HIV Prevention and Treatment: The Evolving Role of the Emergency Department

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Historically, the role of the emergency physician in HIV care has been constrained to treating sick patients with opportunistic infections and postexposure prophylaxis for occupational exposures. However, advances in HIV care have led to medications that have substantially fewer issues with toxicity and resistance, opening up an exciting new opportunity for emergency physicians to participate in treating the HIV virus itself. With this new role, it is crucial that emergency physicians be familiar with the advances in testing and medications for HIV prevention and treatment. To our knowledge, to date there has not yet been an article addressing this expansion of practice. We have compiled a summary of what the emergency physician needs to know, including misconceptions associated with antiretroviral therapy, medication complexity, toxicity, resistance, and usability. Additionally, we review potential indications for prescribing these drugs in the emergency department, including the role of the emergency physician in postexposure prophylaxis, preexposure prophylaxis, and treatment of acute HIV, as well as how emergency physicians can engage with chronic HIV infection. [Ann Emerg Med. 2017;70:562-572.]

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INTRODUCTION

Importance

It is difficult to envision a better medical success story than the progress made in HIV infection since its discovery in 1983. However, despite the development of safe and highly effective therapy for both the treatment and prevention of HIV infection, the epidemic is far from over. The majority of HIV patients remain out of care and do not receive antiretroviral therapy; transmission of HIV from this population is estimated to account for 91.5% of new infections.[1] Our greatest challenge to end the epidemic today is not developing effective therapy but diagnosing, treating, and retaining infected patients in care, and identifying and engaging those most in need of prevention.

Emergency departments (EDs) are the safety net of our health care system, with 1 in 5 Americans using the services of the ED annually.[2] EDs often become the medical home for marginalized patients with chronically uncontrolled HIV and are often a key point of health care access for those with risk factors for or living with undiagnosed HIV.[3-7] This has led EDs across the country to have a greater role in the HIV epidemic and HIV care continuum. Patients with HIV visit the ED at least 3 times as frequently as patients without HIV.[8] Despite this, HIV care has historically been considered outside of the scope of practice of emergency physicians, and involvement in the diagnosis, prevention, and treatment of HIV infection can be anxiety provoking for emergency physicians. Since the beginning of the epidemic, the role of emergency physicians has been largely limited to managing complications of HIV infection and its treatment, and prescribing postexposure prophylaxis for occupational needlestick injuries. Barriers to comprehensive involvement included inefficient testing algorithms, complexity and toxicity of antiretroviral therapy, unknown optimal timing of antiretroviral therapy, lack of continuity between ED and community HIV care providers, and lack of effective preventive measures. For these reasons, more comprehensive care was deferred to the HIV specialist. However, in recent years HIV care has evolved and emergency physicians now have an opportunity to expand their role in the diagnosis and treatment of HIV-infected individuals.

Since 2006, the Centers for Disease Control and Prevention (CDC) has recommended routine nonrisk-based opt-out HIV screening in all health care settings, including the ED, and efforts to scale up routine opt-out screening in the ED are ongoing.[9] Approximately 18% of individuals infected with HIV have received no diagnosis, and many more have but have not been retained in care. These 2 groups unknowingly contribute disproportionately to forward transmission of the virus, and any opportunity to diagnose and treat their HIV infection has potential for a substantial public health benefit.[1] For many of these patients, the ED may be their only interface with the health care system. Thus, ED-based screening provides

a critical opportunity to identify undiagnosed and untreated HIV in patients, link them to care, and, in select cases, initiate treatment from the ED. Although previous generations of HIV tests may not have fit into the work flow of the emergency physician, new HIV-1 and -2 antigen/antibody immunoassay testing provides rapid turnaround times and simultaneously detects both acute and chronic infection, making screening from the ED feasible.[10] These changes have led to an increasing number of newly identified HIV infections in the ED, including an increasing percentage of patients with acute HIV infection.[11] Recently, Hsieh et al[12] examined the role of the ED in the HIV care continuum and argued that EDs and physicians should play an increased role in HIV identification and management. The discussion of HIV screening in the ED is expansive and a detailed discussion is beyond the scope of this article, but we refer the reader to previous issues of this journal for more information on this topic.[13]

Emergency physicians may also experience an increased role in HIV prevention. Requests for postexposure prophylaxis in the community after high-risk sexual encounters are increasing in some high-risk settings.[14] Even more recently, pre-exposure prophylaxis has been shown effective at preventing HIV in high-risk communities. In fact, CDC guidelines in 2014 recommended pre-exposure prophylaxis for those at high risk of acquiring HIV.[15] Since evidence of robust efficacy has become more apparent,[16,17] media exposure has increased community awareness of such prophylaxis, and recent uptake has significantly increased.[18] However, the patients who most need pre-exposure prophylaxis may limit their health care exposure to the ED,[19] focusing high-yield opportunities for prevention to the ED setting.

Today, emergency physicians will increasingly find themselves involved in the prevention or treatment of HIV infection through caring for patients with new diagnoses of HIV, fielding requests for pre-exposure prophylaxis, administering postexposure prophylaxis, or managing complications of untreated HIV. However, myths in regard to HIV therapies are prevalent and need to be addressed before physicians can become comfortable with HIV medications. This article seeks to provide a tool for emergency physicians caring for patients infected with HIV or with risk factors for HIV, dispel existing myths about antiretroviral therapy, review developments in HIV therapies and prevention strategies, and address indications for prescribing antiretroviral therapy from the acute care setting.

DISPELLING ANTIRETROVIRAL THERAPY MYTHS

When triple antiretroviral therapy became available in 1996, for the first time, HIV was transformed from a terminal disease to a chronic infection. Despite being one of the greatest medical success stories of our time, the development of safe and effective treatment for HIV infection during the last 20 years had to overcome significant challenges. The original antiretroviral therapy "cocktails" were cumbersome, poorly tolerated, and riddled with significant adverse effects and toxicity, but these problems were accepted as regrettable trade-offs for survival. Given this history, it is not surprising that only HIV specialists were comfortable prescribing antiretroviral therapy. However, during the last 20 years, significant advances have occurred in antiretroviral therapy, and medications used to prevent and treat HIV today now bear only a slight resemblance to the first generation of antiretroviral therapy drugs, but concerns about toxicity persist.

In the early days of antiretroviral therapy, complex drug interactions resulted in antiretroviral therapy regimens containing up to 25 pills, received up to 5 times throughout the day and night. Pills tasted so bad that patients hid them inside peanut butter or chocolate to be able to swallow them. When the combination pill of efavirenz, emtricitabine, and tenofovir disoproxil fumarate (Atripla) became available in 2006, once-daily single-pill combination regimens became first-line therapy.[20] Now, 6 different 1-pill-a-day regimens are available for patients to maintain viral suppression.[21]

Previously prescribed antiretroviral medications such as didanosine, stavudine, indinavir, or nevirapine not infrequently resulted in severe, sometimes life-threatening adverse effects, including anemia, abnormal fat distribution, liver failure, pancreatitis, severe drug reactions, lactic acidosis, hyperlipidemia, hyperglycemia, and diabetic ketoacidosis. The complexity of the regimen and the adverse-effect profile resulted in very poor adherence. For example, in 2002, Heath et al[22] found that 70% of patients reported intentional nonadherence to antiretroviral therapy because of adverse effects. In stark contrast, current antiretrovirals have much more mild adverse effects, commonly nausea and diarrhea, which are self-limited and improve over time. As a result, recent studies examining patients' experiences with new antiretroviral medications show that few, if any, patients who receive new integrase inhibitor–based antiretroviral therapy regimens experience an adverse event that leads to switching to a new medication regimen.[23] Additionally, significant progress has been made in decreasing pill burden and dosing frequency; many regimens now consist of combination pills that are received only once or twice daily, improving likelihood of medication adherence.

