Median Age at Death due to HIV Infection, United States, 1987–2015



Note: For comparison with data for 1999 and later years, data for 1987–1998 were modified to account for ICD-10 10th instead of ICD-9 rates.

25



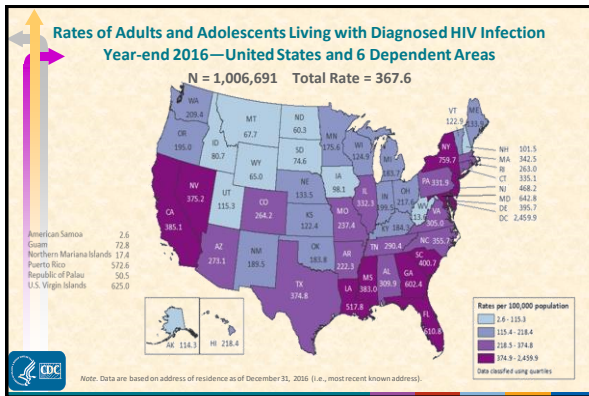
26

### Florida ranks #5 in US

Areas with the highest rates of persons living with diagnosed HIV infection at the end of 2016 were:

- 1. The District of Columbia (2,459.9)
- 2. New York (759.7)
- 3. Maryland (642.8)
- 4. The U.S. Virgin Islands (625.0)
- 5. **Florida (610.8)**

27



28

### Conclusions

- After rapidly increasing since the 1980s, the annual rate of death due to HIV infection peaked in 1994 or 1995 (depending on the demographic group), decreased rapidly through 1997, and continued to decrease much more slowly thereafter.
- Persons dying of HIV infection increasingly consist of:
  - women (26% in 2015)
  - blacks/African Americans (52% in 2015)
  - residents of the South (53% in 2015)
  - persons 45 years of age or older (74% in 2015)
- HIV infection continues to remain among the 10 leading causes of death among persons 25 to 44 years old, particularly among blacks/African Americans.

29

### HIV & AIDS -- What's It All About?

- The Human Immunodeficiency Virus (HIV)
  - Lentiviridae family of retroviruses (slow viruses)
  - Binds to host cells including T helper cells (CD 4 cells), macrophages, monocytes

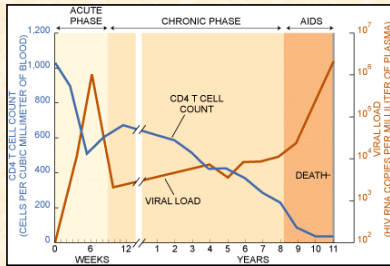
31

### Life Cycle of HIV

- Acquire HIV → seroconversion → viral replication → no antibodies yet → becomes symptomatic (~14 days) → patient develops immunity with profuse viral accumulation → immune system suppresses and partially clears virus → asymptomatic stage (10 years) → immune system wears out → onset of further replication → CD 4 cell count drops → patient become symptomatic → AIDS

32

## Natural Course of HIV Infection



© Scientific American, July 1998

33

## Natural Course of HIV Infection

- Virus is never 'dormant' – virus replicates at 'set point' controlled by immune system
- Replication of HIV causes immune system damage

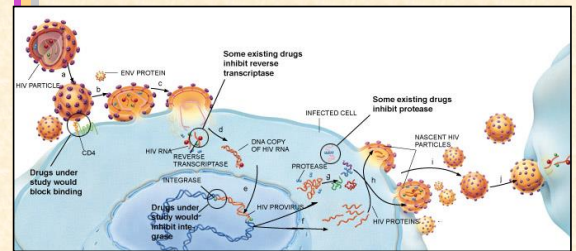
34

## Pathogenesis of HIV Infection

- HIV binds and fuses with host cell (CD 4 cell) → HIV releases viral RNA into nucleus of host cell → viral RNA infects T lymphocytes (as well as glial cells and monocytes) → viral RNA incorporated into cell → enzyme **reverse transcriptase** forms viral DNA from viral RNA in reverse fashion → enzyme **integrase** integrates new DNA into host cell's genetic material → viral genetic material packaged into new viral particles with new viral RNA (requires enzyme **protease**) → released from cell to infect new cells

