ASHP Guidelines on Pharmacist Involvement in HIV Care

Background and Purpose

The epidemic of human immunodeficiency virus (HIV) infection in the United States has changed dramatically since its initial recognition in 1981.[1] Early in the epidemic, the incidence of HIV reached over 130,000 new cases per year, and death as a result of acquired immunodeficiency syndrome (AIDS) was an almost certain prognosis for those infected.[2] Significant advances in the strategies to prevent HIV transmission and in the medical care of patients with HIV infection led to significant reductions in both HIV transmission events and AIDS-related deaths over time. Among these advancements were an understanding of HIV infection pathophysiology, identification of HIV transmission modes, development of public health interventions targeting behavioral changes in high-risk populations, and identification of novel HIV medication targets leading to advances in HIV treatment and eventually combination antiretroviral therapy (ART). Because the application of ART can significantly suppress HIV replication, thereby restoring a patient's immune function, it has resulted in a significant decline in HIV-related mortality. As a result, patients receiving long-term therapy who maintain viral suppression can now manage their infection as a chronic illness and are likely to experience a near-normal life expectancy.[3]

Despite remarkable advances in HIV treatment and prevention, the HIV epidemic in the United States has persisted. While the annual incidence of AIDS and AIDS-related deaths initially declined after the introduction of ART in 1995, the annual numbers of new HIV infections, AIDS diagnoses, and AIDS-related deaths have remained constant since 2000.[4] From 2000 to 2011, there were 45,000–55,000 new cases of HIV infections diagnosed every year in the United States and nearly 15,000 AIDS-related deaths annually. These statistics indicate that significant challenges remain for public health officials and HIV care providers to properly address the HIV epidemic. Furthermore, while long-recognized challenges to successful HIV care remain relevant (e.g., lack of early diagnosis, inadequate linkage to and retention in care, poor adherence to ART, stigma and public perception, disparities in access to care for disenfranchised or socially marginalized populations), new challenges to successful HIV care and prevention are emerging (e.g., HIV in an aging population, the application of novel prevention methods such as preexposure prophylaxis, the optimal timing of ART initiation, management of special patient populations with HIV infection).[5-9]

As the HIV epidemic in the United States evolves and new challenges to successful care and prevention emerge, healthcare providers—including pharmacists—are expanding their roles to ensure optimal patient care.[10,11] Pharmacists have long been recognized as essential members of the HIV patient care team, and their involvement in managing HIV-infected patients has been associated with improved outcomes. Pharmacist activities such as helping the team in selecting individualized HIV treatment regimens, providing patient counseling, monitoring for treatment responses and adverse effects, evaluating regimens for potential drug–drug interactions, and identifying opportunities for regimen simplification are associated with better viral load reductions and CD4+ T-lymphocyte responses, improved ART adherence, simpler regimens, and reductions in medication errors.[12-16] To address emerging challenges, pharmacists will need to apply their traditional expertise within an interdisciplinary healthcare framework in multiple practice settings (inpatient, community, and ambulatory care) as well as identify and establish new roles in evolving areas of care, including HIV testing and diagnosis, medication therapy management, transitions of care, patient retention, acute HIV treatment, preexposure prophylaxis (PrEP), and initiation of ART in key populations, such as those with acute opportunistic infections, hepatitis coinfections, and solid organ transplantation. In developing these roles, it will be essential for pharmacists to remain highly engaged in the rapidly changing field of HIV using reliable resources such as https://aidsinfo.nih.gov——the U.S. Department of Health and Human Services (DHHS) HIV management guidelines—and others, which are listed in the appendix.

