Sep 21st, 9:15 AM - 10:45 AM

Cases in HIV: HIV discussion through interactive case studies

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HIV discussion through interactive case studies

September 22, 2019

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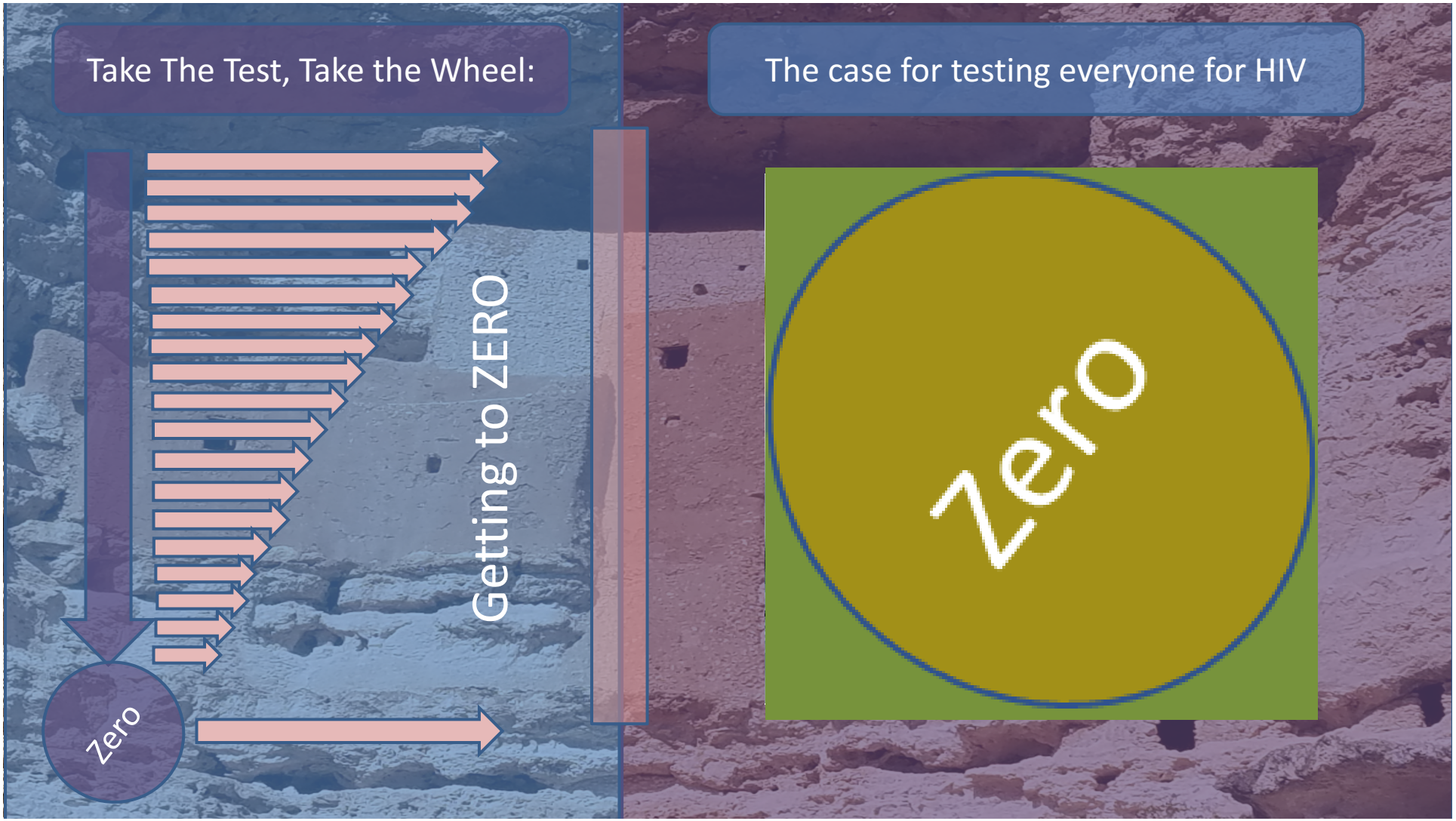
Disclosures

The presenter has no actual or potential conflict of interest in relation to this presentation

Outline

This webinar aims to address the current challenges in “Getting to Zero” and review hot topics and recurrent themes and questions presented throughout the year and within the current literature through interactive audience participation. Cases will be presented in highlighting current HIV care.


