

# Complete Care of the HIV-Infected Outpatient: Antiretroviral Advances and Chronic Care Objectives

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**Activity Type: Knowledge-based**

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**Upon successful completion of this activity, the pharmacist should be able to:**

1. Describe oral rapid diagnostic testing options and methods for establishing point-of-care service.
2. Use a patient's CD4 count or viral load to assess treatment effectiveness or need for treatment revision.
3. Identify community interventions that can increase adherence to combination pill regimens.
4. Select an appropriate fixed-dose or combination regimen for outpatients with new or chronic HIV infection.
5. Initiate strategies to prevent disease complications and chronic concerns in outpatients with HIV infection.

**Upon successful completion of this activity, the pharmacy technician should be able to:**

1. Describe oral rapid diagnostic testing options and methods for establishing point-of-care service.
2. Identify community interventions that can increase adherence to combination pill regimens.
3. Identify OTC medications that may indicate a patient living with HIV infection is experiencing adverse effects from prescription drugs and alert the pharmacist.

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## INTRODUCTION

In the 21st century, human immunodeficiency virus (HIV) and the resulting acquired immunodeficiency syndrome (AIDS) together have become a chronic, treatable condition, instead of an acute, rapidly progressive attack to the immune system that it once was. Because of this transition to longer care, pharmacists must educate themselves about HIV to provide long-term disease management akin to metabolic or pulmonary disorders. Additionally, pharmacists can establish point-of-care (POC) rapid-testing services for diagnosis in the community. These efforts can improve the quality of life for patients with HIV by providing earlier care that reduces damaging secondary complications of retroviral infection. POC screenings in the outpatient pharmacy setting also have the ability to directly reduce infection incidence and treatable disease burden. Barriers to HIV care in the community pharmacy exist—revolving around staff knowledge base and site-specific challenges—but are not insurmountable.

## HIV DISEASE STATE OVERVIEW

Community pharmacists rarely focus on HIV training, but their role is increasingly important as more patients with HIV live longer and receive antiretroviral treatment for decades, often while receiving overlapping treatments for other chronic diseases, such as hypertension or high cholesterol. Pharmacists knowledgeable about the development and progression of HIV can more ably answer patient questions, improve adherence to regimens, and identify drug interactions across a patient's lifespan. For detailed HIV training, the National AIDS Education and Training Center recommends to clinicians the training guidebook, HRSA Guide for HIV/AIDS Clinical Care (available at <http://aidsetc.org/resource/hrsa-guide-hiv-aids-clinical-care>), that includes considerations especially relevant to community pharmacists (such as common drug interactions).

## HIV HISTORY

HIV is an old virus: its original form as a spillover from simian infection (SIV) has been tracked to as early as 1908, and the first people infected with the human-like version lived in Kirshasa, the Congo, in 1959. Two infectious versions, HIV-1 and HIV-2, originated in Africa, but HIV-1 has spread across the globe and become a pandemic disease.

The opportunistic infections indicative of AIDS were first described in the United States as sequelae of this immune deficiency syndrome in 1981, when the rare diseases Kaposi's sarcoma and *Pneumocystis carinii* pneumonia were identified in numerous young gay men in New York and Los Angeles. During the next few years, AIDS occurrences became increasingly documented, and the viral cause of AIDS was eventually isolated as HIV.

HIV is a retrovirus that, like influenza and other common

viruses, lacks its own cellular membrane and requires a host cell to live. Unlike traditional viruses, though, which are overpowered by our body's healthy immune system, HIV attacks the immune system itself. Characteristic of a retrovirus, HIV uses a host cell to synthesize viral DNA from RNA and to incorporate into the immune system CD4 T cells—one type of T cell needed to protect the body during a viral attack. As HIV uses these specialized immune cells, the cells are killed; thus, AIDS becomes inevitable without treatment.

Global treatment and public health initiatives continue to evolve in the 21st century to minimize viral morbidity and AIDS-related illnesses and mortality. Primary efforts are aimed at stopping HIV spread so as to delay damage to entire organ systems through disease or tumor development.

## VIRAL LIFE CYCLE

HIV's stronghold on the human immune system after entering the bloodstream relies on a multimodal approach to CD4+ T cell entry, viral replication, and spread across the host cells. The viral life cycle is efficient, requiring only one host cell to initiate a rapid chain reaction of immune cell infiltration.

The extensive life cycle process begins when HIV first binds to the outside of a CD4+ T cell at two receptors: the CD4 receptor and a coreceptor, either CXCR4 or CCR5. As the bound virus fuses with the host cell, viral RNA enters the cell, and HIV reverse transcriptase enzymes convert the RNA into HIV DNA. The new viral DNA inside the host is then copied, or transcribed, by using viral enzymes and the host cell DNA in the first step of HIV replication. The resultant HIV proteins made from these genetic building blocks are cleaved by the enzyme protease, and each smaller protein develops into its own separate viral particle within the host cell. After cleavage is complete, the particles, together with glycoproteins of the CD4+ T cell outer envelope, break off from the host cell and bind to new CD4+ T cells to begin the infectious replication process again several-fold.

Because the virus incorporates neatly into each step of the immune cell replication process, its eradication is nearly impossible. Visit [www.hhmi.org/biointeractive/hiv-life-cycle](http://www.hhmi.org/biointeractive/hiv-life-cycle) to view an animation of HIV life cycle. Without treatment to minimize the number of infected cells and reduce viral replication, people infected with HIV experience immune system collapse and the onset of AIDS.

## TRANSMISSION METHODS

Although HIV quickly replicates once it enters a host, the virus alone is quite fragile and cannot live outside of a host body. Transmission, therefore, is more limited for HIV than for common viruses like influenza. Unlike the common cold or flu, HIV cannot be transmitted through air particles or

intact skin. Instead, it requires contact directly with the bloodstream or in mucous membranes.

Once HIV is in a person's cellular alphabet, it can be transmitted to anyone through shared bodily fluid, particularly blood, semen, vaginal fluid and breast milk. Mucous membranes are one of the most frequent places to transfer the virus. Vaginal and oral tissues are two sites of thin mucous membrane where HIV can cross from an infected host into a new host. Oral transmission comes from contact with the bodily fluids listed above; it is believed that transmission from saliva alone is extremely rare or nonexistent. Contact with HIV-infected blood—either directly via an open wound or indirectly through contact with contaminated objects—is another primary transmission method. Because forms of transmission are so specific, the high risk populations are specialized.

### **RISK DEMOGRAPHICS AND EPIDEMIOLOGY**

The highest-risk populations for HIV infection include people who interact with bodily fluids more often than the general population. A dominant risk group includes injection drug users (IDUs) who share needles and easily transmit the virus among bloodstreams directly. Men who have sex with men (MSM) comprise one of the highest risk categories for HIV transmission; those who have multiple partners with unknown HIV statuses are most at risk. Similar risk groups are those who have sex for money or drugs and heterosexual people with multiple partners whose statuses are unknown. Secondary populations include newborns born to mothers with HIV who are infected perinatally during delivery, and health care professionals who work directly with blood and objects in contact with these fluids (such as needles, gloves, and swabs). For this latter population, clinical procedures to prevent contact between the professional and an infected blood source, such as double-gloving examination gloves, are essential.