Another significant concern about antiretrovirals is that even short-term prescription of antiretroviral therapy will promote significant development of resistance in patients.

Certain conditions such as nonadherence allow the HIV virus to mutate to "beat" or become resistant to the drug regimen that the patient is prescribed. Earlier drugs were highly susceptible to resistance; very few mutations could easily knock out an entire drug and other drugs within the same class. Drug failure would quickly lead to virus resistance, which would limit future therapy options. In the 1990s, after almost a decade of sequential monotherapy, the majority of HIV-infected patients had resistance to many of the available nucleoside reverse transcriptase inhibitor drugs[24] and patients had to continue receiving failing regimens until newer agents were available. As a consequence, physicians were worried about starting medications in patients for whom adherence might be a question for fear of hastening these resistance patterns. Many of the newer drugs are designed to increase this barrier to resistance. In other words, some of the modern antiretroviral drugs such as protease inhibitors have a higher barrier to resistance. Although it is still important that patients receive all of their medications as scheduled, an occasional missed dose carries a lesser risk of selecting for resistant virus because of suboptimal drug levels.[25-27]

Another myth relates to uncertainty about appropriate timing for antiretroviral therapy in HIV-positive patients. In fact, up until a few years ago, the time to start antiretroviral therapy in HIV patients was unclear. Some HIV specialists did not prescribe antiretroviral therapy until immunosuppression had significantly progressed; for example, CD4 count less than 500 cells/mm^3. Improvements in safety and tolerability of treatment options prompted reexamination of appropriate timing for antiretroviral therapy in HIV infection, leading to abundant public health and clinical data that now support starting antiretroviral therapy as early as possible in every HIV-infected patient. The HIV Prevention Trials Network 052 study demonstrated a 96% reduction in transmission between serodiscordant couples when the HIV-positive partner was virally suppressed with antiretroviral therapy.[28] This led to the 2012 US Department of Health and Human Services guidelines recommendation to start antiretroviral therapy in all patients with HIV regardless of CD4 count.[21] In 2015, the Strategic Timing of Antiretroviral Treatment (START) study showed that beginning antiretroviral therapy regardless of CD4 count led to a decrease in both AIDS-related and non-AIDS-related complications and mortality.[29] These results strengthened the Department of Health and Human Services guidelines of universal treatment to an A1 recommendation and stimulated a change in worldwide recommendations in 2015, calling for treatment of all patients with HIV, regardless of CD4 count.[30]

Regardless of guidelines for treatment, accessibility is of utmost importance for patients and remains a major issue worldwide. However, in the United States, expanded Medicaid and Medicare coverage, as well as the Ryan White Care Act, has significantly reduced barriers to obtaining antiretroviral therapy regardless of socioeconomic or immigration status.

Today, antiretroviral medications have advanced significantly in simplicity, tolerability, and safety. In the current era of widespread usage of antiretroviral therapy in acute and chronically infected patients, as well as patients needing HIV prophylaxis, front-line and acute care physicians will find it easier to care for patients who require these lifesaving medications.

REASONS TO PRESCRIBE ANTIRETROVIRAL THERAPY

Antiretroviral medication is prescribed with 3 principal indications in mind: for postexposure prophylaxis, for pre-exposure prophylaxis in patients at high risk, and for treatment of the HIV-infected patient, whether acutely or chronically infected. In Figure 1, a comparison of antiretroviral therapy by clinical indication is illustrated. Common antiretroviral therapy medications are not foreign to emergency physicians. There is no difference between postexposure prophylaxis and approved drug combinations used for treatment of HIV-infected patients. Thus, an emergency physician who has experience prescribing postexposure prophylaxis also has experience in prescribing a version of antiretroviral therapy that could be used for the HIV-infected patient. Also pre-exposure prophylaxis, a 2-drug combination, is a component of both postexposure prophylaxis and of common treatment regimens for the HIV-infected patient.

Antiretroviral therapy for the HIV-infected patient involves a 3-drug combination composed of 2 nucleoside reverse transcriptase inhibitors and a third active antiretroviral drug from 1 of 3 drug classes: an integrase inhibitor, a protease inhibitor combined with a pharmacokinetic enhancer (ritonavir or cobicistat), or a non-nucleoside reverse transcriptase inhibitor. Figure E1 (available online at http://www.annemergmed.com) more fully details antiretroviral therapy for the HIV-infected patient, including the structure of single-tablet regimens and other possible drug combinations. Single-tablet regimens are prescribed commonly and combine 3 drugs in a once-daily tablet. Figure 2 provides a reference of antiretroviral drugs by class.

Figure 3 highlights a number of drug-drug interactions that are associated with antiretroviral therapy.

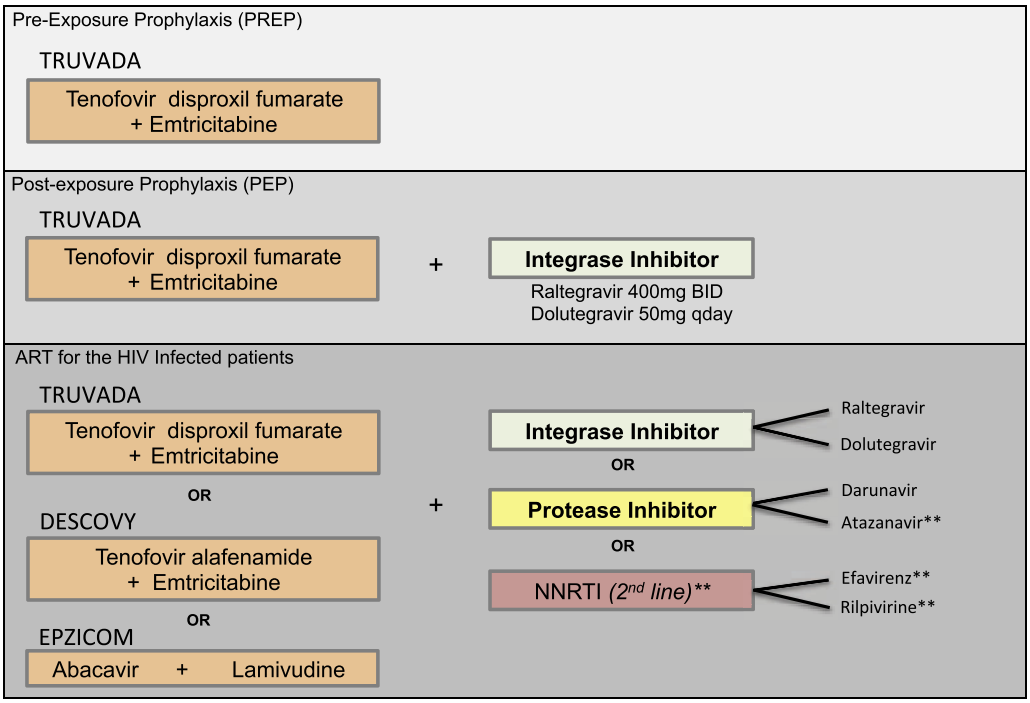

Figure 1. Comparison of antiretroviral therapy by clinical indication. *BID*, Twice daily; *ART*, antiretroviral therapy; *NNRTI*, non-nucleoside reverse transcriptase inhibitors.