In 2003, ASHP published a statement on the pharmacist's role in the care of patients with HIV infection.[17] These current guidelines extend beyond the scope of that document and are intended to provide guidance for all pharmacists and other healthcare professionals involved in the care of patients with HIV. The purpose of these guidelines is to describe the ways in which pharmacists can contribute to the care of patients with HIV while working within a healthcare team. These guidelines emphasize the importance of interdisciplinary teams and collaboration among healthcare professions in order to achieve optimal patient care. Pharmacists may also find these guidelines helpful in establishing or expanding their services in an HIV practice setting. Using primary literature, therapeutic and practice guidelines, national standards, and the consensus of experts in the field of HIV pharmacy practice, these guidelines describe the available evidence for traditional pharmacist roles and identify new areas of emerging significance in which pharmacists can establish novel roles to meet the current and future challenges of the HIV epidemic in the United States. Specifically, these guidelines address in detail the involvement of pharmacists in the following 10 key aspects of HIV prevention, care, and treatment for patients:

- HIV testing
- Treatment of HIV infection
- Treatment of HIV in key patient populations
- HIV treatment failure
- Management of HIV disease state complications
- Treatment and prevention of opportunistic infections
- Prevention of HIV infection
- HIV education
- Social services and HIV infection
- Professional engagement

Pharmacist Involvement in HIV Testing

The need for expanded HIV testing in the United States is demonstrated by the fact that one in six individuals with HIV in the United States is unaware of his or her infection and may therefore present an increased risk of transmission to others.[18] Recommendations from both the Centers for Disease Control and Prevention (CDC) and the U.S. Preventive Services Task Force (USPSTF) stress the importance of routine "opt-out" HIV testing for adults in all healthcare settings; patients are informed about and undergo testing for HIV unless they specifically decline.[19,20] Ubiquity and flexible hours make pharmacies ideal locations for HIV testing. Pharmacists, as advocates for public health, should be involved with HIV testing initiatives by recommending HIV testing, providing and/or counseling on HIV tests, and assisting healthcare providers with test interpretation.

HIV testing and early HIV diagnoses improve access to HIV treatment that prolongs life, preserves health, and prevents transmission to others. To ensure timely HIV testing, pharmacists should recommend HIV testing according to recommendations set forth by CDC and USPSTF and must be knowledgeable about the signs and symptoms of early HIV infection and the behaviors placing an individual at risk for HIV infection. CDC and DHHS maintain websites that list updated HIV testing recommendations, risk behaviors, and common symptoms of early HIV infection (www.cdc.gov/hiv and www.aids.gov, respectively). Pharmacists referring patients for testing should be knowledgeable about community HIV-testing sites. CDC maintains a list of free HIV-testing sites (hivtest.cdc.gov or 800-232-4636). Pharmacists should support routine HIV testing and help educate patients infected with HIV about how to modify their behavior to prevent disease transmission.

HIV testing may not be easily accessible for patients with limited access to healthcare. Community pharmacies are addressing this issue and improving patient access to HIV testing by offering onsite rapid HIV testing and counseling services.[21,22] Pharmacists in community and outpatient settings perform point-of-care HIV tests, provide pretest and posttest patient counseling, counsel patients with a positive result about confirmatory testing, and facilitate a linkage to care.[23] CDC is developing a toolkit for HIV testing in community pharmacies and retail clinics, and the Michigan Pharmacists Association offers an accredited certificate course for pharmacists focused on point-of-care testing in community pharmacies.[24] These training modules set forth a curriculum designed to support pharmacists in the administration of point-of-care HIV testing, including competencies in pretest and posttest patient counseling, performing the actual test, reading and interpreting the HIV test results, and identifying sites for linkage to care and confirmatory testing. When state legislation does not permit pharmacists to perform these activities, these guidelines can be used to advocate for change and improve and standardize pharmacist care nationally. Expanding HIV testing to pharmacies serves to eliminate barriers and reduce stigma by providing convenient, ubiquitous access to testing. Interest in pharmacy-based HIV testing initiatives has been documented from the perspectives of both pharmacy staff and patients.[25-28] The readiness of pharmacies to provide these services calls attention to their ideal accessibility to both urban and rural communities and to hard-to-reach populations not integrated into the formal healthcare system.

In 2012, the first point-of-care home HIV test became available for sale in community pharmacies. The OraQuick In-Home HIV Test provides results in as little as 20 minutes using a sample obtained by swabbing the test strip along the gum lines.[29] This test joined the already available over-the-counter Home Access HIV-1 Test System, which analyzes a mailed dried blood spot and provides telephone results in as little as one day. Community pharmacists should stock over-the-counter HIV test kits and be able to educate individuals about the proper method for administering the test and interpreting the results and to take action on both reactive and nonreactive test results.