HIV affects all genders, ethnicities, socioeconomic groups, and ages. However, blacks are affected more than any other race or ethnicity. At approximately 12 percent of the U.S. population in 2009, 44 percent of people living with HIV infection were black. People who identify as Hispanic or Latino account for 21 percent of the population living with HIV infection.

Although the progression to AIDS has been slowed by attempts at antiretroviral treatments, HIV remains a global epidemic and long-term concern. In 2009, approximately 34,000 people with HIV developed AIDS, and more than 14,000 deaths occurred that year in people with HIV/AIDS diagnoses.

The population living with HIV in the United States likewise remains high in number. In 2008, the estimated population of HIV-infected individuals age 13 years or older in the United States was nearly 1.2 million; and 20 percent of these

individuals remained undiagnosed. Rates of new infections have remained steady for the past 20 years despite public health communication about transmission and prevention. In 2013, the Centers for Disease Control and Prevention estimated the incidence of new infections in the United States at 50,000 each year.

Because infection rates remain high and viral spread is broad, testing for HIV infection is recommended for everyone, not just for high-risk patients. The Emory University AIDSvU.org webpage: "Take the Test, Take Control" allows anyone to view HIV rates where they live, find testing sites and observe the continuum of diagnoses and care. Late diagnoses, in patients who remained unaware of their status for a long time, open the door for increased numbers of infected people. In fact, up to 70 percent of new infections in the United States each year are attributed to transmission from patients who do not know that they have HIV. As more people "know their status," as recommended by the CDC pilot program of the same name, fewer people will transmit the virus unknowingly. To support the CDC initiative and reduce the burden of HIV across the United States, pharmacists now can offer established point-of-care diagnostic services with oral-swab rapid tests.

### **MEASURING THE DISEASE FOR DIAGNOSIS AND TREATMENT EVALUATION**

#### **What to Test**

Because HIV is initially asymptomatic with insidious onset of flu-like symptoms, diagnosis is inherently difficult and relies on laboratory measures instead of clinical evaluation. Two measures are essential for HIV diagnosis and evaluation: the CD4+ T cell count and the HIV RNA level, or viral load.

The CD4 count is a measure of the amount of these immune system T cells in 1 cubic millimeter of blood, and it is a direct reflection of immune health. The CD4 count decreases as HIV spreads, so a baseline measure at diagnosis followed by repeat evaluations every 3–4 months, even while ostensibly healthy, is useful to monitor the disease course. Normal CD4 counts range from 500 to 1,500 cells/mm<sup>3</sup>. The lower the immune count at treatment initiation, the more difficult it is to repair the immune response. Progression to AIDS is more likely when CD4 counts decrease to 200 cells/mm<sup>3</sup> or fewer, and maintaining CD4 counts greater than 500 cells/mm<sup>3</sup> substantially delays HIV/AIDS progression. All patients with CD4 counts of less than 350 cells/mm<sup>3</sup> should begin taking ARV medication with a goal of increasing the CD4 count long term.

Viral load is the level of HIV RNA copies per 1 milliliter of blood, and it is directly proportional to the extent of disease. Its best use is to measure how well treatment against HIV is working; HIV RNA can reach >100,000 copies/mL during the untreated window period, and the load decreases progres-

sively with effective medication. Viral load reflects treatment efficacy and viral activity; baseline and periodic (such as every 4–8 weeks) measures of viral load after treatment begins will dictate medication choices. The goal of an ARV regimen is to achieve an undetectable viral load, measured at <50 copies/mL. Failure to achieve or maintain low viral load with treatment indicates a poor virologic response to the selected drugs. Treatment failure can be determined when previously undetectable loads reach >200 copies/mL despite medication.

Keeping viral load low not only improves patient quality of life and lengthens the time to AIDS development, it also reduces the spread of HIV to others. Transmission rates are proven lower from people with undetectable levels of HIV RNA in their blood, so partners are less likely to develop the disease. The transmission rates are three times greater with every tenfold increase in viral load.

### Whom to Test

The CDC, in its Know Your Status campaign, recommends that every age-appropriate person undergo HIV testing at least once and that high-risk individuals undergo more frequent testing. HIV testing and knowledge of HIV status is applicable to broad population groups. However, HIV transmission carries social and public health stigmas, so health care professionals face steep challenges in motivating individuals to get tested. Offering HIV testing in the pharmacy makes it more readily accessible and may facilitate a higher comfort level than in a clinic setting. Combining HIV testing with evaluation of other conditions, such as hepatitis B or other sexually transmitted diseases, may be prudent, as well.

### Point-of-Care Testing

During the period just after infection, viral load increases drastically, but human antibodies to the virus have not yet developed. The time between initial infection and antibody development at approximately three months after infection is called the window period, during which diagnosis rates are low and unintentional spread of the virus is high. Gold standard tests for HIV use bodily fluid, usually blood, to identify antibodies after the window period; positive ELISA antibody results are then confirmed with Western blot measurement of viral levels.

Rapid diagnostic tests, which can measure plasma HIV RNA as early as nine days after infection, once were reserved for patients in whom transmission was strongly suspected. With advances in HIV rapid tests, though, pharmacists and other health professionals can offer point-of-care testing to achieve the CDC's Know Your Status goal. According to current estimates in the United States, broader availability of point-of-care testing alone might identify 20 percent of patients who are unaware of their positive status.

### Rapid Test Details

Rapid tests often use man-made peptides to which human HIV antibody adheres; a color change signifies a positive reaction. In August 2013, the first rapid test to instead detect HIV-1 antigen itself, which can indicate the presence of infection before any human cell response develops, was approved. The 11 available point-of-care rapid tests use blood or saliva, though cotton-swab saliva kits are more common and more accessible in pharmacy settings. Results are available within 20-40 minutes.

Because rapid tests are still new to pharmacy clinics, pharmacists should be prepared to answer questions about the accuracy of these tools. Today's rapid tests on the market meet the U.S. Department of Health and Human Services requirement of 98 percent sensitivity (in other words, 98 percent of positive results are accurate) and specificity (98 percent of negative results are accurate), and some achieve 99 percent accuracy levels. Regardless, positive point-of-care rapid tests still must be confirmed by traditional ELISA methods.

Rapid point-of-care testing turns a potentially scary experience into a normal procedure for many pharmacy patients; pharmacy clinics for rapid testing are the first step in establishing long-term community-based HIV care and have the potential to close the gap of disparate HIV care across the United States.

### CLIA Waivers

The Clinical Laboratory Improvement Amendment (CLIA) was enacted in 1988, and its standardization of laboratory testing procedures and tools was approved for widespread use in 1992. CLIA Certificates of Waiver for Infectious Disease Tests are required by outpatient pharmacies that intend to conduct basic laboratory testing, including rapid diagnostic HIV testing. CLIA waivers indicate that specialized equipment and complex ability with equipment are not needed to perform testing; facilities that administer CLIA-waived rapid tests do not have to be licensed laboratories.