It is important to have a high suspicion for drug-drug interactions when prescribing for an HIV-infected patient receiving antiretroviral therapy. The order of frequency of HIV drug class interactions with commonly prescribed medications (greatest to least interactions) is protease inhibitor class, non-nucleoside reverse transcriptase inhibitors, and then integrase inhibitors.

Figure 4 displays some of the most common class and drug-specific adverse effects of antiretroviral therapy. Overall, patients tolerate antiretroviral therapy well. They experience few adverse effects, particularly with drug combinations involving the newer classes of drugs such as the integrase inhibitors. Many of the older drugs associated with the most severe adverse effects are rarely prescribed. See Table E1 for adverse effect frequencies and Table E2 for common combination pills and single tablet regimens (available online at http://www.annemergmed.com).

Postexposure Prophylaxis

Postexposure prophylaxis is an important and well-accepted part of emergency physicians' practice. We describe postexposure prophylaxis first, not because the details of postexposure prophylaxis are novel to most emergency physicians, but because the familiar concepts outlined in this section conceptually introduce the medication regimen structure, anticipated adverse effects, and monitoring for antiretroviral drugs that are found in the regimens used in acute and chronic infection, as well as pre-exposure prophylaxis.

Emergency physicians oversee the majority of occupational, sexual, and drug exposures to HIV that prompt requests for postexposure prophylaxis. Data from New York acute care settings showed that the proportion of visits to the ED after an acute sexual or drug-related exposure to HIV has tripled during the last 10 years.[14] HIV exposure is an emergency because infection is established within 24 to 36 hours.[31-33] After an exposure, prompt initiation of postexposure prophylaxis is recommended to decrease the chance of HIV infection.[34] Postexposure prophylaxis is essentially a 1-month course of a standard 3-drug antiretroviral regimen identical to that used to treat patients with chronic HIV infection.[34]

Below is a brief guide to postexposure prophylaxis as approached in the emergency care setting (Figure 5). Online resources for postexposure prophylaxis can be found at http://nccc.ucsf.edu. Postexposure prophylaxis is not always straightforward, and expert consultation is recommended in certain situations, including delayed exposure reports greater than 72 hours, situations in which source HIV status cannot be determined, pregnancy or breastfeeding in the exposed patient, source patient with known drug-resistant HIV, or serious medical illness in the

Drug name *(Brand name)*

Integrase Inhibitors	Protease inhibitors	NRTI's	NNRTI's
Raltegravir *(Isentress)*	Atazanavir *(Reyataz)*	Abacavir *(Ziagen)*	Efavirenz *(Sustiva)*
Dolutegravir *(Tivicay)*	Darunavir *(Prezista)*	Tenofovir disoproxil fumarate *(Viread)*	Rilpivirine *(Edurant)*
Elvitegravir		Tenofovir alafenamide/ Emtricitabine *(Descovy)*	
		Emtricitabine *(Emtrica)*	
		Lamivudine *(Epivir)*	
		Zidovudine *(Retrovir)*	

Figure 2. Antiretroviral drugs by class. *NRTIs*, Nucleoside reverse transcriptase inhibitors.

exposed person.[34-36] If needed, expert consultation is available through the national postexposure prophylaxis hotline at 888-448-4911.

For occupational exposures, the first priority is to assess risk of exposure. Exposures for which administration of postexposure prophylaxis should be considered include an infectious body fluid, such as blood or serum, semen, vaginal secretions, cerebral spinal fluids, and breast milk, and would include the following fluids if visibly bloody: saliva, vomitus, urine, feces, sweat, tears, and respiratory secretions. Exposures must also involve a portal of entry, such as percutaneous, mucous membrane, or cutaneous, with nonintact skin. Next, HIV status of the source patient is considered. Postexposure prophylaxis is always recommended if the source person is HIV infected and should be strongly considered for exposures from a patient with unknown HIV status but with HIV risk factors or living in an area with a high incidence of HIV; in these circumstances, the first dose of postexposure prophylaxis should be administered immediately.[34-36]

Although postexposure prophylaxis for occupational exposures is widely practiced, its administration for people with sexual or injection-drug-related exposures to HIV is more controversial, and its true efficacy is unclear, but it is being increasingly requested and prescribed.[14,37] Appropriate candidates for postexposure prophylaxis include patients who have had unprotected sexual exposure or exposure to HIV-infected blood while injecting drugs who seek care within 72 hours (the benefit of prophylaxis after 72 hours is less clear). Additionally, if the source person has unknown status but is known to be from a group with high prevalence of HIV infection, such as transgender women or men who have sex with men, prophylaxis may be warranted.[37] Postexposure prophylaxis patients who have repeated HIV-related risk behaviors can be counseled about pre-exposure prophylaxis to provide ongoing protection against HIV.

If the decision to pursue postexposure prophylaxis is made, baseline testing should include a rapid HIV test (ideally, an HIV-1 or -2 antigen/antibody immunoassay) for both the source patient and exposed patient, as well as hepatitis B and C testing for both, and renal and hepatic function in the exposed person because tenofovir is indicated for patients with glomerular filtration rate greater than 60.[34] The first dose of postexposure prophylaxis should not be delayed while results of these tests are awaited. The value of rapid HIV testing is primarily to determine whether the source patient is HIV infected. The selected postexposure prophylaxis regimen should be fully active against HIV, so it is less necessary

Higher Risk (for drug interactions)	**Any regimen including ritonavir or cobicistat****
Medium Risk	**NNRTIs Integrase Inhibitors**
Lower risk	**NRTIs**

Check drug-drug interactions with:

Antiepileptic drugs
Statins
Anti-coagulants
Steroids
Acid reducers
Hormones
Any other drug requiring liver clearance

Please refer to the following web site for comprehensive drug interactions between ART and other medications:
http://www.hiv-druginteractions.org/
***See Appendix 1 for regimens including ritonavir or cobicistat*

Figure 3. Important adverse effects by antiretroviral class.

Integrase Inhibitors	Protease inhibitors	NRTIs	NNRTIs
Headache	GI side effects (nausea/diarrhea)	Renal failure (tenofovir alafenamide)	Liver toxicity
Insomnia	Metabolic syndrome	Hypersensitivity reaction (abacavir)	Rash
Rash	Hyperglycemia, DKA, Hyperlipidemia	Anemia (zidovudine)	Neurocognitive effects (efavirenz, rilpivirine)
		Lipodystrophy	

Fewest side effects ----------> More side effects

Figure 4. Important side effects by antiretroviral class.

to know the HIV status of the exposed person before starting postexposure prophylaxis.