Take The Test, Take the Wheel:
Getting to ZERO
Zero
The case for testing everyone for HIV
zero

Georgia Concerns: (2016/2017)

Georgia National Rank	STD	Cases	Rate per 100,000 population
1	HIV	56,789 51,532	31.8 / 24.9
3 / 9	**Gonorrhea**	20,553 22,667	201.2 / 219.8
4 / 4	P&S Syphilis	1,350 1,489	13.2 / 14.4
5 / 6	**Chlamydia**	62,776 65,104	614.6 / 631.4
9 / 10	Congenital Syphilis	21 23	16 / 17.7
10 / 11	P&S Syphilis (women)	113 139	2.2 / 2.6

https://www.cdc.gov/std/stats16/toc.htm / https://www.cdc.gov/hiv/statistics/overview/geographicdistribution.html
https://www.cdc.gov/std/stats17/2017-STD-Surveillance-Report_CDC-clearance-9.10.18.pdf

O.C.G.A. (Official Code of Georgia Annotated) § 31-17-7.1

Prescription drugs; **expedited partner therapy** for patients with venereal diseases

NOT for MSM or women with S/S of PID

§ 31-17-4.2: Georgia HIV/Syphilis Pregnancy Screening Act of 2015; enact

Number & Rates: Persons Living with HIV & AIDS, GA, through December 31, 2017

	HIV Diagnoses		PLWH	
Public Health District	**Count**	**Rate***	**Count**	**Rate***
1-1 Northwest (Rome)	51	7.6	1,089	163.2
1-2 North Georgia (Dalton)	28	5.8	677	141.2
2 North (Gainesville)	40	5.7	829	117.9
3-1 Cobb-Douglas	200	22.2	4,011	445.9
3-2 Fulton	651	62.5	16,770	1,610.3
3-3 Clayton (Jonesboro)	146	51.2	2,708	949.7
3-4 East Metro (Lawrenceville)	218	19.5	4,091	365.7
3-5 DeKalb	374	49.7	9,926	1,317.8
4 LaGrange	125	14.6	2,155	252.3
5-1 South Central (Dublin)	25	16.6	612	406.9
5-2 North Central (Macon)	99	18.8	2,203	417.3
6 East Central (Augusta)	91	18.7	2,257	464.3
7 West Central (Columbus)	119	32.4	1,806	492.1
8-1 South (Valdosta)	68	26.5	1,151	448.1
8-2 Southwest (Albany)	87	25.1	1,779	513.0
9-1 Coastal (Savannah)	133	21.4	2,756	444.2
9-2 Southeast (Waycross)	45	12.2	1,213	328.3
10 Northeast (Athens)	54	10.8	1,008	200.7
Unknown Health District	143	--	1,767	--
Total	2,698		58,808	

*per 100,000 population

Georgia DPH Resource HUB

https://www.gacapus.com

A 28 yo F in excellent health presents with concerns about a high-risk sexual exposure 6-days ago. She was tested 3-months & 6-months ago for HIV & was seronegative. She has no symptoms.

Which of the following is likely to give the earliest evidence of HIV infection?