35

## HIV Life Cycle



© Scientific American, July 1998

36

## HIV Life Cycle

- HIV replicates 10 billion particles/day
  - Want viral load to be below 10,000 copies
  - Best to be undetectable (< 200 copies)
  - Undetectable viral load may still have virus in semen and may cause infection\*\*
- 2017: medical authorities are now agreeing that those with undetectable viral loads cannot transmit the virus.
  - 9/27/17: CDC releases statement that those taking daily medication and maintain an undetectable viral level "have effectively no risk of sexually transmitting the virus to an HIV-negative partner".
- U=U: Undetectable = Untransmittable

37

## HIV Life Cycle

- Primary HIV infection:
  - Highest viral titers during primary stage (1st 14 days)
  - Most likely to transmit virus
  - Patient unaware of infection
- Acute retroviral syndrome:
  - Fever, fatigue, sore throat, muscle pain, nausea
  - Symptoms equate to viral load and progression to AIDS

38



## Acquired Immune Deficiency Syndrome (AIDS)

- Emphasizes CD4 count in categorization of HIV-related problems
- Expanded AIDS case definition
- Progression from infection to AIDS: 8 mos. to 18 years
- Long-term non-progressors: viral load stays down and T cells stay up.
- Rapid progressors: viral load is high and T cells are low

39

## Acquired Immune Deficiency Syndrome (AIDS)

- Study of blood frozen early in disease (mid 1980's)
  - Those with initial viral load < 3,000: only 10% developed AIDS at this point
  - Those with initial viral load > 110,000: 75% developed AIDS
- High initial viral load most predictive of AIDS development
- High viral load 6 months after infection predicts rapid progression
  - These patients can be converted to non-progressors

40

## Systemic Manifestations of HIV & AIDS

- Initial infection causes mild, self-limited condition:
  - upper respiratory infection; 1-2 weeks duration
  - generally asymptomatic course (months to years) until immune system becomes depressed
- AIDS defined by:
  - CD4+ T-lymphocyte count below 200/L, AND/OR
  - development of other recognized secondary infections or conditions

41

## AIDS and the Eye

- If CD4 count < 200:
  - 1st year: 33% incidence of opportunistic infection
  - 2nd year: 58% incidence of opportunistic infection
- If CD4 count < 100
  - 1st year: 25% incidence of CMV retinitis

42

## AIDS and the Eye

- Follow up for patients with no retinal pathology:
  - CD4 > 600: Annually
  - CD4 599-300: 6 months
  - CD4 299-100: 3-4 months
  - CD4 < 100: 2-3 months
  - Systemic CMV: 2-3 months

43

## Transmission, Prevention, Testing, Reporting, and Management

44

## Modes of Transmission

- HIV can be isolated from the following body fluids:
  - Blood
  - Semen and vaginal secretions
  - CSF, synovial fluids, pleural fluid, pericardial fluid, amniotic fluid, tears
  - Transmission occurs via *“exposure of mucous membranes to visible blood or body fluids...”*
    - Sexual contact
    - Sharing of needles by IV drug users
    - Blood transfusion

45

## Modes of Transmission

- è **Negligible risk** of HIV transmission by exposure of:
  - Vagina, rectum, eye, mouth or other mucous membrane, intact or non-intact skin, or percutaneous contact
- WITH**
  - Urine, nasal secretions, saliva, sweat or **TEARS**, if not physically contaminated with blood

Source: Morbidity Mortality Weekly Report January 21, 2005

46

## Modes of Transmission

- è Accidental exposure to contaminated vectors by medical personnel
  - Most common is needle stick
  - 51 cases of transmission and conversion in health care workers
  - Can be contracted through broken skin or open lesions
  - Universal precautions should be used when dealing with known HIV-infected samples

47

## Prevention

- Hand Washing
  - With soap and water after EACH patient
  - Dry with FRESH towel
- Gloves
  - Used if open wound, weeping lesions, dermatitis or exposure to tears or mucous membranes
  - Discard after EACH patient
  - Double glove if risk of needle stick
  - Double glove removes inoculum from needle
- Gowns & Masks
  - Unnecessary for routine exam
  - Used only if splashing of blood or blood products anticipated (ER)