Administration of the first dose of antiretroviral therapy is time sensitive and should be initiated immediately, ideally within the hour of presentation, even if baseline testing is pending. Most clinicians use a 72-hour time frame postexposure as the outer limit of opportunity. However, efficacy beyond 72 hours is unknown, and thus we recommend consultation with an HIV specialist in this setting. All exposures that merit prophylaxis now require a full 3-drug regimen, fundamentally identical to that used for many chronically infected HIV patients. The current

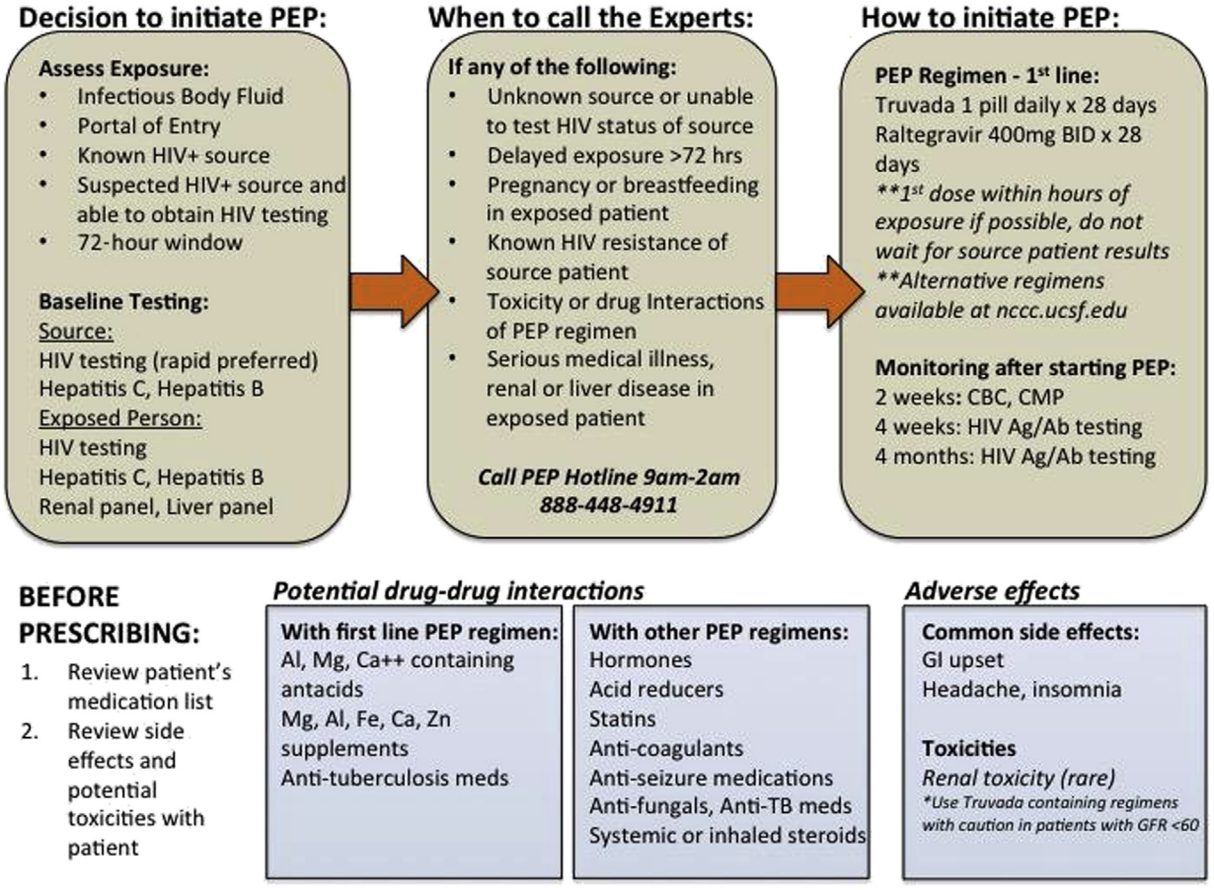

Figure 5. Example postexposure prophylaxis protocol. *GI*, Gastrointestinal.

preferred 3-drug regimen includes a once-daily combination pill of tenofovir disoproxil 300 mg+emtricitabine 200 mg (Truvada) plus an integrase inhibitor, either raltegravir 400 mg twice daily or dolutegravir 50 mg once daily. Alternatively, darunavir 800 mg+ritonavir 100 mg could replace the integrase inhibitor. Postexposure prophylaxis is given for 28 days. Patients should be counseled to follow up with a primary care provider within 2 weeks for laboratory monitoring and subsequent HIV testing.[35,36]

Adverse effects are generally mild and self-limited, and discontinuation rates for the first-line regimen are lower than those of previously used postexposure prophylaxis regimens.[38] The most common adverse effects experienced with the above first-line regimen are mild nausea, vomiting, or diarrhea and can be treated symptomatically to allow a full course of prophylaxis. Toxicity with the first-line regimen is rare but includes occasional renal toxicity from the tenofovir component of tenofovir disoproxil 300 mg+emtricitabine 200 mg, which should not be routinely used for patients with underlying kidney disease; we recommend HIV specialty consultation in this setting. Either before or immediately after initiation of postexposure prophylaxis, it is wise to review the patient's preexisting medication list to ensure that no potentially harmful interactions exist.

Pre-exposure Prophylaxis

Pre-exposure prophylaxis is one of the most exciting developments in the effort to prevent HIV infection. It is easy to administer, involves one pill daily, and, when received effectively, can prevent up to 92% of new infections; most recent data show a number needed to treat of 13 to prevent one HIV infection.[16,17] Media exposure has followed suit and awareness and uptake of pre-exposure prophylaxis has significantly increased in some high-risk groups.[18] At-risk communities have become very aware of pre-exposure prophylaxis and demand has increased significantly. Access to the health care system for many of the patients at the highest risk for acquiring and transmitting HIV infection is limited to that of urgent or emergency care settings[19]; as a result, emergency physicians will very likely experience an increase in the number of requests for pre-exposure prophylaxis in EDs. Under the correct set of circumstances, it is reasonable to initiate pre-exposure prophylaxis in the ED as long as the patient has good follow-up and the physician is familiar with the medications being prescribed. Brief counseling by informed emergency physicians could significantly increase the number of patients who successfully access pre-exposure prophylaxis, which could have a substantial public health influence in the future.

Currently, the Food and Drug Administration-approved method of pre-exposure prophylaxis includes once-daily administration of tenofovir disoproxil 300 mg+emtricitabine 200 mg, which is an oral fixed-dose combination pill that includes 2 active antiretrovirals: tenofovir disoproxil fumarate 300 mg and emtricitabine 200 mg (and is also one of the most commonly used pills as part of a 3-drug regimen in HIV infection). Pre-exposure prophylaxis efficacy varies according to risk groups. In men who have sex with men, incidence of new HIV infection is decreased by 86% to 92% when drug levels are detectable (indicating adherence of at least 4 pills per week); one recent study found that the number needed to treat was 13 patients for one year to prevent one infection.[16,17] Additionally, an actual demonstration of pre-exposure prophylaxis in men who have sex with men who were Kaiser patients revealed zero new infections in 657 patients engaging in high-risk practices who were enrolled in pre-exposure prophylaxis during a 3-year period.[39] Efficacy in women seems to be lower overall, but studies with women have been limited by adherence.[40-42] Pre-exposure prophylaxis has been shown to decrease incidence of new infections of injection drug users by 70%.[42]

Pre-exposure prophylaxis with daily oral tenofovir disoproxil 300 mg+emtricitabine 200 mg was approved by the Food and Drug Administration in 2012 and is currently recommended both nationally and internationally by the CDC and the World Health Organization for certain high-risk populations: men who have sex with men or male-to-female transgender patients with recent sexually transmitted infection or condomless anal intercourse, heterosexual men and women with condomless sexual intercourse, those with a high number of partners or recent sexually transmitted infections, commercial sex workers, HIV-serodiscordant couples, and injection drug users. In general, any patient who is asking for pre-exposure prophylaxis likely has at least some risk for HIV and should be considered for treatment.[15]

A key aspect of pre-exposure prophylaxis is that one must prove that someone is HIV negative before prescribing it. This avoids incomplete treatment of an HIV-infected individual. Before prescribing of pre-exposure prophylaxis to clinically eligible patients, they should have a documented negative HIV test result (ideally with an HIV-1 or -2 antigen/antibody immunoassay) within 3 days of initiation and no signs or symptoms of acute HIV infection. For patients with negative or indeterminate HIV test results and recent transmission risk behavior or signs or symptoms of acute HIV infection, send an HIV ribonucleic acid (RNA) viral load test by polymerase chain reaction to rule out acute HIV infection.