A. p24 antigen
B. HIV RNA viral load
C. HIV 1/2 EIA
D. HIV1/2 IgM antibody test
E. CD4 count

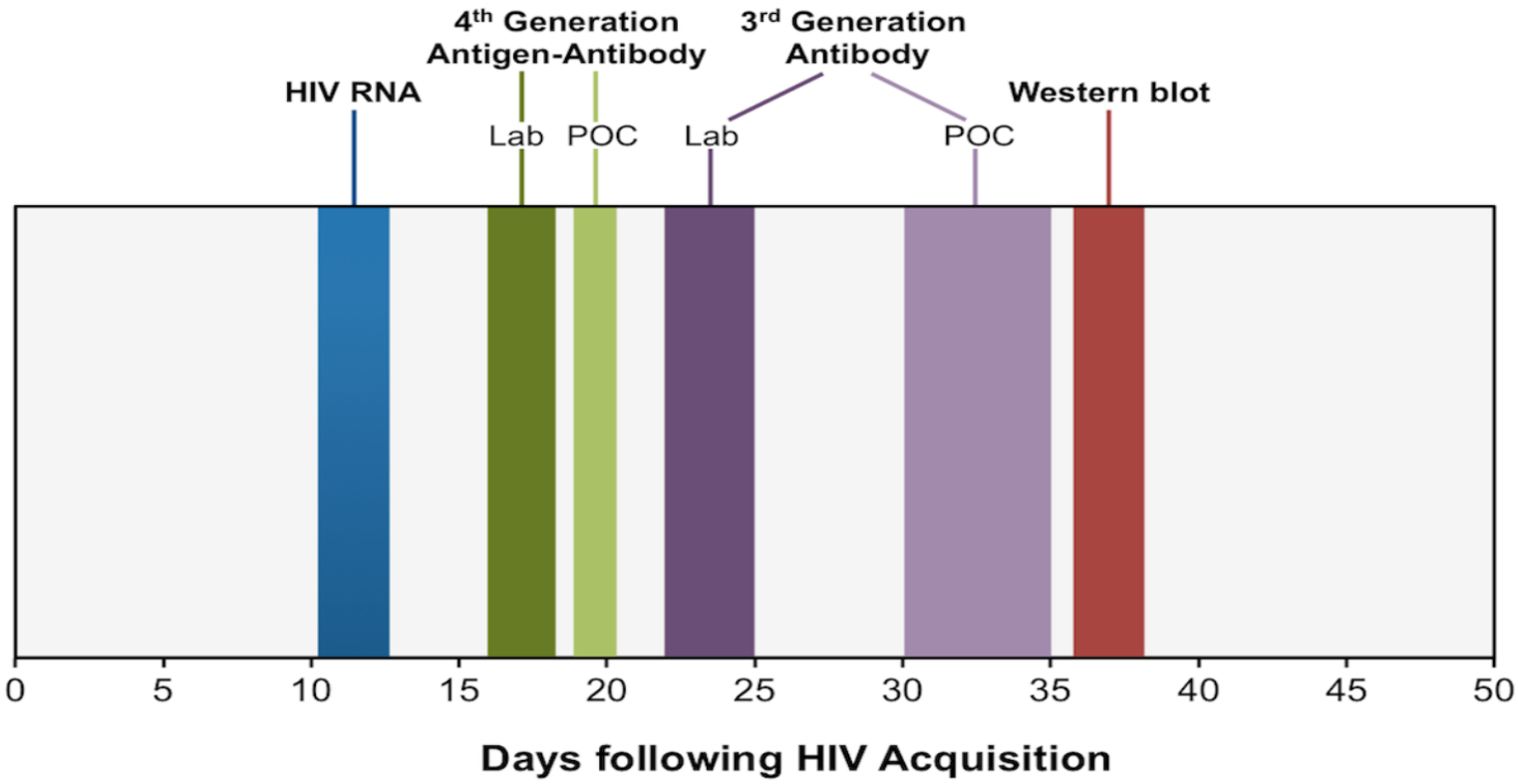


Figure 2 - Timing of Positivity for HIV Diagnostic Tests
Abbreviation: POC = point of care

Source: modified from Centers for Disease Control and Prevention and Association of Public Health Laboratories. Laboratory Testing for the Diagnosis of HIV Infection: Updated Recommendations. Published June 27, 2014.

The signs and symptoms of acute HIV infection appear 6 to 56 days after exposure.
Viremia can be detected as early as 4 days post exposure by RT-PCR of serum.

https://www.hiv.uw.edu/go/screening-diagnosis/diagnostic-testing/core-concept/all

64-yo HIV+ F doing well (VL<20, CD4 =400 cells) on long-term primary ARVs of TDF, FTC and unboosted atazanavir. She experiences an acute major GI bleed.

- Advised to switch to boosted ATV but insists on remaining on unboosted ATV.
- In the hospital; continues ARVs & found to be helicobacter(+) on gastric biopsy & treated with metronidazole, clarithromycin plus omeprazole.
- She is sent home on day 17 with her preadmission ARVs + omeprazole.
- Routine visits 2-weeks & 6-weeks after hospitalization; VL is >25000 copies on each occasion, & her CD4 count is falling despite perfect adherence.

The most likely cause of the rise in HIV viral load and reduced CD4 count?

A. Metronidazole
B. Clarithromycin
C. Omeprazole
D. Poor absorption of antiretroviral drugs due to unsuccessful eradication of helicobacter
E. Direct effect of helicobacter on HIV replication rate

- ATV is not recommended without boosting (ritonavir or cobicistat)
- Omeprazole interferes with the absorption of a variety of drugs. Unboosted ATV should not be used with omeprazole since ATV plasma levels may not be adequate. Boosted ATV would probably be adequate.
- ATV requires acidic gastric pH for adequate absorption. Acid-lowering drugs (proton pump inhibitors, histamine-2 antagonists, antacids) may significantly impair ATV absorption, & thus reduce ATV efficacy.
- The degree of impairment depends on the dose & half-life of the acid-lowering product, the duration of acid lowering effect, & the timing between taking these agents & ATV.

A man from Cameroon W. Africa is referred for evaluation. He had an episode of PCP & was successfully treated. The hospital documented:

- HIV Elisa Positive for HIV: 1/2
- Viral Load: <50 copies/ml
- CD4 Count: 125 cells/uL
- CBC and Chem 12: Unremarkable
- The HIV Elisa was confirmed positive for HIV 1/2 at another commercial laboratory.
  - This laboratory confirmed the viral load <50 copies/ml.

How would you interpret these results and manage the patient?