48

## Disinfecting Equipment

- Goldmann tonometer
  - 70% alcohol, wiped vigorously, washed with water, air dry OR
  - Soak in fresh 3% hydrogen peroxide for 5 minutes OR
  - Soak in fresh 1:10 dilution of bleach for 5 minutes
- Gonio prisms (& other instruments)
  - Wiped clean, then
  - Disinfected with above regimen
- Trial contact lenses
  - Any commercially available Peroxide system OR
  - Heat disinfection: 80 degrees X 10 minutes (may warp RGP's)

49

## Florida Statutes Pursuant to HIV Infection

- Sections 381.004 and 384.25
  - 381.004 refers to testing for HIV
- The state must facilitate informed, voluntary, and confidential use of HIV testing
- Florida DOH has established a network of voluntary HIV testing programs in every county.
  - Also provides for counseling
  - Program is anonymous and confidential

50

## Florida Statutes Pursuant to HIV Infection

- ❑ Results of these tests may not be used to:
  - ❑ Determine eligibility for disability, health, or life insurance
  - ❑ Screen or determine suitability for, or discharge a person from, employment
- ❑ HIV testing must be preceded by informed consent; must inform patient that:
  - ❑ All test results are treated as confidential information
  - ❑ Positive results are reported to county health department
  - ❑ Centers are available for anonymous testing should the patient desire

51

## Florida Statutes Pursuant to HIV Infection

- ❑ The individual ordering the HIV test is obligated to inform the patient of the test results as well as:
  - ❑ Availability of treatment and support services
  - ❑ Importance of notifying partners who may have been exposed
  - ❑ Methods of preventing transmission of HIV
- ❑ HIV test results may be released only to the individual patient or the patient's LEGALLY AUTHORIZED REPRESENTATIVE

52

## Florida Statutes Pursuant to HIV Infection

- ❑ Penalties:
  - ❑ Violation of the confidentiality provisions is a 1<sup>st</sup> degree misdemeanor
  - ❑ "Anyone who...identifies an individual who has a sexually transmissible disease including HIV...and maliciously, or for monetary gain, disseminates this information...commits a felony of the 3<sup>rd</sup> degree..."
- ❑ It is illegal for any medical facility to require or utilize HIV testing as a condition for admittance or treatment

53

## Florida Statutes Pursuant to HIV Infection

- ❑ 384.25 – refers to reporting of HIV test results
  - ❑ STD's must be reported to the DOH within 2 weeks
    - Includes physicians who diagnose a patient or begin treatment for STD as well as laboratories which obtain positive results
- ❑ To ensure confidentiality, reports of HIV infection as well as AIDS must follow protocol of the HIV/AIDS Reporting System (HARS) as developed by the CDC

54

## Case History Questions

- è When were you first diagnosed?
- è Have you had or been treated for any opportunistic infections?
- è What medications are you taking?
  - ù Are you compliant with your medications?
- è When was your last blood work done?
- è What is your T-Cell or CD4 count?
- è What was the viral load?

55

## Clinical Management of HIV Infection

- è Treatment Goals:
  - ù Maintain viral load as low as possible
    - may never get viral load to undetectable level, esp if load high
  - ù Maintain CD4 count as high as possible
  - ù Manage opportunistic infections

56



## Clinical Management of HIV Infection

- Treatment Goals:
  - Maintain viral load as low as possible
    - may never get viral load to undetectable level, esp if load high
  - Maintain CD4 count as high as possible
  - Manage opportunistic infections

57

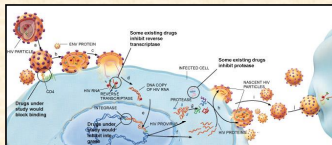
## Established Medical Therapies

- **Nucleoside reverse transcriptase inhibitors (NRTIs)**- prevents infection of new cells: incorporated into viral DNA and prevents further synthesis
  - Zidovudine- **AZT, ZDV** (Retrovir): 300 mg PO BID
  - Zalcitabine- **ddC**, (Hivid)
  - Didanosine- **ddl**, (Videx) also enteric coated ddl EC
  - Lamivudine- **3TC**, (EpiVir): reverses AZT resistance
  - Lamivudine + Zidovudine – **CBV** (Combivir)
  - Acabavir – **ABV, ABC** (Ziagen)
  - Stavudine – **d4T** (Zerit) also available as extended release Zerit XR
  - Emtricitabine – **FTC** (Emtriva)
  - Tenofovir – **TNF, TDF** (Viread)
  - Lamivudine+Acabavir+Zidovudine – **TZV** (Trizivir) 3TC+ABV+AZT