Baseline renal and liver function test results should be normal, pregnancy test result should be negative, and patients should be tested and treated for other sexually transmitted infections because the presence of a sexually transmitted infection can increase HIV transmission by up to 5 times per exposure. Documentation of hepatitis B infection or hepatitis B vaccination status is also important. Tenofovir disoproxil 300 mg+emtricitabine 200 mg is active against hepatitis B, and discontinuation or intermittent hepatitis B virus treatment can lead to serious hepatic consequences because of reactivation of the virus after its suppression from the tenofovir therapy. Consider referral to a liver specialist for all patients with hepatitis B who request pre-exposure prophylaxis. The long-term safety of pre-exposure prophylaxis to a fetus has not yet been determined; thus, the pregnant patient seeking such prophylaxis should be referred to an HIV specialist.

After a well-structured plan for follow-up is in place, the prescription of pre-exposure prophylaxis includes daily oral doses of tenofovir disoproxil 300 mg+emtricitabine 200 mg, given initially in a 1-month supply and never more than a 3-month supply. Patients receiving pre-exposure prophylaxis need follow-up visits every 3 months for serial testing for HIV, sexually transmitted infection, pregnancy, and renal and hepatic function, as well as medication adherence counseling. If pre-exposure prophylaxis is used, patients must receive pre-exposure prophylaxis daily, not merely as needed.[15]

Acute HIV Infection

Acute HIV infection is a medical and public health emergency that is now often recognized in the ED and merits immediate treatment with antiretroviral therapy.[43] Previously, given the nonspecific nature of acute HIV infection and older first-line HIV testing that would not routinely detect HIV infection at very early points, emergency physicians would rarely knowingly encounter acute HIV infection, and, even if it was encountered, treatment was considered to be supportive. Now, with recent scaling up of efforts for routine HIV testing in EDs, and the development of the HIV-1 and -2 antigen/antibody immunoassay tests that detect acute and chronic infections, increasing numbers of patients with acute infections are identified in the ED.[11] Immediate treatment of acute HIV infection with antiretroviral therapy results in public health benefits that are vital to ending the HIV epidemic and important lifelong clinical benefit for the patient.

Identification of patients with acute HIV infection is imperative to facilitate immediate treatment. Patients with acute HIV infection present differently from those with chronic HIV infection. Although patients with chronic HIV infection are often asymptomatic, 40% to 90% of those with acute HIV infection develop acute symptoms.[21] Symptomatic patients with acute HIV may have a mono- or flulike illness[44] between 1 and 6 weeks after exposure. Small studies revealed acute HIV infection in 1% of at-risk patients presenting to the ED with symptoms of a flu- or monolike illness.[45,46] Most frequent complaints include but are not limited to fever, lymphadenopathy, rash, headache, fatigue, pharyngitis, diarrhea, myalgias, and arthralgias.[21,47] This acute, highly infectious period occurs before formation of antibodies against the virus. Previous HIV antibody-only tests such as enzyme-linked immunosorbent assay and Western blot frequently missed acute infection; however, newer antigen/antibody immunoassay testing for HIV can detect both acute and chronic HIV as early as 10 days after initial exposure.[48]

Despite the improved ability to identify acute HIV infection with the antigen/antibody immunoassay test, in patients with high suspicion for acute HIV for whom the test comes back negative or indeterminate, an HIV-1 viral load test by RNA may pick up a small subset of patients whose viral load is positive anywhere from 1 to 3 days before the antigen/antibody immunoassay results are returned. Additionally, because not all medical centers necessarily have antigen/antibody immunoassay testing available, HIV-1 viral load testing by RNA may be used for patients for whom acute HIV treatment is being considered but antigen/antibody immunoassay testing is not available.

Immediate treatment in acute infection has critical clinical benefits compared with treatment delaying the start of antiretroviral therapy during chronic infection. As the viral load increases during the acute infection period, the virus seeds viral reservoirs, making the virus present in various hidden parts of the immune system, such as cerebrospinal fluid and lymphoid tissue, that make it nearly impossible to eradicate once seeded. This causes chronic immune activation and dysfunction that lead to increased cardiovascular risk and mortality even in the absence of immunosuppression or AIDS.[49-51] Very early treatment of acute HIV may limit the size of these viral reservoirs,[52,53] which restores normal immune responses for the patient, likely decreasing the long-term risks.[53]

These viral reservoirs established in the first few weeks to months after exposure to HIV render it incurable despite antiretroviral therapy and effectively determine the HIV viral burden in the body.[53-55] The size of these viral reservoirs affects how quickly the virus rebounds after medications are stopped and how high the baseline viral load "set point" is in untreated patients; people with bigger viral reservoirs usually have higher viral loads when not

receiving treatment, and their viral loads will increase very rapidly on stopping antiretroviral therapy. Multiple studies have found that treating with antiretroviral medications very early in HIV infection decreases the size of these viral reservoirs and results in lower viral loads when patients cease treatment, as well as viral levels that more slowly increase after patients stop their medications.[56] Some patients who were treated in early infection have maintained temporary control of their HIV.[57] Despite stopping antiretroviral therapy, their bodies were able to naturally keep their virus at undetectable levels for up to 2 years.[57] The concept of treatment in acute and early HIV infection is now a major part of ongoing HIV cure research.

Another critical argument for immediate treatment of HIV infection with antiretroviral therapy is its effect on public health. In the first 6 weeks after exposure, levels of virus in the blood exceed 1 million copies/mL. As a result, transmission of HIV is significantly increased in acute HIV; an estimated 50% of new HIV infections are acquired during acute HIV infection.[58] Immediate administration of antiretroviral therapy in patients who present during acute infection begins to decrease the viral load and significantly decreases the amount of time it takes to reduce HIV virus to undetectable levels,[59] thereby decreasing the risk of transmission during acute infection.

Immediate treatment of acute HIV identified in the ED under the supervision of an HIV or infectious disease specialist is safe and feasible, as demonstrated by recent data from our study conducted in a large urban ED, as well as that of the Rapid ART Program Initiative for HIV Diagnoses (RAPID) program in San Francisco.[43,59] Antiretroviral therapy in acute infection is identical to that used in chronic infection, which consists of a 3-drug regimen with a nucleoside reverse transcriptase inhibitor backbone plus either a protease inhibitor or integrase inhibitor (see Figure E1, available online at http://www.annemergmed.com).[21] If treatment of acute HIV in the ED is being considered, administration of antiretroviral therapy should be conducted in consultation with an HIV or infectious disease specialist, with appropriate patient counseling, baseline laboratory tests (HIV RNA viral load, CD4 count, HIV genotype testing, and baseline chemistry panel and CBC count with differential), as well as a coordinated plan for close follow-up.

The combination of ongoing efforts to increase ED-based HIV testing, increasingly recognized critical public health and clinical benefits of treating acute HIV infection, and feasibility of immediate treatment of acute HIV infection promises a future that involves widespread implementation of immediate treatment of acute HIV infection, which will involve the front-line care of emergency physicians.