CLIA waivers introduce diagnostic tests and follow-up care to hard-to-reach communities and patient populations, but they are not a reflection of the positive or negative accuracy of any test. A list of all CLIA-waived tests can be found on the FDA website: <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfClia/analyteswaived.cfm>.

### Developing a Clinic

Implementing a rapid test program can be approached similarly to establishing an immunization program. Before any services are provided, the pharmacist should develop protocols, research physical and logistical needs, and train all involved staff on procedures and ethics.

During an initial needs assessment, identify the population base for outreach; the physical space available for a private diagnostic and counseling area; and existing paper or technologic capabilities for recording the process, result, and related dispensing or counseling procedures. If physical structures, such as enclosed rooms, secure file storage, or secure laptop access are not available, determine how to develop or adapt the location to meet these privacy and documentation needs.

Because training and knowledge about HIV diagnosis and treatment are often inconsistent across pharmacists and their staff, group or individual training courses are essential before a clinic is made available to the public. Training should involve disease background review, laboratory evaluation comprehension, and explanation of HIV diagnostics. Additionally, ethical or social services training about how to approach a patient with a positive diagnosis and how to ensure patient privacy throughout the process can ensure a smoothly run clinic. Often, nearby colleges or group health practices can collaborate on staff training; free resources are available from the AIDS Education and Training Center (<http://www.aetc.org>) and from the CDC that are developed specifically for pharmacists.

Pharmacists must determine which CLIA-waived test kit they prefer that fits the needs of the population and the ability of the pharmacist providers. Literature is not widely available to compare the available tests, but warranty-replacement and manufacturer-specific details, as well as size of the kits and pharmacy storage space limitations, may help pharmacists select their best fit. Additionally, any pharmacy implementing a testing program must complete a CLIA Application for Certification (Form CMS-116), which is available on the Centers for Medicare & Medicaid Services (CMS) website at <http://www.cms.gov/cmsforms/downloads/cms116.pdf>, and pay its accompanying fee. The application process can take up to three months and may include CMS inspection of the ambulatory site.

Documentation standards and goals for the program should be determined before testing is underway. Set short- and long-term goals for a testing program. A short-term goal example is to screen five patients per month, whereas a long-term goal could involve chronic care objectives for patients who test positive in the clinic. When all of the above steps are completed, the pharmacy is ready to advertise its new clinic.

### Steps in the Clinic

Although rapid HIV tests have quick-turnaround results, they are not instantaneous. The 20-40 minutes between testing and results can be used for basic counseling and Q&A interaction. For example, when patients approach the clinic for HIV testing, they should complete a risk factor questionnaire that can be the basis of a counseling discussion while waiting for test results. Point-of-care testing should not be an isolated event,

but should be combined with risk assessments; disease state or lifestyle risk counseling; and discussions about treatment, adherence, and chronic care if HIV test results are positive.

A positive test result is only the beginning of a relationship between the pharmacist and patient. When a patient tests positive in the outpatient clinic, the pharmacist should be prepared to offer continuity of care that is crucial to improving long-term care and public health. Initially, the pharmacist should be able to counsel the patient on what a positive rapid test means and must refer the patient to follow-up care to confirm diagnosis and establish a regular provider relationship. Some examples include escorting patients with positive tests (voluntarily) to local HIV clinics or establishing a referral appointment by telephone with a primary care physician as soon as possible after the rapid test date. Later in the relationship, at scheduled follow-up visits, pharmacists can address ongoing patient questions about treatment initiation, regimen changes, daily care, transmission risks, and adherence.

### Procedural Logistics

When patients approach the pharmacist for HIV testing, they should expect a private setting for both the swab sample collection and the results consultation. Patient-identified concerns include worry about undergoing HIV testing in an open clinic, such as those established beside pharmacy counters to give vaccinations during flu season.

During testing, staff procedures should be observed for continuing education and good clinical practice. Each patient should receive a new rapid testing kit, and reusable materials (such as pens and tables) should be disinfected after each patient is tested. To minimize the real risk associated with contact of infectious body fluids during testing, pharmacists should observe universal precautions (the same safety procedures for every patient regardless of test result) to reduce exposure. HIV is not transmitted casually, but protection often involves sterile gloves and disinfectant use at a minimum.

Documentation is essential when testing outpatients for HIV status. Keep records of the methods, patients, and results on file and secured in the pharmacy. Positive tests often must be reported to state departments of health for incidence tracking. These data also can be useful for risk reduction strategies to control HIV spread by encouraging partner notification of anyone who was sexually active with the newly diagnosed person.

### Pharmacist Opinions on Rapid Tests and Point-of-Care Programs for HIV

Overall, a majority of polled pharmacists (up to nearly 80 percent) support in-pharmacy HIV testing as a convenient

and accessible provision of care. Pharmacists who provide counseling, vaccinations, and other public health services are more likely to promote point-of-care HIV testing. This favorable view appears shared by technicians and staff, also. Polled pharmacists have stated that peer opinions about the acceptability of pharmacist-based HIV testing seem to vary but are likely positive in recently trained pharmacists.

However, barriers exist for initiating and continuing a diagnostic clinic. As early as 2003, pharmacists and the AIDS Education and Training Center (AETC) identified one of the largest challenges: lack of knowledge about HIV. Training about medication regimens, test accuracy, specimen collection, test interpretation, and available resources for patients who test positive are not provided during a typical university program and change with relative frequency. Instead, pharmacists must rely on educational tools available online, such as those provided by AETC and its regional associations. As expected, insufficient time and staff are two ongoing challenges to running an HIV testing clinic; not enough time to provide counseling is a specific concern of pharmacists. A related concern is the lack of space to provide a private testing and results counseling session, especially for pharmacists and patients who might not be comfortable discussing HIV-positive test results. Finally, concerns about the lack of third-party payer compensation for medication therapy management services to HIV patients remain.

HIV testing requires training, dedicated counseling time, and higher levels of community engagement to reduce stigma and increase testing rates. However, point-of-care rapid tests are increasingly viewed by pharmacists as a useful addition to pharmacy's role in chronic disease community care.

## **TREATMENT DISCOVERIES AND ADVANCES**

When HIV emerged, no treatment options in existence could tackle the retrovirus mechanism or mutation rate. HIV changes its genetic code frequently as a result of natural errors during its own transcription as well as in response to external factors (such as drug therapy) that threaten virus survival. This resistance to drug therapy can extend across individual drugs within a class and sometimes across drug classes, which makes HIV more formidable to treat as it remains in the body longer. Because resistance is not reversible, and because resistance can spread across an entire drug class, additional HIV mutations strongly protect the virus and limit any secondary treatment options. Drug therapy that uses multiple mechanisms of attack is most effective at combating HIV mutations. Antiretroviral treatment options have expanded greatly since the first drug—zidovudine—was approved in 1987. Six classes that contain more than 20 drugs now attack HIV at varying points along the viral life cycle.