A. Patient is not infected with HIV-1 or HIV-2
B. Patient is infected with HIV-2; has low-level viremia & needs no therapy now
C. Patient should be started on Tenofovir-3TC-Efavirenz
D. Patient should be started on emtricitabine-tenofovir & Darunavir-Ritonavir
E. Patient is infected with HIV-1; does not need therapy as he is a long term non-progressor

32 yo F HIV(+) is taking TDF/FTC/efavirenz with routine follow-up labs one month ago revealing a CD4 count of 905 cells/uL & an HIV RNA <20 copies/ml.

After missing her period, she does a home pregnancy test which is positive & is subsequently confirmed to be pregnant by her primary care provider who estimates that she is in her first trimester. She intends to continue the pregnancy.

What should be done with her antiretroviral drug regimen?

A. Stop antiretrovirals until the second trimester
B. Stop antiretrovirals until labor
C. Change the efavirenz to atazanavir/ritonavir
D. Change the tenofovir/emtricitabine to zidovudine/lamivudine
E. Continue the current regimen

DHHS 2018 Guidelines

Recommendations for Use of Antiretroviral Drugs during Pregnancy

	NRTIs	NNRTIs	PIs	Entry Inhibitors	Integrase Inhibitors
Preferred	ABC*/ 3TC TDF/ (3TC or FTC)		ATV/r DRV/r (twice daily)		RAL (twice daily) DTG Triumeq™
Alternate	ZDV/ 3TC	RPV Complera™ EFV*** Atripla™ Symfi™	LPV/r (twice daily)		
Insufficient Data	TAF/FTC	Odefsey™ DOR		IBA	Biktarvy™
Not Recommended	ABC*/3TC/ZDV ddI + d4T# ddC	NVP** ETR	FPV SQV/r IDV/r TPV/r NFV RTV (as single PI)	T20 MVC	Prezcobix™ Symtuza™ Stribild™ Genvoya™ Evotaz™ Cobicistat

**** Use ABC only for HLA-B*5701 negative patients***

***** Use with caution: use only if CD4 count < 250***

****** anencephaly, microphthalmia, cleft palate***

 # Implicated in death of a client: severe lactic acidosis with hepatic steatosis with or without pancreatitis

25 yo M HIV(+) is seen for routine HIV care. He has received his initial regimen with TDF, FTC, & efavirenz for the past year but has a history of a poor response & currently has a viral load of 10,000 copies on repeated determinations despite his assurances of adherence.

- Resistance profile on his current regimen includes:
  - Nucleoside: M184V
  - Non nucleoside: K103N
- Phenotype: fully susceptible to all protease inhibitors
- He is hepatitis B surface antigen (HBsAg) positive.

The most prudent management strategy for this patient would be?

A. Discontinue current regimen & repeat genotype after being off ARVs for 4 weeks
B. Change his regimen to Abacavir, Darunavir-ritonavir, and Raltegravir
C. Change his regimen to Zidovudine, Lamivudine, Darunavir-ritonavir
D. Change his regimen to TAF, FTC, Darunavir-ritonavir
E. Change his regimen to Abacavir, Lamivudine, Darunavir-ritonavir

45 yo TG-MTF HIV(+) presents for routine care.

Screening labs revealed:

HDL = 38 mg/dL

Triglyceride = 1,200 mg/dL.

LDL could not be calculated

Her current ARVs includes darunavir/ritonavir & tenofovir/emtricitabine.

Which of the following triglyceride lowering approaches using standard unadjusted doses would be the preferred next step?

A. Simvastatin
B. Pravastatin
C. Fenofibrate
D. Simvastatin + Omega 3 fatty acid
E. Dietary counseling

- Boosted DRV will augment simva-, lova-, & pravastatin levels; enhanced toxicity
  - Greatly enhanced statin levels can cause muscle pain, or even fatal rhabdomyolysis
- When Triglycerides exceed 1000 mg/dl, either fibrate or niacin should be the first line therapy &, therefore, "dietary counseling" is wrong
- Markedly elevated triglyceride levels are independent risk factors for both cardiac disease & pancreatitis.
- Once TG are below 500 mg/dL, LDL can be calculated.
  - LDL goal - < 70 mg/dL
- Atorvastatin can be started with the lowest dose & titrated upward based on lipid responses & side effects. Pravastatin & Fluvastatin have the least interactions & can be used safely with most protease inhibitors; however, Darunavir has been shown to increase pravastatin levels substantially.

55 yo HIV(+) M, who has excellent virologic control with darunavir/ritonavir, abacavir/lamivudine called your office to request a prescription for Vardenafil (Levitra™). He has never been on any drugs for erectile dysfunction (PDE-5 inhibitors).

Which of the following opinions would you give this patient?