58

## Established Medical Therapies

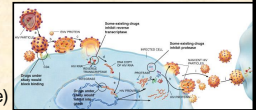
- **Non-nucleoside reverse transcriptase inhibitors (NNRTIs)**: directly inhibits reverse transcriptase
  - Nevirapine – **NVP** (Viramune): rapid resistance; not indicated for monotherapy
  - Delavirdine- **DLV** (Rescriptor)
  - Efavirenz- **EFV** (Sustiva)



59

## Established Medical Therapies

- **Protease inhibitors**- prevents assembly of new virus cells- leads to a dramatic reduction in viral load
  - Saquinavir – **SQV** (Invirase Hard gel cap) (Fortovase Soft gel cap)
  - Ritonavir – **RTV** (Norvir)
  - Indinavir- **IDV** (Crixivan)
  - Nelfinavir- **NFV** (Viracept)
  - Amprenavir – **APV** (Agenerase)
  - Atazanavir – **ATV** (Reyataz)
  - Fosamprenavir – **FPV, 908** (Lexiva)
  - Lopinavir + Ritonavir – **LPV** (Kaletra)



60

## Highly Active Anti-Retroviral Therapy (HAART)

- 2 nucleoside RNA reverse transcriptase inhibitors + protease inhibitor or...
- A non-nucleoside reverse transcriptase inhibitor + 2 nucleoside reverse transcriptase inhibitor or...
- 2 protease inhibitors + one or two nucleoside reverse transcriptase inhibitor or...
- 3 nucleoside reverse transcriptase inhibitor
  - Reduces mutations
  - Gets viral load down to zero
- HAART is unforgiving of non-adherence to drug schedules

61

## Treatment Guidelines

- Monotherapy unacceptable due to resistance
- Drugs are not titrated up- begin polytherapy immediately → HAART
- More drugs are needed when viral load is high
  - suppress disease → 2 drugs
  - Eradicate virus → 2 nucleoside RTI + protease inhibitor + non-nucleoside RTI
- Deferred therapy is not acceptable
  - But, if viral load low and CD4 high, short term monitoring acceptable.

62

## Treatment Guidelines

- Combination therapy is patient's best option:
  - synergistic effects can improve effectiveness of each med
  - lower dosages may be possible
  - decrease in resistance
  - better penetration of all body compartments
- Convergent (drugs within same family) and divergent therapy (drugs in different families)

## Treatment Guidelines

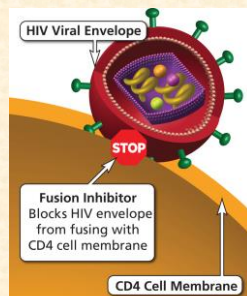
- CAN NOT MISS DOSAGES! THIS WILL LEAD TO RESISTANCE!
  - Up to 1 million mutations occur daily
  - Signs of drug failure:
    - development of opportunistic infection
    - decreasing T cells
    - increasing viral load
- When doing combination therapy, do not stop individual drugs due to resistance. Stop all 3 and start 3 new drugs.
- All pregnant patients get AZT at least → reduces vertical transmission to infant
  - Decreases perinatal transmission by 90% to < 100 cases annually

63

64

## New Medical Therapies

- Entry (Fusion) Inhibitors (not an integrase inhibitor)
  - Enfuvirtide- T20 (Fuzeon)
  - Injected
- FDA Approved March 2003



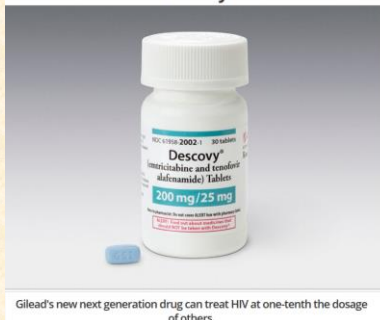
## Integrase Inhibitors

- Dolutegravir (*Tivicay*)
  - 50 mg tablets as a once or twice daily add on to concurrent HAART therapy.
- Elvitegravir (*Vitekta*)
- Raltegravir (*Isentress*)

65

66

## FDA Approves a New, Safer HIV Drug Called Descovy



Gilead's new next generation drug can treat HIV at one-tenth the dosage of others.