## **Available Antiretroviral Drug Classes**

Drugs in two of the first available antiretroviral classes work by stopping reverse transcriptase, the enzyme used by HIV to form viral DNA within the host cell. Non-nucleoside reverse transcriptase inhibitors (NNRTIs) and nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs) act at similar locations in the genetic transcription process to halt viral activity. Despite HIV resistance mutations, NRTIs together with NNRTIs remain important components of a successful ARV treatment backbone. Protease inhibitors prevent the HIV enzyme protease from forming functional, small-chain HIV proteins near the end of the viral life cycle. As a class, protease inhibitors are poorly absorbed, so most of the available protease inhibitors are supplemented, or boosted, with low-dose ritonavir (such as 100 mg) for optimal activity. Table 1 lists individual, marketed members of each drug class, with the most recent approval dates noted. The following web page from the Food and Drug Administration also contains useful information ([www.fda.gov/ForConsumers/byAudience/ForPatientAdvocates/HIVandAIDSActivities/ucm118915.htm](http://www.fda.gov/ForConsumers/byAudience/ForPatientAdvocates/HIVandAIDSActivities/ucm118915.htm).)

Although many approved drugs continue to fall into one of the three standard treatment classes, new developments still seek to expand alternative mechanisms and broaden the range of antiretroviral possibilities. For example, the fusion inhibitor T-20 prohibits HIV from entering a host CD4+ T cell after the virus binds to the CD4 receptor, and the entry inhibitor maraviroc, approved in 2007, prevents HIV entry into a CD4+ T cell by binding to the CCR5 co-receptor on the outside of the host cell. Raltegravir, also approved in 2007 as the first available integrase inhibitor, blocks yet another step of the HIV life cycle by stopping the integration of HIV DNA into the host cell genetic material for replication. In 2013, dolutegravir was approved as a new integrase inhibitor for use in patients without prior treatment with that drug class.

## **Treatment Initiation Timing and Goals**

The timing of first-line therapy depends in part on patient ability to maintain treatment and largely on CD4 evaluation. Patients with CD4 counts less than 500 cells/mm<sup>3</sup>, anyone with HIV and hepatitis B coinfection, and patients older than 50 years of age, and any pregnant woman who is HIV positive should initiate HAART.

The overall goals of ARV therapy are to maximally and durably suppress the virus, which will allow recovery of the immune system and reduce the emergence of HIV resistance. To combat widespread single-agent resistance, effective combination therapy with drugs from different mechanistic classes, known as highly active antiretroviral therapy, or HAART, quickly became the best form of therapy to prevent progression to AIDS. HAART is now considered essential, as the most effective

**Table 1. ARV Drugs by Mechanistic Class**

<b>NRTI</b>	<b>NNRTI</b>	<b>PI</b>	<b>Other</b>
Emtricitabine	Efavirenz	Ritonavir	Raltegravir (integrase inhibitor, 2007)
Tenofovir	Nevirapine	Lopinavir	Maraviroc (entry inhibitor, 2007)
Abacavir	Delavirdine	Tipranavir	Enfuvirtide (T-20; fusion inhibitor)
Lamivudine	Etravirine (2008)	Saquinavir	Dolutegravir (integrase inhibitor, 2013)
Zidovudine	Rilpivirine (2011)	Indinavir	
Didanosine		Nelfinavir	
Stavudine		Atazanavir	
		Fosamprenavir	
		Darunavir	

means of combating the spread of HIV within and between individuals. HAART combinations for first-line treatment, when observed correctly, can maintain undetectable viral loads and prolong the quality of life for patients with HIV.

Today, at least three active drugs, usually from two different classes, are required to achieve therapeutic goals. Initial regimens typically contain one of the following combinations of drug classes: 2 NRTIs + 1 NNRTI; 2 NRTIs + 1 PI; or 2 NRTI + 1 integrase inhibitor. Monotherapy with any agent and combinations that include only one drug class are always contraindicated because these options confer poor antiviral coverage and high rates of viral resistance. Similarly, regimens of three NRTI with a single NNRTI are not proven more effective than other first-line options, so they are best avoided as well. In the United States and developing countries, simplified HIV regimens in the form of fixed-dose pills or co-packaged drugs (such as blister packs) may facilitate distribution and improve patient adherence.

### Second-Line Regimens

Although effective HAART immediately reduces viral loads in patients with HIV, maintaining that effect is not always as simple. Antiretroviral treatment is a life-long effort to prolong the immune system destruction by HIV and the development of AIDS. The timing and selection of individual drugs included in the first-line and any subsequent, second-line, HAART regimens require careful ongoing consideration of the virus's rapid and multimodal drug resistance mechanisms as well as the role of patient adherence to treatment. ARV revision is necessary in most patients with HIV and is nearly inevitable over time.

Sometimes, first-line regimens are not effective at reducing viral load to undetectable levels. This can be caused by existing viral mutations present at diagnosis or by outdated

treatment regimens, or it can develop gradually as a result of poor adherence to the first-line regimen. During susceptibility testing, drugs that remain active against a newly mutated HIV strain are identified as secondary treatment options. Testing within four weeks of stopping the failing regimen ensures an accurate reflection of the viral mutations at the time of treatment failure. Addition of a single new agent onto an existing regimen is not recommended because resistance mutations to the new drug will develop rapidly. Thus, secondary regimens typically require an entirely new antiretroviral combination—sometimes another first-line recommended combination—with a steadfast HAART goal of viral load suppression.

The need for second-line regimens may be determined according to viral load, which should be measured at four weeks and at 3-6 months after the initiation of a first-line regimen to confirm load reduction. Regimen failure is considered if viral load remains detectable without decrease at these measured time periods; evaluation of adherence or mutation genotyping is warranted.

### Advances in Fixed-Dose Regimens

Fixed-dose combinations (FDCs) are the 21st century answer to some barriers of effective HAART treatment. FDCs combine the most effective ARV regimens into one formulation. Benefits of these once- or twice-daily pills include improved adherence, lower medication costs, and reduced pill burden—essential elements of therapy as patients live with the disease and its treatment longer and require continuous care across youth, teen, and adult ages.