In addition to recommending and providing HIV testing, clinical pharmacists can assist healthcare providers with interpreting HIV test results. HIV infection can be diagnosed by serologic assays that detect antibodies against HIV and by assays that detect HIV antigens or RNA. Reactive screening tests are always confirmed by a supplemental test. Pharmacists' expertise is useful when clinicians are faced with discordant HIV test results, especially during the period between exposure and seroconversion. Clinicians may have questions about which additional tests are necessary. New HIV diagnostic algorithms incorporating the use of fourth-generation HIV testing assays are increasingly implemented within U.S. institutions following updated recommendations from CDC.[30] Pharmacists should familiarize themselves with evolving HIV testing diagnostics; CDC maintains a website of HIV-testing recommendations (www.cdc.gov/hiv/guidelines/testing.html). At the Clinician Consultation Center, clinical pharmacists practicing in HIV medicine, and physicians are on staff to assist with healthcare provider telephone inquiries regarding HIV testing.[31,32]

HIV testing is the first step in linking persons to HIV care and prevention. Pharmacists should encourage HIV testing as part of routine care and familiarize themselves with testing methods performed at local medical facilities, at pharmacies, or at home. Pharmacist endorsement of HIV testing is important for the expansion of HIV prevention and treatment services.

Pharmacist Involvement in HIV Treatment

Patient Assessment and Laboratory Testing. As ambulatory care transitions to the patient-centered medical home model, it is becoming increasingly important for interdisciplinary healthcare teams to provide both comprehensive HIV care and primary care for HIV-positive patients. As a member of the team, a pharmacist should therefore be familiar with both HIV and primary care management guidelines (appendix) and help to ensure that laboratory testing and monitoring of patients with HIV include parameters specific to HIV as well as primary care. It is also essential that pharmacists have the ability to interpret laboratory test results and recommend appropriate treatment or additional testing when necessary in collaboration with the patient care team. Pharmacists should understand how certain laboratory test results may influence the management of HIV (e.g., the presence of baseline dyslipidemia, renal dysfunction, or hepatitis B coinfection among other conditions may influence the selection of antiretroviral agents or perhaps the timing of ART initiation). Among the laboratory tests

that should be obtained at baseline in a patient with HIV are CD4+ T-lymphocyte count; viral load; HIV genotype test; hepatitis, tuberculosis, and sexually transmitted infection testing; varicella, cytomegalovirus, and toxoplasmosis serologies; complete blood count with differential; chemistry and liver panels; and fasting lipid profile.[33,34] Many of these laboratory values will require periodic assessment or ongoing monitoring, particularly the HIV viral load and CD4+ T-lymphocyte count to assess HIV disease progression or treatment response. After the initiation of ART, the HIV viral load and CD4+ T-lymphocyte count are closely monitored, though over time the frequency of monitoring may decline once a patient demonstrates a durable virological and immunologic response. For example, after receiving ART for two years and consistently achieving HIV RNA suppression and a CD4+ T-lymphocyte count of greater than 500 cells/mm^3, viral load monitoring can be extended to every six months and CD4+ T-lymphocyte count monitoring is considered optional.[35] Pharmacists should be intimately familiar with laboratory values that require periodic assessment or ongoing monitoring in HIV-positive patients and recommend that appropriate assessment and monitoring occurs. Specific laboratory testing may also be necessary before the use of specific antiretroviral agents. For example, if abacavir is considered for therapy, the patient should be tested for the presence of the human leukocyte antigen B*5701 allele to determine his or her risk for abacavir hypersensitivity; for maraviroc, an HIV tropism assay should be performed to predict the patient's response to therapy.