## Descovy

- Unique design which allows it to enter the patient's cells in a more efficient manner than prior drugs, and leaves significantly less tenofovir in the patient's body.
- Descovy is a prodrug which lowers the amount of HIV in a user's blood more efficiently than older antiretrovirals. In clinical trials, Descovy was able to lower the HIV in someone's body as well as Viread, but by using one-tenth the size dosage.

67

68

**GoodRx** | Type your drug name (or Abbreviation, Strength, etc) | How GoodRx Works | Discount Card | More | Help | Sign In

**Descovy** Emtricitabine and Tenofovir Alafenamide Fumarate ▲ Specialty Drug

EMTRICITABINE, TENOFOVIR ALAFENAMIDE is 2 antiretroviral medicines in 1 tablet. It is used to treat HIV. This medicine is not a cure for HIV. This medicine can lower, but not fully prevent, the risk of spreading HIV to others. The lowest GoodRx price for the most common version of Descovy is around \$1,656.78, 17% off the average retail price of \$2,014.05. Compare HIV NRTIs.

Prescription Settings | Inset - | Tablet - | 200mg/25mg - | 30 tablets - | SHARE

Prices and coupons for 30 tablets of Descovy 200mg/25mg

Set your location for drug prices near you

Store	Price	Coupon
Kmart	\$1,656.78 with free coupon	GET FREE COUPON
Winn-Dixie	\$1,667.43 with free coupon	GET FREE COUPON
Costco	\$1,667.43 with free coupon	GET FREE COUPON
Safeway	\$2,014 not retail price   \$1,718.81 with free coupon	GET FREE COUPON

69

## Genvoya and Odefsey

- Genvoya: Elvitegravir + tenofovir alafenamide + emtricitabine + cobicistat
- Odefsey: Rilpivirine + emtricitabine + tenofovir alafenamide (one non-nucleoside reverse transcriptase inhibitor (NNRTI) and two nucleoside reverse transcriptase inhibitors (NRTIs)).
- Once-a-day dosing

70

□ GENVOYA® is indicated as a complete regimen for the treatment of HIV-1 infection in patients 12 years and older who have no antiretroviral (ARV) treatment history or to replace the current ARV regimen in patients who are virologically-suppressed (HIV-1 RNA <50 copies/mL) on a stable ARV regimen for ≥6 months with no history of treatment failure and no known resistance to any component of GENVOYA

71

**GoodRx** | Type your drug name (or Abbreviation, Strength, etc) | How GoodRx Works | Discount Card | More | Help | Sign In

**Genvoya** COBICISTAT, ELVITEGRAVIR, EMTRICITABINE, TENOFOVIR ALAFENAMIDE is 3 antiretroviral medicines and a medication booster in 1 tablet. It is used to [treat](#) HIV. This medicine is not a cure for HIV. This medicine can lower, but not fully prevent, the risk of spreading HIV to others. The lowest GoodRx price for the most common version of Genvoya is around \$2,906.32, 10% off the average retail price of \$3,246.59. Compare HIV NRTI + NNRTI + integrase strand transfer inhibitor combinations.

Prescription Settings | Inset - | Tablet - | 150mg/100mg/200mg/10mg - | 30 tablets - | SHARE

Prices and coupons for 30 tablets of Genvoya 150mg/100mg/200mg/10mg

Set your location for drug prices near you

Store	Price	Coupon
Kmart	\$2,906.32 with free coupon	GET FREE COUPON
Winn-Dixie	\$2,924.59 with free coupon	GET FREE COUPON
Costco	\$2,924.59 with free coupon	GET FREE COUPON
Safeway	\$3,246 not retail price   \$3,014.06 with free coupon	GET FREE COUPON

72

**GoodRx** | Type your drug name (or Abbreviation, Strength, etc) | How GoodRx Works | Discount Card | More | Help | Sign In

**Odefsey** EMTRICITABINE, RILPIVIRINE, TENOFOVIR ALAFENAMIDE is 3 antiretroviral medicines in 1 tablet. It is used to treat HIV. This medicine is not a cure for HIV. This medicine can [lower](#), but not fully prevent, the risk of spreading HIV to others. The lowest GoodRx price for the most common version of Odefsey is around \$2,645.68, 10% off the average retail price of \$3,226.70. Compare HIV NRTI + NNRTI combinations.