A. PDE-5 inhibitors are contraindicated in HIV-infected patients as they may increase HIV replication
B. Vardenafil is a substrate of CYP 3A4, thus, vardenafil dosage should be reduced when used with darunavir/ritonavir
C. Vardenafil is an inducer of CYP3A4, thus, vardenafil may reduce the virologic efficacy of darunavir/ritonavir
D. Vardenafil is an inhibitor of CYP3A4, thus, may increase darunavir level and increase darunavir toxicities.

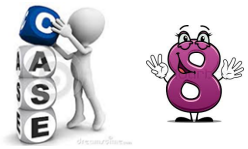
- All phosphodiesterase type 5 (PDE-5) inhibitors (Levitra™, Viagra™, Cialis™);
  - are substrates of CYP3A4 enzyme system & are prone to significant interactions with CYP3A4 inhibitors such as darunavir/ritonavir.
- PDE-5 drug levels increase dramatically, especially vardenafil (Levitra™)
- These drugs are vasodilators, hypotension can occur, especially when serum levels exceed therapeutic targets. Hypotension is the major association with ritonavir-boosted regimens unless doses are appropriately adjusted.
- Patients who take standard doses of vardenafil & boosted protease inhibitors will be more likely to experience hypotension, cardiac toxicities related to poor cardiac perfusion, headache, nausea, visual changes including irreversible blindness, hearing loss, & prolonged priapism.
- Thus, if these drugs are used for patients receiving protease inhibitors, especially boosted protease inhibitors, the dose must be started low & carefully selected from one of the many pharmacology reference sources.

A cardiac surgeon comes to you for advice.

- She has recently found out that she is HIV infected (CD4 =70 cells/uL, Viral load 300,000 copies) but her viral load is now <50 copies on ART. She feels well, states that she has the best surgical outcomes at her hospital, and would like to keep operating.

What other advice would you give her?

A. Cease to perform surgery because of the magnitude of risk of transmission of HIV to patients regardless of HIV-VL
B. Cease to perform surgery because of likely cognitive impairment, regardless of the results of current neurocognitive testing
C. Cease to perform surgery because most state laws prohibit such practice by an employee who is HIV infected
D. Continue to practice if she adheres to hospital policies regarding HIV infected employees, has viral loads <50 copies, follows infection control guidelines, has satisfactory performance reviews, & there is no evidence of HIV transmission.
E. May practice however she chooses at her own discretion since most hospital policies & state laws do not permit discrimination against workers with disabilities.



- No state or Federal laws prohibit the practice of surgery based on HIV status
  - Society of Healthcare Epidemiologists of America offer guidelines (SHEA)
- No scientific or ethical reason why this surgeon cannot continue to practice assuming that her results meet usual & customary standards, & she adheres to recommended infection control practices & her viral load is <50 copies.
- If she has a viral load >50 copies, there are professional society guidelines & some hospital policies that indicate a need to restrict the infected healthcare professional from “procedures with definite risk of blood borne pathogen transmission”
- Since the sensational news about a Florida dentist transmitting HIV to his patients were reported in 1993, which has never been satisfactorily explained, there have been only 3 other likely cases of transmission from healthcare provider to patient. Thus, HIV transmission from healthcare provider to patient is very rare in the current era & less common of HBV or HCV transmission.

Recommendations for Managing Healthcare Providers Infected with HBV, HCV, and/or HIV

Virus, circulating viral burden	Categories of clinical activities	Recommendation	Testing
HBV			
$<10^4$ GE/mL	Categories I, II, and III	No restrictions (1)	Twice per year
$\geqslant 10^4$ GE/mL	Categories I and II	No restrictions (1)	NA
$\geqslant 10^4$ GE/mL	Category III	Restricted (2)	NA
HCV			
$<10^4$ GE/mL	Categories I, II, and III	No restrictions (1)	Twice per year
$\geqslant 10^4$ GE/mL	Categories I and II	No restrictions (1)	NA
$\geqslant 10^4$ GE/mL	Category III	Restricted (2)	NA
HIV			
$<5\times10^2$ GE/mL	Categories I, II, and III	No restrictions (1)	Twice per year
$\geqslant 5\times10^2$ GE/mL	Categories I and II	No restrictions (1)	NA
$\geqslant 5\times10^2$ GE/mL	Category III	Restricted (3)	NA

1. Next slide
2. These procedures permissible only when viral burden is $<10^4$ GE/mL.
3. These procedures permissible only when viral burden is <5×1025×102 GE/mL.