The pill count options of initial regimens for treatment-naïve patients can decrease from as high as 10-23 pills/day to only 1-4 daily with fixed-dose formulations. If used during first-line treatment, the potential for adherence and sustained viral

### Online and mobile tools for professionals

- Clinical Education Initiative of the New York State Department of Health AIDS Institute: The Provider guide to HIV Testing (available online or on smartphones).
- Ambulatory Surgical Center Quality point-of-care assessment toolkit used by Centers for Medicare & Medicaid Services to assess clinic point-of-care standards at <http://www.ascquality.org/PointofCareDevicesToolkit.cfm> provides posters (<http://bit.ly/pocposting>, <http://bit.ly/pocclean>) for professionals to hang in the clinic about proper disinfectant procedures and power-point slides to train staff (<http://bit.ly/pocpowerpoint>).
- The AIDS Education and Training Center (AETC) links providers who are ready to develop an HIV POC clinic with tools from established clinics around the country, including the Pocket Guide to Giving HIV Test Results (4/2012) at <http://www.mpaetc.org/Products/Giving-HIV-Test-Results> and a brochure about how to retain patients after HIV diagnosis for care (11/2013) at <http://www.mpaetc.org/Products/Retention-in-HIV-Care>. These help keep pharmacists up-to-date and marketable about types and combinations of ARVs, how to assess at-risk patients, and which codes to use for billing of POC services.

suppression on a single regimen is high, which helps preserve and delay other treatment options.

For prescribers, fixed-dose combinations are equally as beneficial. Combined formulations have simplified prescribing options and minimized the numerous drug interactions possible within and between antiretroviral classes. By using a fixed-dose pill instead of hand-selected combinations of individual drugs, the prescriber also ensures that the most effective dosages are being used according to published data. Consistency of the HAART regimen among the HIV population reduces the likelihood of multiple mutant HIV strains developing and spreading harder-to-treat infections across wide patient groups.

Because fixed-dose combinations typically contain antiretroviral drugs that have already been approved by the FDA, these new formulations do not require the same time to receive FDA approval. Instead, fixed-dose pills require proof of bioequivalency with the individual components. In addition, fixed-dose combinations are compatible with each other and with similar meal restrictions, and their drug interaction or adverse event profiles are not synergistically burdensome. The combination tablets are not significantly larger than individual components of HAART, so swallow impacts are minimal.

Since 2006, two triple-medication and one four-drug options have been marketed. Atripla contains, in one pill taken once daily, the NNRTI efavirenz combined with Truvada, a dual-NRTI combination of tenofovir and emtricitabine. Atripla was the first fixed-dose formulation to combine drugs in two

different classes and to provide an all-in-one HAART regimen for select patients. In 2011, the second all-in-one fixed-dose formulation was approved. Complera combines Truvada with a newer NNRTI, rilpivirine, in one tablet and is also prescribed once daily; the combination tablet is indicated for treatment-naïve adults and has been studied against available first-line combinations, including Atripla. Stribild, the once-daily, four-drug combination of elvitegravir + cobicistat + tenofovir + emtricitabine was approved by the FDA in 2012 for HIV-1 infection in adults who are treatment-naïve.

Rilpivirine is active against HIV that is resistant to older NNRTIs, but, as a part of Complera, comes with important caveats. Its effectiveness wanes in the presence of extreme viral loads, when treatment failure rates increase dramatically. The resultant viral resistance is significant, and it is not limited to the fixed-dose Complera regimen. Cross resistance is prevalent both within the NNRTI class and into the NRTIs and at viral loads >100 copies/mL can introduce resistance mutations to emtricitabine/ lamivudine, etravirine, and nevirapine.

An established priority group for fixed-dose treatment options, to ensure optimal adherence, comprises HIV-positive pregnant or nursing women whose disease is stable on the combination administered as multiple pills. Transition from multiple drugs to a fixed-dose tablet in any patient with virologically stable disease requires careful management and pharmacy stock maintenance to avoid missing or overlapping doses.

Fixed-dose tablets also provide benefits to newly diagnosed and poorly adherent patients. In April 2013, treatment guidelines first recommended fixed-dose combinations for patients as first-line care, at the initiation of HAART, regardless of CD4 count. Patients who maintain better adherence on fixed-dose regimens than multiple-pill HAART appear to retain positive adherence levels of 95 percent significantly more often than patients on multiple pills, even when another NRTI is added to the fixed-dose regimen.

### Prophylaxis

As is the case with any prophylaxis regimen, the goal here is to prevent HIV infection and the morbidity and mortality that follow. There are prophylaxis regimens for patients who are at high risk for exposure but have not yet been exposed and regimens for patients who have been exposed or have engaged in behavior with a high risk of exposure to the virus.

### Pre-Exposure Prophylaxis (Pr-EP)

Pre-exposure prophylaxis guidelines have long been needed, and in May 2014 the U.S. Public Health Service released the first Pre-Exposure Prophylaxis for the Prevention of HIV Infection in the United States guidelines. The guidelines Provider Supplement is a useful packet of information for the provider



and patient. Recommended indications include MSM, heterosexually active men and women with an infected partner (sometimes called a “heterosexual HIV-discordant couple”) and injection drug users. Dosing for three medications (tenofovir, emtricitabine and the combined tenofovir + emtricitabine product) and monitoring guidelines are also stated. PrEP does not negate the need to undergo HIV testing periodically and is just one method of minimizing risk that can be up to 92 percent effective with continuous use. Intermittent PrEP is not as effective, and combination of PrEP with other prevention methods, such as using condoms, is a best practice.

### **Post-Exposure Prophylaxis (PEP)**

Post-exposure prophylaxis is divided into occupational and non-occupational exposure. Occupational exposure guidelines applies to health care personnel, paid or unpaid, who may be exposed to infectious material; pharmacists, pharmacy technicians and pharmacy students may fall under this definition. Exposure might be any needlestick, contact with mucous membrane, or contact with damaged skin that could introduce infected material. The preferred regimen is raltegravir plus tenofovir + emtricitabine, but several alternative regimens may be considered for individual patients.

Non-occupational exposure applies to sexual contact, injection drug use or other non-occupational situations such blood transfusion, or as an infant might have during delivery. Guidelines provide many drug options for a 28-day course of therapy that should be started within 48-72 hours of exposure.

### **Managing Adverse Reactions**

One of the biggest roles that pharmacists can play in the management of HIV therapy is identifying and managing side effects of antiretroviral medications. For example, 30 percent of all HIV-positive patients experience daily episodes of diarrhea. This side effect can greatly reduce quality of life, but is manageable. It is important to counsel the patient to replace lost fluids and electrolytes lost from diarrhea. There are many choices between sports drinks and rehydration solutions. Soluble fiber drinks that contain psyllium husk or methylcellulose can help prevent diarrhea by adding bulk to the stool. Loperamide may be a good OTC choice for patients with acute symptoms. Prescription therapy was recently approved by FDA. Crofelemer (Fulyzaq) is indicated for the symptomatic relief of non-infectious diarrhea in adult patients living with HIV infection on anti-retroviral therapy. If cost is a barrier, then diphenoxylate/atropine may serve as another option. HIV medications can increase the patient’s risk of hyperlipidemia by raising cholesterol and triglyceride levels. Appropriate cholesterol screening should be advised in this population. Recommending fish oil may be an option for appropriate patients. Certain HIV medications can cause changes in bone mineral density, leading to thinning of the

bones. Screening for osteoporosis early can help patients prevent fractures. Because these medications can cause drug induced nutrient depletion of Vitamin D, supplementation may be appropriate for patients with low levels.