Prescription Settings | Inset - | Tablet - | 200mg/25mg/25mg - | 30 tablets - | SHARE

Prices and coupons for 30 tablets of Odefsey 200mg/25mg/25mg

Set your location for drug prices near you

Store	Price	Coupon
Kmart	\$2,645.68 with free coupon	GET FREE COUPON
Winn-Dixie	\$2,662.37 with free coupon	GET FREE COUPON
Costco	\$2,662.37 with free coupon	GET FREE COUPON
Safeway	\$2,743.89 with free coupon	GET FREE COUPON

73

## HIV Post Exposure Prophylaxis (HIV PEP)

- AIDS can be prevented in a substantial number of cases
- Needle stick is second highest exposure risk (after HIV blood transfusion- 90% conversion rate)
- 0.3% convert (1/300)
  - Conversion dictated by amount of inoculum and patient's viral load
  - As of 2010, 57 documented transmissions and 143 possible transmissions had been reported in the United States.
  - HIV virus not hearty; killed by most antiseptics

74

## HIV Post Exposure Prophylaxis (HIV PEP)

- Antiretroviral agents from five classes of drugs are currently available to treat HIV infection . These include:
  - the nucleoside reverse transcriptase inhibitors (NRTIs)
  - nucleotide reverse transcriptase inhibitors (NtRTIs)
  - nonnucleoside reverse transcriptase inhibitors (NNRTIs)
  - protease inhibitors (PIs)
  - and a single fusion inhibitor.

75

Exposed to HIV? The clock is ticking!

**72**  
hours

To be effective, **PEP** must begin **within 72 hours** of exposure

You can get **PEP** from your doctor's office, emergency rooms, urgent care clinics, or a **local HIV clinic.**



76

## HIV Post Exposure Prophylaxis (HIV PEP)

- Soak affected part in Betadine, alcohol, peroxide immediately after exposure
- HIV PEP is highly recommended
  - Triple therapy of AZT (200 mg PO Q8H on empty stomach), 3TC (150 mg PO BID), and Crixivan (800 mg PO Q8H on empty stomach)
  - **Must begin within 72 hours after exposure (sooner better)**
  - Should be continued for four weeks
  - Reduces the conversion rate by approximately 80%
- Can not test patients blood for HIV without consent after needlestick

77

## HIV Post Exposure Prophylaxis (HIV PEP)

- Clinicians caring for health care workers who've had a possible exposure can call the PEPline (1-888-448-4911), which offers around-the-clock advice on managing occupational exposures to HIV, as well as hepatitis B and C. Exposed health care workers may also call the PEPline, but they should seek local medical attention first.

78

## PEP Regimen

- Basic Regimen
  - Zidovudine (Retrovir™; ZDV; AZT) + lamivudine (Epivir®; 3TC); available as Combivir™
  - Preferred dosing
- ZDV: 300 mg twice daily or 200 mg three times daily, with food; total: 600 mg daily
- 3TC: 300 mg once daily or 150 mg twice daily
- Combivir: one tablet twice daily

79

## PEP Regimen

- Basic Regimen
  - **Truvada or Descovy**
    - Viread tenofovir disoproxil fumarate (tenofovir DF or TDF) (300 mg) with Emtriva emtricitabine (200 mg) once daily
    - **Plus**
  - **Isentress** raltegravir (RAL) 400 mg twice daily or **Tivicay** dolutegravir (DTG) 50 mg daily.
    - Preferred dosing
- All persons offered PEP should be prescribed a 28-day course of a 3-drug antiretroviral regimen

80





## Truvada

- Truvada® is approved for daily use as PrEP to help prevent an HIV-negative person from getting HIV from a sexual or injection-drug-using partner who's positive. Tenofovir/ emtricitabine
- FDA has approved Truvada® for PrEP for HIV-negative adults and adolescents weighing at least 35 kg (approximately 77 lbs.)
- Studies have shown that PrEP is highly effective for preventing HIV if it is used as prescribed.
- PrEP is much less effective when it is not taken consistently.