https://www.jstor.org/stable/10.1086/650298#metadata_info_tab_contents

No restrictions recommended, so long as the infected healthcare provider

(1) is not detected as having transmitted infection to patients;
(2) obtains advice from an Expert Review Panel about continued practice;
(3) undergoes follow-up routinely by Occupational Medicine staff (or an appropriate public health official), who test twice per year to demonstrate the maintenance of a viral burden of less than the recommended threshold;
(4) also receives f/u by a personal physician who has expertise in the management of her/his infection & who is allowed by the provider to communicate with the Expert Review Panel about the provider's clinical status;
(5) consults with an expert about optimal infection control procedures (and strictly adheres to the recommended procedures, including the routine use of **double-gloving** for Category II and Category III procedures and frequent glove changes during procedures, particularly if performing technical tasks known to compromise glove integrity [e.g., placing sternal wires]), and
(6) agrees to the information in & signs a contract or letter from the Expert Review Panel that characterizes her/his responsibilities

Category I: Procedures with de minimis risk of bloodborne virus transmission

- Routine dental preventive procedures
- Routine rectal or vaginal examination
- Lower GI tract endoscopic examinations & procedures; sigmoidoscopy & colonoscopy

Category II: Procedures for which bloodborne virus transmission is theoretically possible but unlikely

- Bronchoscopy
- Minor gynecological procedures (colposcopy)
- Upper GI tract endoscopy

Category III: Procedures for which there is definite risk of bloodborne virus transmission or that have been classified previously as "exposure-prone"

- General surgery/oral surgery
- Cardiothoracic surgery
- Ob/gyn: cesarean delivery, hysterectomy

- 27-yo AAF office worker from Savannah (no travel/exposure history), presents with 3-weeks of incr. severe midabdominal cramping non-radiating pain, associated with nausea & occasional emesis the past 2-days. No fever.
- Diagnosed 2-months earlier with HIV; VL 861,000 & CD4 8
- Begun on TMP/SMX & TAF/FTC/DRV/r with good adherence.
- Afebrile, obese, distended abd. with slight tenderness, no rebound & good bowel sounds
- Labs: VL 54,000 & CD4 72.
- Surgical consultation felt laparotomy was unnecessary & percutaneous needle aspiration was declined by radiology

A. Empirical therapy for MAC
B. Empirical therapy for lymphoma
C. Empirical therapy for histoplasmosis
D. Stop all the antiretrovirals
E. Change darunavir to lopinavir

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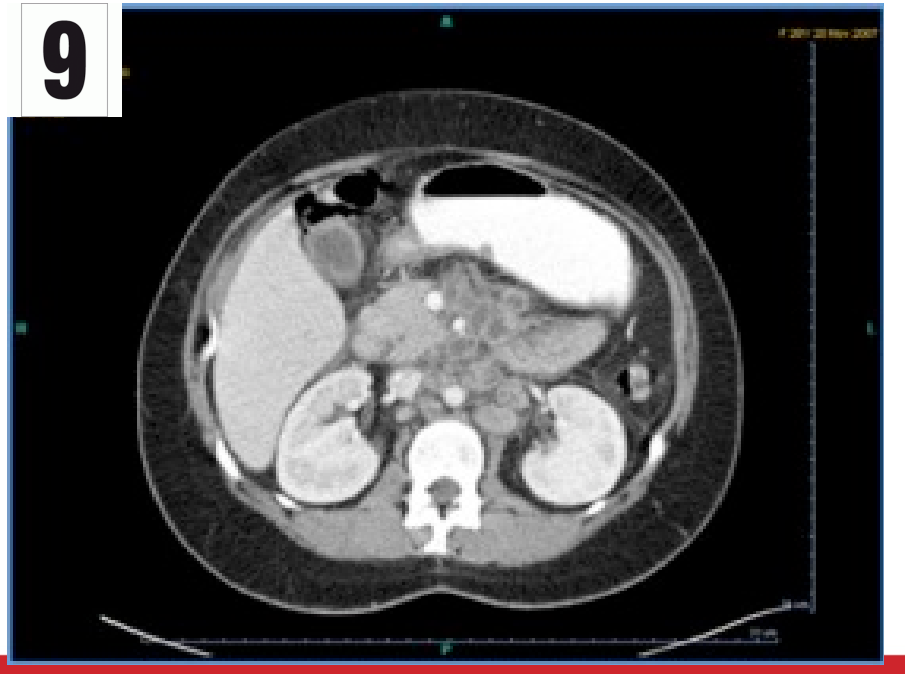


- Clinical presentation: c/w IRIS from MAC mesenteric lymphadenitis
- Some might opt to wait to see if this resolves w/o MAC therapy, but since she has never been treated for MAC, the best option would be to treat
- Some would use a regimen with activity against both MAC & MTb. However, no history of TB exposure, & TB is uncommon to be acquired in the US except in prisons, homeless shelters, or certain other settings with high risk individuals (e.g. hospitals, long-term care facilities).
- CT shows necrotic nodes.