Another common side effect of HIV medication is anemia. If a patient living with HIV infection complains of feeling more tired or worn out than usual, a pharmacist needs to be able to make this connection and have the patient follow up. Up to 50 percent of patients taking efavirenz, which is a component of the three drug combo Atripla, develop psychiatric side effects such as vivid dreams and nightmares. The patient should be counseled that these are most likely to occur in the first 2-4 weeks and should diminish after that point. If bothersome dreams do continue, consider dosing the medication in the morning.

### **Managing Drug Interactions**

Clinical decision support tools at the point of prescribing and point of dispensing flag major drug interactions and contraindications. Pharmacists should use the comprehensive medication review (CMR) model to identify all the prescription drugs, over-the counter drugs and dietary supplements that patients take. An accurate personal medication record (PMR) helps all providers make appropriate treatment decisions. Drug interactions that are less likely to be caught by a computer include OTC antacids, OTC H2-blockers, and OTC proton pump inhibitors (which affects drug absorption), and St. John’s Wort (speeds up antiretroviral drug metabolism). Protease inhibitors affect methadone metabolism, paradoxically lowering plasma levels. Methadone treatment clinics should be aware of methadone drug interactions, but pharmacists who process orders for changes in protease inhibitor therapy should counsel the patient on signs of withdrawal or over-medication.

### **Longevity of Care: Answering Chronic Care Questions**

Patients with HIV, and their partners and family, now understand AIDS as a state that can be detained for months, years, or even decades. To delay AIDS and maintain a positive quality of life for such long durations, though, patients and caregivers must remain knowledgeable about current and future advances in HIV care. Their questions and needs focus on how to maintain treatment without resistance, how to safely manage a drug holiday, and how to get involved in new approaches that simplify treatment and improve quality of life even more.

Routine community programs enhance drug safety, maintain adherence, and introduce patients to useful tools and support groups. As professionals and patients view HIV as a chronic and treatable condition, secondary complications and opportunistic infections become even less common. As routine POC testing becomes a standard, the incidence of

HIV can be reduced; regular monitoring of ARV adherence and efficacy will support the goal of eradicating HIV/AIDS.

### **MONITORING RESISTANCE IN THE POC CLINIC**

Patients with HIV are nearly as familiar with resistance concerns as clinicians. Whenever the virus sees an opportunity, it will mutate and become resistant to the drugs attacking it. Failure to observe ARV therapy is one of the most common causes of viral resistance and treatment failure. ARV regimens, even those with minimal pill burdens and fixed-dose options, are notoriously difficult to maintain long-term: costs, adverse effects, and drug interactions are three dominant reasons. Secondary factors that impede consistent long-term ARV therapy include patient wellbeing (such as feeling too well to need medications), complicated treatment schedules when fixed-dose options are not available, and the management of drug holidays to assuage patient burden of therapy, or pill fatigue, without allowing viral rebound to occur. Adherence rates of less than 95 percent are low enough to open the door to resistance. In fact, even improved adherence that remains below 95 percent compliance is considered suboptimal: resistance is still highly likely when patients increase adherence from 50-85 percent, because the 95 percent threshold is not crossed.

A basic checklist of questions asked by the pharmacist can guide counseling when medications are refilled and can evaluate patient needs efficiently after treatment is initiated. At 3-6 months after treatment initiation, patients should have achieved stable or increasing CD4 levels and undetectable viral loads. To contribute to this laboratory monitoring regimen, the pharmacist can ask the following when medications are prescribed or refilled:

1. Has the patient had CD4 and viral load measures in the past two weeks?
2. Is the viral load suppressed?
3. How are adherence (per patient and as assessed by pharmacist on site) and tolerability (per patient)?
4. How affordable is the prescribed regimen for the individual patient?
5. Does the patient have an appointment for laboratory follow-up after receiving the medications? For clinician follow-up? For support services consultations?

### **IMPROVING ADHERENCE**

Adherence to therapy—taking each medication exactly as directed every time, on a regular basis—ensures that HIV has few chances to mutate. An inconsistent attack on HIV occurs with adherence less than 95 percent of the time, and this provides the retrovirus an opportunity to mutate rapidly and in multiple locations to withstand the regimen.

Adherence to complicated or fixed-dose HAART regimens relies on patient involvement; its benefits include dramatic

improvement in quality of life, continuous viral load suppression, and stable immune system health associated with consistent treatment. However, its difficulties are several-fold: First, the high cost of many antiretroviral drugs can impede consistent treatment, especially for patients with limited finances. Poor tolerance of one or more antiretroviral drugs contributes to irregular use as well through skipped dosages, frequent drug changes and discontinuations, and adverse effects or drug interactions that minimize ARV blood levels to insufficient activity. Finally, HAART regimens can involve an enormous number of pills, called a cocktail, that are complicated to store, transport, and take regularly. This high pill burden is identified by the NIH as one of the greatest barriers to long-term adherence. Patient-identified barriers to ARV adherence revolve more around the dosing schedules. At least one-third of patients report one of the following as a reason for nonadherence: forgetting a dose, sleeping through a dose, being in a public setting during a scheduled dose, and not eating a meal at the usual dose time.

In 2011 the CDC identified evidence-based initiatives to improve adherence in patients with HIV. Documented adherence initiatives significantly reduce viral load in an outpatient setting. In CDC-guided testing of five counseling sessions concurrent with initial HAART, patients were observed for adherence changes resulting from the increased communication. A pretreatment evaluation by a health care professional of the patient's social setting and daily schedule needs were keys to improving adherence from the start. Similarly, involving a partner and measuring medication use with MEMS (medication even monitoring system) pill bottle caps proved adequate reminders to maintain dosages correctly. Medication therapy management (MTM) administered and billed apart from dispensing services in the pharmacy help pharmacists collaborate with other clinicians to maintain continuity of care and help improve patient knowledge. Examples of techniques proven to enhance adherence are using prefilled pill boxes, or prepackaged strip regimens; requiring patients to repeat back medication instructions before leaving the pharmacy; using MEMS caps; and counting pills that remain between refills.

Similar examples of useful adherence tools are pillbox beepers, refill reminder phone calls, and direct adherence counseling. Direct observation of therapy may be employed for patients who have serious barriers to adherence. Because pharmacists are likely more approachable by patients about adherence topics, the burden is on them to communicate problems or patient needs to the prescriber.