Antiretroviral Therapy Refills in the ED

Emergency physicians may encounter requests for antiretroviral medication refills from chronically infected HIV patients. In the case of a patient with well-controlled HIV, it is reasonable for emergency physicians to refill medications. For patients whose disease is not well controlled and who are out of care, the emergency physician should consult an HIV specialist about the appropriateness of antiretroviral refills and assist the patient with follow-up care.

For the HIV patient with established adherence to antiretroviral therapy who is requesting a routine refill, emergency physicians may safely refill antiretrovirals without consultation. The physician should review the chart to confirm the patient's engagement in care. Routine HIV care visits within the last 3 to 6 months and an undetectable HIV RNA viral load within the previous 6 months support patient reports of adherence. After confirmation of normal renal and liver function, a refill of a 30-day supply of the patient's current antiretroviral regimen is appropriate, along with instructions for follow-up care within the next 2 weeks.

The more common scenario in the ED involves patients who have ceased HIV care and are either nonadherent or intermittently adherent to antiretroviral therapy. In these instances, consultation with an HIV or infectious disease specialist to establish follow-up care in an HIV clinic is crucial. Once that has been addressed, it may be appropriate to prescribe antiretroviral therapy, but in consultation with an HIV specialist. This may require involvement of interdisciplinary support, including social work, to address barriers to care. Many patients marginally engaged in care may be unsure of their complete medication regimen, and prescription of a partial regimen or the incorrect regimen could promote drug resistance and lead to treatment failure.

CONCLUSION

The role of emergency physicians in HIV care has been limited for decades. However, with advances in HIV prevention, detection, and treatment, there is an expanded opportunity and role of the emergency physician in the care of HIV patients. Our goal in this review is to arm the emergency physician with the tools needed to care for these patients so that they can embrace this expansion to their scope of practice. Postexposure prophylaxis has long been within the scope of emergency medicine. This review

demonstrates how antiretroviral therapy for pre-exposure prophylaxis and acute HIV infection is a natural extension of postexposure prophylaxis. Pharmaceutical advances and improvement in diagnostic testing have broken down the barriers keeping emergency physicians from adequately treating the true emergency of HIV exposure and acute infection. Antiretroviral therapy regimens have become simplified and the drugs themselves carry less concern for dangerous adverse effects and invoking resistance. Advances in HIV detection and treatment have led to new opportunities for patient care in the acute care setting and a potential for emergency physicians to have a greater role in quelling the HIV epidemic.

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REFERENCES

1. Skarbinski J, Rosenberg E, Paz-Bailey G, et al. Human immunodeficiency virus transmission at each step of the care continuum in the United States. *JAMA Intern Med*. 2015;175:588-596.
2. National Center for Health Statistics. *Health, United States, 2014: With Special Feature on Adults Aged 55-64*. Hyattsville, MD; United States Government Printing Office: 2015. Available at: https://www.cdc.gov/nchs/data/hus/hus14.pdf. Accessed December 27, 2016.
3. Mohareb AM, Rothman RE, Hsieh YH. Emergency department (ED) utilization by HIV-infected ED patients in the United States in 2009 and 2010—a national estimation. *HIV Med*. 2013;14:605-613.
4. Centers for Disease Control and Prevention. Vital signs: HIV prevention through care and treatment-United States. *Morb Mortal Wkly Rep*. 2011;60:1618-1623.
5. Kelen GD, Hexter DA, Hansen KN, et al. Feasibility of an emergency department–based, risk-targeted voluntary HIV screening program. *Ann Emerg Med*. 1996;27:687-692.
6. Rothman RE, Ketlogetswe KS, Dolan T, et al. Preventive care in the emergency department: should emergency departments conduct routine HIV screening? a systematic review. *Acad Emerg Med*. 2003;10:278-285.
7. Coil CJ, Haukoos JS, Witt MD, et al. Evaluation of an emergency department referral system for outpatient HIV testing. *J Acquir Immune Defic Syndr*. 2004;35:52-55.
8. Bozzette SA, Berry SH, Duan N, et al. The care of HIV-infected adults in the United States. HIV Cost and Services Utilization Study Consortium. *N Engl J Med*. 1998;339:1897-1904.
9. Sullivan PS, Lyons MS, Czarnogorski M. Routine screening for HIV infection in medical care settings: a decade of progress and next opportunities. *Public Health Rep*. 2016;131(Suppl 1):1-4.
10. Centers for Disease Control and Prevention. Laboratory testing for the diagnosis of HIV infection: updated recommendations. 2014. Available at: http://stacks.cdc.gov/view/cdc/23447. Accessed December 16, 2016.
11. Jacobson KR, Glick N, Giordano T, et al. Acute HIV discovered during routine screening in six urban emergency department. Paper presented at: International AIDS Society; July 18-22, 2016; Durban, South Africa.
12. Hsieh Y-H, Kelen GD, Laeyendecker O, et al. HIV care continuum for HIV-infected emergency department patients in an inner-city academic emergency department. *Ann Emerg Med*. 2015;66:69-78.
13. Rothman R, Lyons MS, Branson B, et al. HIV screening in the emergency department. *Ann Emerg Med*. 2011;58(Suppl):S1-176.
14. Ngai S, Edelstein Z, Myers J, et al. Tracking HIV post-exposure prophylaxis using syndromic surveillance in NYC emergency departments. *Online J Public Health Informatics*. 2015;7:e89.
15. US Preventive Services Task Force. Preexposure prophyaxis for the prevention of HIV infection in the United States—2014: a clinical practice guideline. 2014. Available at: http://www.cdc.gov/hiv/pdf/prepguidelines2014.pdf. Accessed May 13, 2016.
16. Grant RM, Lama JR, Anderson PL, et al. Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. *N Engl J Med*. 2010;363:2587-2599.
17. McCormack S, Dunn DT, Desai M, et al. Pre-exposure Prophylaxis to Prevent the Acquisition of HIV-1 Infection (PROUD): effectiveness results from the pilot phase of a pragmatic open-label randomised trial. *Lancet*. 2016;387:53-60.
18. Hood JE, Buskin SE, Dombrowski JC, et al. Dramatic increase in preexposure prophylaxis use among MSM in Washington State. *AIDS*. 2016;30:515-519.
19. Underhill K, Operario D, Skeer M, et al. Packaging PrEP to prevent HIV: an integrated framework to plan for pre-exposure prophylaxis implementation in clinical practice. *J Acquir Immune Defic Syndr*. 2010;55:8-13.
20. Julg B, Bogner JR. Atripla—HIV therapy in one pill. *Ther Clin Risk Management*. 2008;4:573-577.
21. Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Department of Health and Human Services. 2016. Available at https://aidsinfo.nih.gov/contentfiles/lvguidelines/adultandadolescentgl.pdf. Accessed December 16, 2016.
22. Heath KV, Singer J, O'Shaughnessy MV, et al. Intentional nonadherence due to adverse symptoms associated with antiretroviral therapy. *J Acquir Immune Defic Syndr*. 2002;31:211-217.
23. Kim MJ, Kim S-W, Chang H-H, et al. Comparison of antiretroviral regimens: adverse effects and tolerability failure that cause regimen switching. *Infect Chemother*. 2015;47:231-238.
24. World Health Organization. WHO HIV drug resistance report. 2012. Available at: http://apps.who.int/iris/bitstream/10665/75183/1/9789241503938_eng.pdf. Accessed May 13, 2016.
25. Scherrer A, Böni J, Yerly S, et al. Long-lasting protection of activity of nucleoside reverse transcriptase inhibitors and protease inhibitors (PIs) by boosted PI containing regimens. *PLoS One*. 2012;7:e50307.