Initiating and Maintaining ART. In initiating ART, current HIV management guidelines state that treatment should be offered to all patients regardless of CD4+ T-lymphocyte count to reduce the risk of HIV transmission and disease progression. Treatment is no longer based on the patient's CD4+ T-lymphocyte count but rather on the patient's willingness and interest in starting and adhering to his or her first ART regimen.[35] The pharmacist, as part of the healthcare team, should contribute to assessing a patient's willingness to initiate ART and provide a readiness assessment. This assessment should include the identification of potential adherence barriers, such as substance abuse, depression, and an unstable social or housing situation. Once potential barriers are identified, the pharmacist should help patients and providers resolve adherence barriers, providing ongoing adherence assessments and barrier management as necessary. This role includes monitoring for adverse effects after ART initiation and implementing adverse-effect management strategies with the patient and provider to improve regimen tolerability and maintain ART adherence.

In selecting an initial ART regimen, convenience, patient preference, cost, comorbidities, baseline viral load, CD4+ T-lymphocyte count, the potential for adverse effects, resistance testing, and concomitant medications must be considered.[35] Performing a thorough medication history and assessing for potential drug interactions are essential functions of the pharmacist.

Antiretroviral agents may interact with other antiretrovirals, concomitant medications, foods, nutrients, and herbal supplements. These interactions may be complex, occurring through multiple mechanisms, and may result in diminished treatment efficacy or an increased risk for toxicity. Drug interactions that are not clinically relevant, will not cause patient harm, or will not impact treatment outcomes may also occur. The pharmacist is uniquely positioned to evaluate potential drug interactions using appropriate resources and determine the clinical significance of each interaction identified. To ensure the safety and efficacy of a patient's initial ART regimen and other medications, the pharmacist should perform thorough initial and ongoing assessments of potential drug interactions, including prescription and nonprescription medicines, recreational drugs, and nutritional and herbal supplements. The results of this assessment should be communicated to the healthcare team and used to help determine the most appropriate ART regimen for the patient. When nonprescription medication, food, or nutritional supplement interactions are identified, the pharmacist should educate the patient and ensure his or her understanding of any safety and efficacy concerns that may be present.

To ensure the accurate assessment of drug interactions, the pharmacist should consult primary resources specific to HIV medications as well as the primary drug interaction literature when necessary. Because drug interaction literature is constantly expanding and may be difficult to access for efficient decision-making, the pharmacist should identify alternative resources that are current, reliable, and easily accessible and that provide an efficient assessment of drug interaction information. These sources include (but are not limited to) the DHHS HIV Treatment Guidelines for Adults and Adolescents (https://aidsinfo.nih.gov/guidelines), the UCSF HIV InSite Drug Interaction Database (http://arv.ucsf.edu), the University of Liverpool HIV Drug Interactions website and mobile application (www.hiv-druginteractions.org), and the Toronto General Hospital Immunodeficiency Clinic website (www.hivclinic.ca/main/drugs_interact.html) (appendix). Since drug interactions are considered a subset of medication errors, preventing drug interactions should lead to better patient outcomes. Patients with HIV are at high risk of medication errors, and the identification and correction of these errors by pharmacists has been instrumental in improving the care of HIV-positive patients.[36-39]

Pharmacist Involvement in HIV Treatment of Key Patient Populations

The management of HIV infection can pose unique challenges in key patient populations. These populations include women and children, patients with comorbid conditions or coinfections, patients receiving solid organ transplantation, and immigrants and refugees. These populations often have specific medical and medication needs and regularly require coordinated interdisciplinary care. Pharmacists are essential members of these interdisciplinary teams and can help to ensure optimal patient outcomes.

Women. Twenty percent of all new HIV infections annually in the United States occur in women, and nearly 25% of all persons living with HIV in the United States are women. The majority of women living with HIV and those who are newly infected in the United States are between the ages of 13 and 45, or child-bearing age.[40,41] The proper use of ART in women of child-bearing age requires several important considerations. First, it is important for pharmacists and other healthcare practitioners to identify patients who should receive preconception counseling, including all women of