Because the cost of medication may affect adherence, it is important for pharmacists to be prepared to give information on AIDS Drug Assistance Programs (ADAPs). The majority of, if not all, ADAPs participate in the 340B program. Each

**Table 2: Select Resources Available on Patient-Centered Websites About Living With HIV**

The Body		AIDSMap	
URL	Description	URL	Description
<a href="http://www.thebody.com/surveys/sexsurvey.html?ic=tools">http://www.thebody.com/surveys/sexsurvey.html?ic=tools</a>	Assess Your Risk for HIV: online quiz that encourages diagnostic testing	<a href="http://www.aidsmap.com/apps">http://www.aidsmap.com/apps</a>	Smartphone tools, including treatment initiation plans, drug charts, and up-to-date news about research
<a href="http://www.thebody.com/content/art33794.html?ic=4003">http://www.thebody.com/content/art33794.html?ic=4003</a>	A Handbook for Communicating About Today's Epidemic: useful information about the state of HIV/AIDS today for providers and patients	<a href="http://www.aidsmap.com/resources/apps/Get-set-for-HIV-treatment/page/2648613/#intro">http://www.aidsmap.com/resources/apps/Get-set-for-HIV-treatment/page/2648613/#intro</a>	Get Set for HIV Treatment: an introduction to treatment initiation timing and options for patients newly diagnosed with HIV, including how each ARV class works and why specific drugs are combined into regimens (updated frequently to reflect current guidelines)
<a href="http://www.thebody.com/reminders/?ic=tools">http://www.thebody.com/reminders/?ic=tools</a>	Personal Reminder Service: a mobile program (online, by text, or by email) to notify patients about HIV medication schedules and related events (registration required)	<a href="http://www.aidsmap.com/resources/apps/Talking-points/page/2648612/">http://www.aidsmap.com/resources/apps/Talking-points/page/2648612/</a>	Talking Points: A Checklist for You and Your Doctor: a monthly resource (online or mobile) that helps patients approach clinicians about different disease management topics with checklists and questionnaires

state operates its own ADAP, with eligibility criteria, formulary and budget resource elements varying by state.

**PROLONGING THE ONSET OF SECONDARY COMPLICATIONS**

Patients with HIV are more susceptible both to generalized infections and to rare, opportunistic infectious diseases that signify the onset of AIDS. As the patient's immune system is worn down by constantly fighting the adaptive presence of HIV, it loses the ability to build a defense against other pathogens. Common infections that occur at high rates in patients with HIV include bacterial skin infections, varicella zoster, and candidiasis. Otherwise rare diseases like tuberculosis, Kaposi's sarcoma, and PCP, as harbingers of irreversible AIDS, are associated with increasing viral loads and reduced CD4 counts; these opportunistic infections are most likely when the CD4 count decreases to less than 350 cells/mm<sup>3</sup>. Preventing development of these infections is crucial to maintaining chronic quality of life and health stability. The best preventive method remains adherence to HAART.

**PREVENTING DISEASE: VACCINATION ADVANCES**

Research into HIV prevention continues to explore investigational or partially effective concepts, such as microbicides combined with physical barrier methods or vaccination against HIV. The most advanced vaccines in development use sections of the HIV or SIV genes embedded into nonin-

fectious viruses, called vectors, to allow the human immune system to develop an antibody response to HIV. So far, no viable options for vaccination are marketed, but live vector vaccines are in advanced, Phase III trials.

**ERADICATING HIV: CURABLE REGIMENS**

A true viral cure is typically defined as total eradication of the virus from the body's cells. In HIV, this cure is not currently achievable; even HAART only reduces viral burden to undetectable levels. However, functional cures have been described in a handful of patients. Some patients who receive effective ARV treatment immediately after infection—particularly infants known to be at high risk because of maternal infection with ARV prophylaxis at delivery—might experience extremely low viral loads. This early treatment could prevent HIV from forming latent reservoirs in long-lasting immune cells. Without a reservoir to reactivate, HIV could be functionally eradicated from the host even after ARV treatment ends. However, long-term evaluation of adult or infant patients who appear to be functionally cured of HIV is not yet available.

Case studies of patients with HIV who underwent bone marrow transplantations support the profound difficulty in eradicating HIV from a host. In two adults who maintained undetectable viral levels after transplantation with continued ARV therapy, symptoms of an acute retroviral syndrome developed after ARV was interrupted. Even undetectable

residual HIV, down to a single cell, was enough to rebound the infection after transplantation.

### SHARING TOOLS WITH PATIENTS AT A POC CLINIC

One of the most important ways that a pharmacist can support patients living with HIV infection in the community outside of direct medication management is by providing the patients with approachable sources of tools and knowledge to become informed patients. In addition to printable booklets available from the CDC or National Institutes of Health, online patient-oriented sites provide thriving communities that help patients with HIV learn to approach their disease in a manageable, chronic-care lifestyle. Two well-established patient forums are The Body and AIDSMap; both sites offer toolkits, interactive quizzes, charts and booklets, suggestions for speaking with health professionals at any stage of disease, and more. Table 2 lists a selection of the available tools that pharmacists can suggest to their patients living with HIV and that can inform pharmacists about topics important to their patients.

### CONCLUSION

HIV remains a global pandemic and national health crisis. However, with new treatment advances, AIDS mortality is delayed and numerous morbidities are prevented. Treatment regimens are well-established and have enormous benefits but require careful evaluation, selection, and monitoring. In the more than 20 years since HAART took hold in the United States, treatment of HIV has become at once more diverse in its options and more streamlined in its selection. The move to combine proven-effective agents into an easy, and potentially once-daily, regimen has enabled people living with HIV to live longer, better, and safer by increasing adherence, reducing drug interactions, and lowering transmission rates. As future agents continue to be developed, the likelihood of more first- and second-line fixed-dose combination formulations is high.

Both patients and clinicians can be encouraged by efforts in the government and industry to reduce the stigma of HIV infection, to increase awareness of HIV status, and to plan for increasing long-term care needs of people living with HIV. ■

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**Editor's Note: For the list of references used in this article, please contact *America's Pharmacist* Managing Editor Chris Linville at 703-838-2680, or at [chris.linville@ncpanet.org](mailto:chris.linville@ncpanet.org).**

## Continuing Education Quiz

Select the correct answer.

- Which of the following patients in your pharmacy is considered at highest risk for contracting HIV?
  - A white, 39-year-old man with a history of injection drug use who denies current use and has never been tested
  - A Hispanic, 27-year-old married woman expecting her first baby in three months
  - A black, 24-year-old bisexual man with multiple and changing sexual partners and a negative HIV test at age 17 years
  - A black, 32-year-old woman who works as a laboratory technician but observes double-glove precaution while dealing with bodily fluids
- Which of the following statements best characterizes the current state of the HIV epidemic in the United States?
  - HIV progression to AIDS has been halted almost 100 percent by appropriate use of HAART across the country.
  - An estimated 240,000 teenage and adult people in the United States who are living with HIV remain undiagnosed.
  - Deaths occurring in people with HIV/AIDS diagnoses in the 21st century have decreased to fewer than 10,000 annually.
  - New infection rates, as estimated by the CDC, continue to approach 100,000 each year.
- Which patients who come to your pharmacy should be tested for HIV with a point-of-care rapid test?
  - Only those with the most risk factors, because the tests are expensive for patients and the pharmacy
  - Only those with physical signs or symptoms of HIV/AIDS
  - Every pregnant woman, so that no infants will risk perinatal exposure because of unknown status of the mother
  - Every patient who enters the pharmacy, in keeping with the CDC Know Your Status program and the Emory University AIDSvU project
- As a retrovirus, HIV differs from traditional viruses in what ways?
  - HIV has its own cell wall.
  - HIV requires a host to replicate.
  - HIV inserts RNA into the host cell.
  - HIV can be eradicated from the host.