26. Gupta R, Hill A, Sawyer AW, et al. Emergence of drug resistance in HIV type 1–infected patients after receipt of first-line highly active antiretroviral therapy: a systematic review of clinical trials. *Clin Infect Dis*. 2008;47:712-722.
27. Gordon L, Gharibian D, Chong K, et al. Comparison of HIV virologid failure rates between patients with variable adherence to three antiretroviral regimen types. *AIDS Patient Care STDS*. 2015;29:384-388.
28. Rodger AJ, Cambiano V, Bruun T, et al. Sexual activity without condoms and risk of HIV transmission in serodifferent couples when the HIV-positive partner is using suppressive antiretroviral therapy. *JAMA*. 2016;316:171-181.
29. Lundgren J, Babiker A, Gordin F, et al. Initiation of antiretroviral therapy in early asymptomatic HIV infection. *N Engl J Med*. 2015;373:795-807.
30. World Health Organization. Guideline on when to start antiretroviral therapy and on pre-exposure prophylaxis for HIV. 2015. Available at: http://aidsinfo.nih.gov/contentfiles/lvguidelines/AdultandAdolescentGL.pdf. Accessed May 13, 2016.
31. Tsai CC, Follis KE, Sabo A, et al. Prevention of SIV infection in macaques by (R)-9-(2-phosphonylmethoxypropyl)adenine. *Science*. 1995;270:1197-1199.
32. Otten RA, Smith DK, Adams DR, et al. Efficacy of postexposure prophylaxis after intravaginal exposure of pig-tailed macaques to a human-derived retrovirus (human immunodeficiency virus type 2). *J Virol*. 2000;74:9771-9775.
33. Wade NA, Birkhead GS, Warren BL, et al. Abbreviated regimens of zidovudine prophylaxis and perinatal transmission of the human immunodeficiency virus. *N Engl J Med*. 1998;339:1409-1414.
34. Kuhar DT, Henderson DK, Struble KA, et al. Updated US Public Health Service guidelines for the management of occupational exposures to human immunodeficiency virus and recommendations for postexposure prophylaxis. *Infect Control Hosp Epidemiol*. 2013;34:875-892.
35. Thomas R, Galanakis C, Vézina S, et al. Adherence to post-exposure prophylaxis (PEP) and incidence of HIV seroconversion in a major North American cohort. *PLoS One*. 2015;10:e0142534.
36. Bock I, Felsen U, Catalano M, et al. Tolerability, adherence and completion of new occupational post-exposure prophylaxis regimen (tenofovir+emtricitabine and raltegravir). Paper presented at: ID Week 2014, Philadelphia, PA, October 8-12, 2014.
37. Centers for Disease Control and Prevention. Updated guidelines for antiretroviral postexposure prophylaxis after sexual, injection-drug use, or other nonoccupational exposure to HIV—United States, 2016. *Morb Mortal Wkly Rep*. 2016;65:458.
38. Ford N, Kranzer K, Hilderbrand K, et al. Early initiation of antiretroviral therapy and associated reduction in mortality, morbidity and defaulting in a nurse-managed, community cohort in Lesotho. *AIDS*. 2010;24:2645-2650.
39. Volk JE, Marcus JL, Phengrasamy T, et al. No new HIV infections with increasing use of HIV preexposure prophylaxis in a clinical practice setting. *Clin Infect Dis*. 2015;61:1601-1603.
40. Baeten JM, Donnell D, Ndase P, et al. Antiretroviral prophylaxis for HIV prevention in heterosexual men and women. *N Engl J Med*. 2012;367:399-410.
41. Van Damme L, Corneli A, Ahmed K, et al. Preexposure prophylaxis for HIV infection among African women. *N Engl J Med*. 2012;367:411-422.
42. Choopanya K, Martin M, Suntharasamai P, et al. Antiretroviral prophylaxis for HIV infection in injecting drug users in Bangkok, Thailand (the Bangkok Tenofovir Study): a randomised, double-blind, placebo-controlled phase 3 trial. *Lancet*. 2013;381:2083-2090.
43. Jacobson KR, Arora S, Walsh KB, et al. High feasibility of empiric HIV treatment for patients with suspected acute HIV in an emergency department. *J Acquir Immune Defic Syndr*. 2016;72:242-245.
44. Schacker T. Clinical and epidemiologic features of primary HIV infection [published correction appears in *Ann Intern Med*. 1997;126:174]. *Ann Intern Med*. 1996;126:257-264.
45. Pincus JM, Crosby SS, Losina E, et al. Acute human immunodeficiency virus infection in patients presenting to an urban urgent care center. *Clin Infect Dis*. 2003;37:1699-1704.
46. Rosenberg ES, Caliendo AM, Walker BD. Acute HIV infection among patients tested for mononucleosis. *N Engl J Med*. 1999;340:969.
47. Daar ES, Pilcher CD, Hecht FM. Clinical presentation and diagnosis of primary HIV-1 infection. *Curr Opin HIV AIDS*. 2008;3:10-15.
48. Branson BM. The future of HIV testing. *Immune Defic Syndr*. 2010;55(suppl 2):S102-S105.
49. Kaplan RC, Sinclair E, Landay AL, et al. T cell activation and senescence predict subclinical carotid artery disease in HIV-infected women. *J Infect Dis*. 2011;203:452-463.
50. Kaplan RC, Sinclair E, Landay AL, et al. T cell activation predicts carotid artery stiffness among HIV-infected women. *Atherosclerosis*. 2011;217:207-213.
51. Hunt PW, Cao HL, Muzoora C, et al. Impact of CD8+ T-cell activation on CD4+ T-cell recovery and mortality in HIV-infected Ugandans initiating antiretroviral therapy. *AIDS*. 2011;25:2123-2131.
52. Eriksson S, Graf EH, Dahl V, et al. Comparative analysis of measures of viral reservoirs in HIV-1 eradication studies. *PLoS Pathogens*. 2013;9:e1003174.
53. Jain V, Hartogensis W, Bacchetti P, et al. Antiretroviral therapy initiated within 6 months of HIV infection is associated with lower T-cell activation and smaller HIV reservoir size. *J Infect Dis*. 2013;208:1202-1211.
54. Katlama C, Deeks SG, Autran B, et al. Barriers to a cure for HIV: new ways to target and eradicate HIV-1 reservoirs. *Lancet*. 2013;381:2109-2117.
55. Kulpa DA, Chomont N. HIV persistence in the setting of antiretroviral therapy: when, where and how does HIV hide? *J Virus Eradication*. 2015;1:59-66.
56. Li JZ, Etemad B, Ahmed H. The size of the expressed HIV reservoir predicts timing of viral rebound after treatment interruption. *AIDS*. 2016;30:343-353.
57. Sáez-Cirión A, Bacchus C, Hocqueloux L, et al. Post-treatment HIV-1 controllers with a long-term virological remission after the interruption of early initiated antiretroviral therapy ANRS VISCONTI Study. *PLoS Pathogens*. 2013;9:e1003211.
58. Brenner BG, Roger M, Routy J-P, et al. High rates of forward transmission events after acute/early HIV-1 infection. *J Infect Dis*. 2007;195:951-959.
59. Pilcher CD, Ospina-Norvell C, Dasgupta A, et al. The effect of same-day observed initiation of antiretroviral therapy on HIV viral load and treatment outcomes in a US public health setting. *J Acquir Immune Defic Syndr*. 2017;74:44-51.