89



90

Store	Price	Discount
Kmart	\$1,656.78	with free coupon
Winn-Dixie	\$1,667.43	with free coupon
Costco	\$1,667.43	with free coupon
Walmart	\$1,716.30	with free coupon

91

Store	Price	Discount
Publix	\$46.00	with free coupon
Safeway	\$49.28	with free coupon
Costco	\$51.77	with free coupon
Walmart	\$55.72	with free coupon

92

Store	Price	Discount
Kmart	\$535.73	with free coupon
Winn-Dixie	\$539.55	with free coupon
Costco	\$539.55	with free coupon
Walmart	\$554.24	with free coupon

93

## Eradicating HIV and Curing AIDS

- 50-500 billion viral particles are produced per day in untreated patients
- Free viral particles have half life of minutes
- Actively infected CD4 T cells have half life of 1 day (17 days in non-infected cell)
- HIV infected macrophages have half life of 14 days
- In regards to these cells, HIV is curable

94

## Eradicating HIV and Curing AIDS

- Memory CD4 T cells are reservoir for HIV virus to hide – half life 40-50 months – allows for viral latency
- It would take 60 years of treatment (assuming average half life of 43.9 months for memory T cells) in order to completely eradicate virus due to viral latency in memory T cell reservoirs
- Patients treated for years with HAART therapy and undetectable viral loads all break through with cessation of therapy

95

## The Future of Treatment

- Integrase inhibitors
- Biomodulators
  - Need to find a way to activate HIV virus latent in memory T cells so that HAART therapy can kill virus
  - Need to find out what keeps virus in transcriptionally silent state

96

## The Future of Treatment

- CCR5 antagonists
  - Chemokine receptors – CCR5 targeted by HIV
  - All transmissions involve CCR5 receptors on CD4 T cells
- Experiment of nature
  - 2-5% of Caucasians (mostly Northern European descent) have CCR5 mutation
  - Individuals who are homozygous for this mutation have healthy immune systems and are very resistant to HIV infection
  - Binding site not available for HIV

97

## Eradicating HIV

- In 2008, one man, Timothy Ray Brown, also known as the "Berlin patient," was considered cured of his infection after receiving two bone-marrow transplants to treat a separate disease he had been diagnosed with a few years earlier: acute myeloid leukemia.
- The bone marrow he received came from a donor whose genes carried a rare mutation that made them resistant to HIV, known as CCR5-delta 32, which was transferred on to Brown.
- Traces of the virus were seen in his blood a few years later, but remained undetectable despite him not being on antiretroviral treatment, meaning he was still clinically cured of his infection, according to his clinicians.

98

## Eradicating HIV

- Timothy Ray Brown was given very harsh chemotherapy, had intense complications, and nearly died.
  - Was put into medically induced coma
  - Received massive destruction to immune system
- Now there is "The London Patient" - who remains anonymous
- London Patient had Hodgkin's lymphoma and underwent bone marrow transplant from a CCR5 mutation donor
- Also received much less aggressive immunosuppression

99

## Eradicating HIV

- London Patient stopped anti-retroviral drugs in 9/17
  - Remains undetectable levels
- Transplant destroyed cancer cells
- Transplanted immune cells now are resistant to HIV
- Indicates that patients don't have to 'nearly die' to be cured.

100

## Eradicating HIV

- 2016- new set of HIV positive patients whose reservoirs of HIV have fallen to very low levels after receiving a range of stem cell transplants similar to Brown's.
- The study is part of the EPISTEM project (now iciStem), a European project to investigate the potential for an HIV cure using stem cell transplantation
- Everyone included in the project is in need of stem cell transplantation to cure severe blood disorders, in addition to being infected with HIV.

101

## Eradicating HIV

- iciStem maintains database of 22,000 donors with CCR5 HIV-resistant mutation (called delta 32).
- Tracking 38 HIV-infected patients who have received bone-marrow transplants
  - 6 are from donors without the mutation
- London Patient is #36 on list
- "Dusseldorf Patient" is #19 on list and has been off anti-virals for several months
  - Considered #3 patient cured of HIV (3/19)

102

## Eradicating HIV

- All HIV-infected patients that received a stem cell transplantation had a significant reduction of the viral reservoir in their body.
  - This has not been demonstrated with other cure strategies
- The minute levels of the virus that have been seen to date were not considered competent enough to replicate
- Time will tell...

104