## CE QUIZ

- 5.** Patient W.K., who has maintained undetectable viral levels on his existing HAART regimen for 23 months, was late to pick up his last refill and did not return multiple phone call reminders. When he visits the pharmacy, what are some likely explanations for his nonadherence that you should discuss during counseling?
- High cost
  - High pill burden
  - High HIV infection illness burden
  - Both A and B
- 6.** W.K. admits that the expense of his triple-drug combination, with a burden of more than 10 pills daily, has become difficult to maintain now that he has moved into a new apartment by himself. Which laboratory tests should be performed to determine the effect of his nonadherence on the virus and to identify second-line options that are not resistant to the virus?
- CD4 count and viral load
  - CD4 count and liver enzymes
  - Viral load and susceptibility testing
  - Viral load and liver enzymes
- 7.** Viral load testing has confirmed that HIV levels in W.K. have rebounded. Which of the following general approaches, pending susceptibility test results, is reasonable for a second-line regimen?
- A third NRTI can be added to the failing first-line regimen.
  - A different first-line treatment regimen can replace the failed regimen.
  - A drug that is now resistant can be removed from the regimen without replacement.
  - An unboosted protease inhibitor can replace two NRTIs as a treatment backbone.
- 8.** W.K. might be eligible for a fixed-dose second-line regimen that would provide antiretroviral coverage at a lower cost. In addition, pill burden can be reduced from greater than \_\_\_\_ pills to as low as \_\_\_\_ with some all-in-one fixed-dose formulations.
- 20, 1
  - 20, 6
  - 40, 1
  - 40, 6
- 9.** The newest individual agent to treat HIV as part of HAART is \_\_\_\_\_, a(n) \_\_\_\_\_ approved in \_\_\_\_\_.
- Dolutegravir, integrase inhibitor, 2013
  - Raltegravir, integrase inhibitor, 2014
  - Rilpivirine, integrase inhibitor, 2013
  - Maraviroc, protease inhibitor, 2014
- 10.** All recommended backbones of first-line HAART regimens include how many drugs of which class?
- Two nucleoside reverse transcriptase inhibitors
  - Two non-nucleoside reverse transcriptase inhibitors
  - Three nucleoside reverse transcriptase inhibitors
  - One protease inhibitor
- 11.** Which fixed-dose combination pill contains a second-generation NNRTI?
- Epzicom
  - Truvada
  - Atripla
  - Complera
- 12.** Your patient, D.K., is on a stable and effective ARV regimen. He returns to the pharmacy for a refill of his HAART and has his latest lab results with him. He has not been to see his primary care physician since receiving the results. What is a logical next step in addressing treatment for D.K., given the following measures: CD4, 325 cells/mm<sup>3</sup>; and VL, 125 copies/mL?
- Refill his existing regimen and remind him to make an appointment with his physician in the next month.
  - Refuse to refill his existing regimen, because his lab results indicate potential treatment failure, and send him to his physician for consultation.
  - Consult with his physician on the telephone to share D.K.'s lab results; refill his existing medication if the physician requests, and set up an appointment for D.K. to see the physician for susceptibility testing and evaluation for salvage therapy.
  - Refill his regimen and counsel him that treatment failure might have developed. Ask D.K. about adherence issues and follow-up with him when he visits the pharmacy again next month.
- 13.** During consultation, D.K. mentions that he has a new partner who had not been tested for HIV yet. What can you tell D.K. to encourage him to bring his partner to the pharmacy for testing?
- CLIA-waived tests available for HIV achieve at least 98 percent sensitivity and specificity, which means they confidently identify both negative and positive individuals.
  - CLIA waivers mean that pharmacy HIV tests are more accurate than laboratory blood draws.
  - Pharmacy testing negates the need for standard testing.
  - Pharmacy tests work in as few as five minutes and do not require high levels of privacy to administer or interpret.

- 14.** To apply for a CLIA-certificate of waiver for point-of-care testing, pharmacies must
- Identify one pharmacist to administer all of the tests and register with the FDA
  - Complete a request form available from the Centers for Medicare & Medicaid Services
  - Complete a request form available from the state board of pharmacy
  - Complete a certification program specific to the practice site's state
- 15.** Fixed-dose combinations logically improve adherence compared with triple-ARV regimens that use separate pills for each drug. When a third agent was added to an existing fixed-dose regimen,
- Adherence decreased significantly to less than 50 percent.
  - Adherence was similar to rates observed when NRTI combinations were given as separate pills.
  - The 95 percent adherence standard required to maintain effective HIV therapy was more difficult to achieve with the fixed-dose regimen, because pill boxes were not used.
  - The 95 percent adherence standard required to maintain effective HIV therapy was achieved in almost 50 percent more patients who received fixed-dose regimens than in those who received separate NRTI pills.
- 16.** Patient-identified barriers to HAART adherence, regardless of pill burden, include
- Dosing during social outings
  - Dosing during the night
  - Dosing that changes each day of the week
  - Dosing that was stored incorrectly
- 17.** Opportunistic infections, or otherwise rare diseases, are most likely to develop when the CD4 count falls below
- 500 cells/mm<sup>3</sup>
  - 450 cells/mm<sup>3</sup>
  - 400 cells/mm<sup>3</sup>
  - 350 cells/mm<sup>3</sup>
- 18.** Pre-exposure prophylaxis with Truvada once daily is a logical prevention method
- Alone for all health care workers who interact with patients
  - In combination with barrier methods for every sexually active adult with multiple partners
  - In combination with barrier methods for partners of people who are HIV positive
  - Alone in people who are injection drug users so that they do not have to get tested for HIV periodically
- 19.** Patient H.G. approaches you to ask about curing her HIV. She began HAART six weeks after her diagnosis and has maintained undetectable viral load on her initial first-line regimen for nearly five years. What facts can you share about the likelihood of eradicating HIV in her body?
- Bone marrow transplantation is a fairly certain way of clearing HIV from her system, because residual HIV is unlikely to rebound after the procedure.
  - HIV that rebounds after bone marrow transplantation causes acute symptoms when ARV therapy is discontinued, possibly because the virus is not recognized by the newly transplanted cells.
  - Latent reservoirs of HIV are more likely to form in short-lasting immune cells, so eradication is possible in people like H.G., who have consistently adhered to long-term therapy.
  - HIV functional cures that appear to eliminate latent viral reservoirs have proven long-term efficacy in both adults and infants.
- 20.** Poor treatment response (in other words, treatment failure) can be documented by a rebound of \_\_\_\_\_ to greater than \_\_\_\_\_.
- CD4 count, 50 cells/mm<sup>3</sup>
  - CD4 count, 500 cells/mm<sup>3</sup>
  - Viral load, 50 copies/mL
  - Viral load, 200 copies/mL