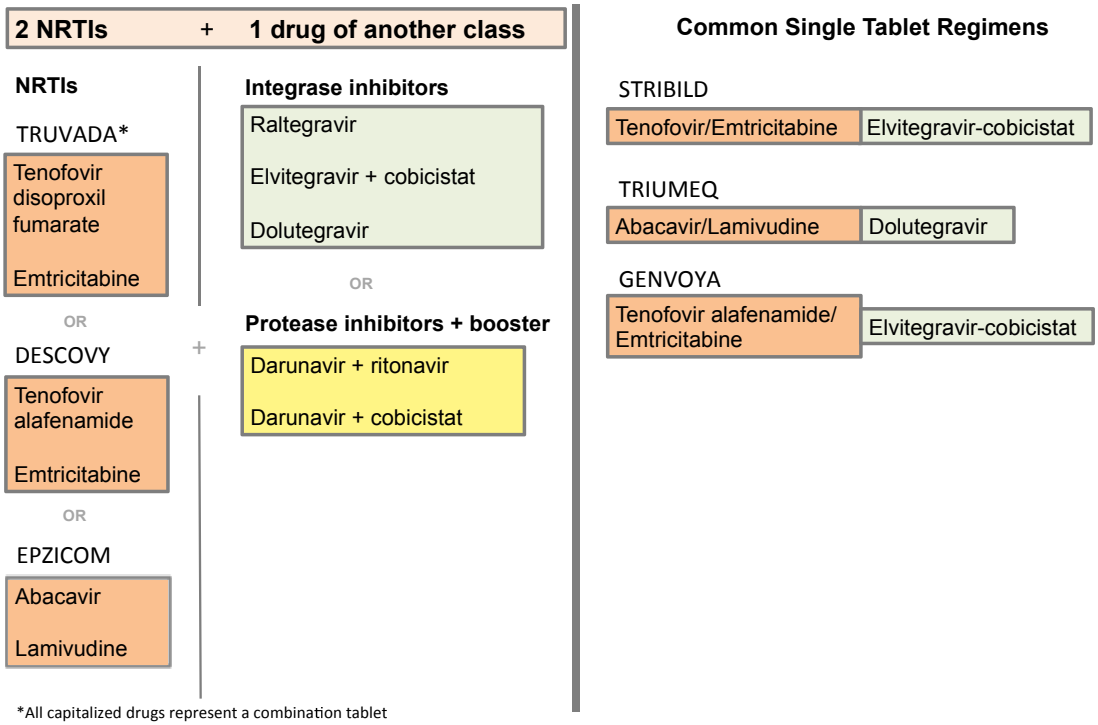

Figure E1. Department of Health and Human Services guidelines: recommended antiretroviral therapy for HIV infection: a 3-drug combination.

Table E1. Available antiretroviral therapy.

Drug Name	Brand Name	Adverse Effects, %	Dose	
NRTIs				
Abacavir	Ziagen	Potentially fatal hypersensitivity reaction (8%); do not rechallenge; CV risk	600 mg qday or 300 mg BID (either dose OK)	Must be HLA-B5701 negative because of potentially fatal HSRs
Tenofovir disoproxil fumarate	Viread	Renal failure (7%), osteomalacia (28%)	300 mg qday	Use in CrCL >60
Tenofovir alafenamide/ emtricitabine	Descovy	Renal failure Osteomalacia	TAF 25 mg/ETC 200 mg	Use in CrCl ≥30
Emtricitabine	Emtrica	Hyperpigmentation/skin discoloration (2%–4%)	200 mg qday	
Lamivudine	Epivir		300 mg qday	
Zidovudine	Retrovir	Macrocytic anemia (1%), BM suppression (2%) Lactic acidosis Hyperlipidemia/glycemia	300 mg BID	
NNRTIs				
Efavirenz	Sustiva	Rash, SJS, hepatotoxicity, hyperlipidemia Neurocognitive (2%–9%) Teratogenic; avoid first trimester (unless previously prescribed)	600 mg qday	Avoid in pts with psych comorbidity Suicide risk
Rilpivirine	Edurant	Rash (3%), SJS, hepatotoxicity (18%) Neurocognitive	25 mg qday	Take with food; cannot be taken with PPIs
PIs				
Atazanavir	Reyataz	Prolonged PR interval, indirect hyperbili (35%–49%), Hepatotoxicity, hyperlipidemia/glycemia nephro/cholelithiasis	300 mg qday+100 mg ritonavir	Take with food
Darunavir	Prezista	Sulfa drug, rash, SJS Diabetes (2%), hepatotoxicity, Hyperlipidemia/glycemia triglyceridemia (3%–10%)	800 mg qday+100 mg ritonavir (600 mg BID if preexisting resistance to other PIs)	Take with food
Integrase inhibitors				
Raltegravir	Isentress	HSR, CPK elevation, fever, nausea (3%), headache (2%–9%), depression, SI	400 mg BID	Used in PEP
Dolutegravir	Tivicay	HSR, insomnia (2%), headache (1%–7%) Depression, SI	50 mg qday	Used in PEP
Elvitegravir		Nausea (4%), diarrhea (7%) Depression, SI	Found only in combination tablets Stribild and Genvoya	Used in PEP

HSR, Hypersensitivity reaction; *CV*, cardiovascular; *BM*, bone marrow; *SJS*, Stevens-Johnson syndrome; *PPI*, proton pump inhibitor; PI, *protease inhibitor*; CPK, *creatine phosphokinase*.

Table E2. Common combination pills and single-tablet regimens.

Drug Name	Combination	Dosing	Considerations
Truvada*	Tenofovir disoproxil fumarate (300 mg)/emtricitabine (200 mg)	1 tablet qday	Used as PREP
Epzicom*	Abacavir (600 mg)/lamivudine (300 mg)	1 tablet qday	Used as NRTI backbone
Stribild†	Elvitegravir (150 mg)/cobicistat (150 mg)/emtricitabine (200 mg)/tenofovir disoproxil fumarate (300 mg)	1 tablet qday	Take with food, not recommended in patients with baseline CrCl <70
Triumeq†	Dolutegravir (50 mg)/abavavir (600 mg)/lamivudine (300 mg)	1 tablet qday	Must be HLA-B5701 negative
Genvoya†	Elvitegravir (150 mg)/cobicistat (150 mg)/emtricitabine (200 mg)/tenofovir alafenamide (10 mg)	1 tablet qday	Take with food
Atripla†	Efavirenz (600 mg)/tenofovir disoproxil fumarate (300 mg)/emtricitabine (200 mg)	1 tablet qday at or before bedtime	Because of neurocognitive effects, taken at night. No longer recommended as first-line regimen.
Complera†	Rilpivirine (25 mg)/tenofovir disoproxil fumarate (300 mg)/emtricitabine (200 mg)	1 tablet qday	Take with food
Odefsey†	Rilpivirine (25 mg)/tenofovir alafenamide (25 mg)/ emtricitabine (200 mg)	1 tablet qday	Take with food

*Combination pill: Combines 2 pills into 1 drug. Not a complete regimen and still needs to be received with other drugs.
†Single-tablet regimen: Combines multiple drugs into one pill, received once daily. Constitutes a complete regimen.