February 15, 2019

DMAC:

Primary prophylaxis: if immediately initiate ARVs, then prophy. is not recommended, regardless of CD4 cell count

35-yo M from Ethiopia presents to the hospital with fever, cough & hemoptysis, & is found to have pulmonary Tb & HIV infection.

The patient denies prior knowledge of either

- CD4= 23 cells/mm^3, VL= 350,000 copies/ml
- He is placed on a 4-drug regimen: INH, RIF, ETHb, & PZA (+pyridoxine) - RIPE
- Assuming that his HIV is pan sensitive, which of the following drugs would be the best choice for this patient to combine with emtricitabine plus tenofovir **&** when should they be started in regards to RIPE?

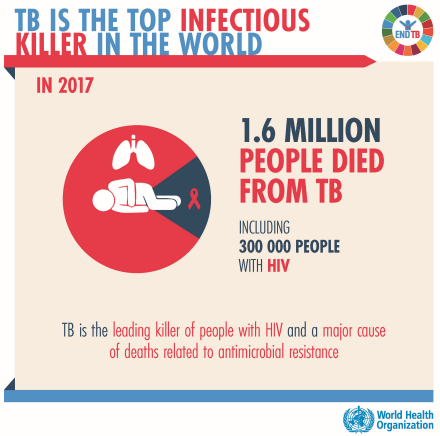
A. Elvitegravir/Cobicistat within 2 weeks
B. Atazanavir/ritonavir within 2 to 4 weeks
C. Lopinavir/Ritonavir within 4 to 8 weeks
D. Efavirenz within 2 weeks
E. Dolutegravir within 2 to 4 weeks

- Among NNRTIs, rifampin may be used with Efavirenz.

  Drug of choice in minimizing interactions when starting both TB tx & ART, assuming that there are no resistance issues.

  Some clinicians would increase the dose of EFV from 600 mg daily to 800 mg daily if the patient weighs >60 kg.

- ART-naïve: start ARVs within 2-weeks after TB tx initiation when CD4 is <50 cells/mm^3 &, within 8-weeks of starting anti-TB treatment in those with higher CD4 counts.



- 29-yo HIV(+) M with a baseline CD4 count: 205, HIV RNA level: 36,000 + HLA-B*5701 positive started on tenofovir/FTC/elvitegravir/cobicistat & by 24-wks had a CD4 count: 355 & an HIV RNA level: <20 copies/ml. On routine follow-up 3-months later, he admits to missing 2-3 doses a week & his HIV RNA level: 13,000. Two weeks later, his repeat HIV RNA level: 32,000 & an HIV genotype reveals **M184V**, **Y143R** and **Q148R**.

  He requests a once-a-day regimen.

Which of the following is the optimal subsequent antiretroviral regimen?

A. tenofovir/emtricitabine + dolutegravir
B. tenofovir/emtricitabine + efavirenz
C. tenofovir/emtricitabine + darunavir/ritonavir
D. abacavir/lamivudine + atazanavir/ritonavir

- Q148R confers reduced activity to dolutegravir.
- Efavirenz: low barrier to resistance & must be combined with 2 fully active agents for maximal virologic efficacy & to avoid the emergence of resistance; the M184V would confer complete resistance to emtricitabine, so this is a suboptimal regimen
- HLA*B5701 positive is a contraindication to abacavir

76-yo HIV(+) M on TDF/FTC + DRV/r for a year & is without side effects. HIV RNA was originally 123,000 & is now persistently suppressed below detection. CD4 originally was 235, & is 200-300 persistently over the past year with no clear upward trend.

What do you recommend?

A. Continue current regimen
B. Change tenofovir/emtricitabine to abacavir/lamivudine
C. Change darunavir/ritonavir to efavirenz
D. Add maraviroc to current regimen
E. Add dolutegravir to current regimen

- Patient has optimal virologic response with ARV therapy, but a suboptimal CD4 cell recovery. Older age (among other reasons) has been associated with a suboptimal CD4 response. There is no proven strategy to treat a suboptimal CD4 response.
- Specifically, changing or adding antiretroviral drugs, including maraviroc or an integrase inhibitor has not been associated with benefit.
- The patient should be reassured and the current antiretroviral drug regimen continued.

- 37-yo M lab tech presents 60 minutes after exposure to a needlestick from an HIV(+) man undergoing routine blood draw
- The patient whose blood was being drawn takes ABC/3TC + DRV/r with his last HIV RNA 62 copies/ml & CD4 553

What do you recommend as initial management?

A. No post-exposure prophylaxis
B. Start tenofovir/emtricitabine/efavirenz X 4 weeks
C. Start tenofovir/emtricitabine + atazanavir/ritonavir X 4 weeks
D. Start tenofovir/emtricitabine + dolutegravir X 4 weeks

What if the Lab Tech was a woman?

- Occupational exposure to HIV should prompt careful evaluation of the exposure, the source patient, & the healthcare worker. A needlestick exposure is a reason to start post-exposure prophylaxis (PEP). The source patient has a low, but not completely suppressed, HIV RNA.

- The CDC recommended regimen for PEP is tenofovir/emtricitabine + dolutegravir or raltegravir.

58 yo F presents with shortness of breath, fever, & CXR with bilateral interstitial infiltrates. Bronchoscopy reveals cysts of Pneumocystis & is started on trimethoprim-sulfa + corticosteroids.

  - HIV antibody test is positive, CD4 is 110, & HIV RNA is 285,000

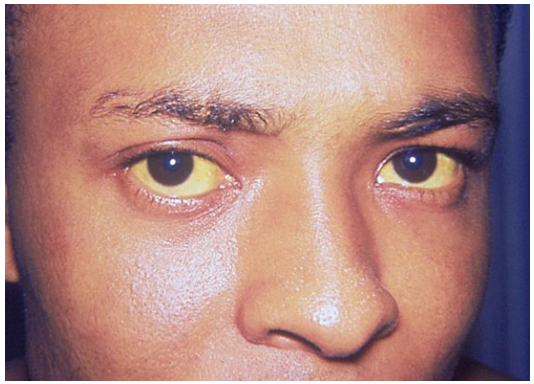
- She improves over 2 weeks & is started as an outpt on TDF/FTC & ATV/r
- Two weeks later, she develops jaundice
  - AST 38, ALT 55, alkaline phosphate 141, bilirubin 3.8 (direct 0.4)

What is the most likely cause of her jaundice and hyperbilirubinemia?

A. Trimethoprim-sulfa
B. Tenofovir (TDF)
C. Emtricitabine
D. Atazanavir
E. Ritonavir

- Jaundice with hyperbilirubinemia (all indirect) is a known effect of ATV, due to its inhibition of the hepatic UGT1A1 enzyme
- Atazanavir-associated indirect hyperbilirubinemia is intermittent and NOT associated with other liver function test abnormalities, but the jaundice may cause concerns for patients, occasionally requiring a change in ART.

Bilirubin is a yellow compound that occurs in the normal catabolic pathway that breaks down heme in vertebrates. This catabolism is a necessary process in the body's clearance of waste products that arise from the destruction of aged or abnormal red blood cell



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26 yo M recently diagnosed HIV disease is eager to start ART

Initial work-up: HIV RNA 2.5 million copies/ml CD4 110

HLA-B*5701 positive Genotype: L63P

His only medication is a fluticasone inhaler for asthma

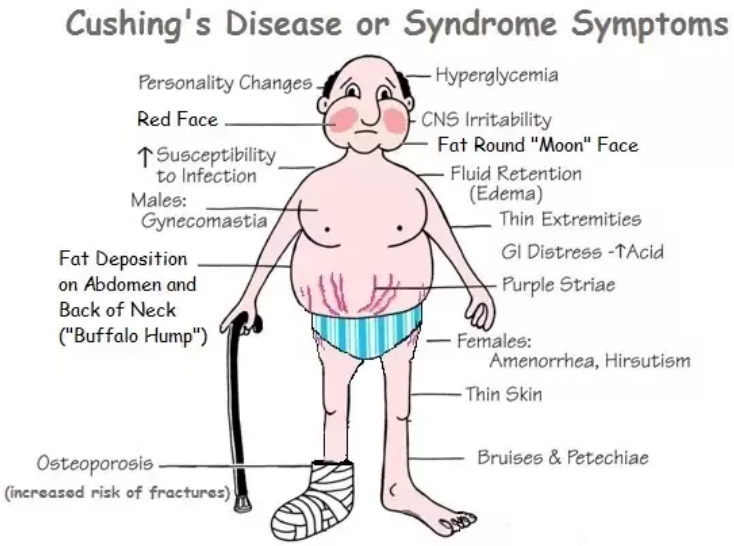
He prefers one pill, once-daily therapy, if possible

Which of the following regimens do you recommend?

A. tenofovir/emtricitabine + darunavir/ritonavir
B. tenofovir/emtricitabine/elvitegravir/cobicistat
C. tenofovir/emtricitabine/Rilpivirine
D. tenofovir/emtricitabine + dolutegravir
E. abacavir/lamivudine + efavirenz

Choices A & B both have a pharmacologic booster which can increase the systemic levels of fluticasone and can lead to Cushing's syndrome

Choice C, the rilpivirine-based regimen, and Choice E, the abacavir-containing regimen, would not be appropriate with a baseline HIV RNA level of >100,000 copies/ml; also abacavir is contraindicated with HLA-B*5701 positive.



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That which is not good for the bee-hive cannot be good for the bees.
Marcus Aurelius