child-bearing age in HIV-concordant or serodiscordant relationships. To accomplish this, pharmacists should first be familiar with resources related to preconception counseling in HIV-positive women, including the DHHS Guidelines for the Treatment of HIV-Infected Pregnant Women and Prevention of Perinatal Transmission (appendix).[42] In addition, pharmacists should be engaged in the decision-making process with providers and patients regarding the use of ART to prevent HIV transmission. As part of the healthcare team, pharmacists can initiate discussions with HIV-positive patients regarding fertility, including a patient's potential desire to become pregnant or her desire to initiate or maintain contraceptive methods such as hormonal contraception. Multiple complex drug interactions exist among ART agents and commonly used oral hormonal contraceptives; therefore, it is essential for pharmacists to identity potential drug interactions and provide proper counseling to patients before initiating ART.[35] In contrast, for patients who express a desire to become pregnant or are inconsistent with contraception, the proper selection of an ART regimen that is safe during pregnancy becomes very important.

The initiation of ART is indicated for all HIV-infected pregnant women regardless of CD4+ T-lymphocyte count as a means to prevent vertical HIV transmission. Pharmacists should be knowledgeable about current treatment guidelines for the use of ART antepartum and intrapartum for the mother as well as postpartum for the infant, including the safety and efficacy of individual antiretroviral agents as well as the recommendations for preferred ART combinations.[42] When appropriate, pharmacists should report outcomes of ART exposures to the Antiviral Pregnancy Registry (www.apregistry.com), which monitors the teratogenic effects of antiretrovirals.

Pharmacists should be acutely aware of the importance of careful and frequent monitoring for ART efficacy, tolerability, and adherence for pregnant patients. They should also be aware of physiological changes that could impact the pharmacokinetics and dosing of certain ART agents, particularly in the third trimester of pregnancy.[42] Pharmacists should also consider the pregnancy-related safety of concomitant agents that are often prescribed to patients with HIV infection, including agents used for the treatment or prevention of opportunistic infections. Postpartum, pharmacists should reinforce DHHS recommendations for women to abstain from breastfeeding, even in the presence of a fully suppressive ART regimen.[42] Pharmacists should also continue to provide adherence support and encouragement for HIV-positive women dealing with the challenges associated with being a new mother.

Pediatric Patients. To make meaningful contributions to the management of established HIV infection in infants and children, pharmacists must first develop interprofessional partnerships with pediatric HIV specialty care providers. They must also have a thorough understanding of the differing immunologic and virological patterns associated with HIV infection in children and how they compare to adults and adolescents. For example, within weeks to months following acute HIV infection, very high HIV RNA levels decline rapidly in adults, whereas high HIV RNA levels persist in perinatally infected infants for prolonged periods, decreasing slowly over years after the first year of life.[43,44] The different virological pattern in infants likely reflects an immature but developing immune system's relative inability to contain viral replication compared to that of an adult. Immunologically, while declines in CD4+ T-lymphocyte counts and percentages are expected to occur in both adults and children with advancing HIV infection, absolute CD4+ T-lymphocyte counts in children younger than age five years are generally higher than their adult counterparts. However, the risk of disease progression associated with specific CD4+ T-lymphocyte counts or percentages varies with the age of the child. For any given CD4+ T-lymphocyte count or percentage, younger children, particularly those in the first year of life, face a higher risk of disease progression than other children and adults.[45-48] As a result, pharmacists and other specialty care providers must consider the age of the child in addition to HIV-specific laboratory values when determining the risk of disease progression and the need to initiate ART.

As with adults, treatment of pediatric HIV infection is a dynamic field with constant change and progression, requiring pharmacists to be knowledgeable of constantly evolving guidelines and treatment recommendations. This is particularly true for data regarding the use of specific antiretroviral agents in young children. Pharmacists must be aware of existing and emerging data describing the efficacy and safety of specific antiretroviral agents in this population. Pharmacists must also be knowledgeable about the pharmacokinetic differences that occur in children as a result of developing physiology and maturation of organs involved in the metabolism and clearance of medications.[49] These factors, in addition to developmental differences in absorption and body composition, often require that children receive higher weight-based dosing of antiretroviral agents than adults. In addition to weight, pharmacists must also be acutely aware and knowledgeable about antiretroviral agent–specific dosing recommendations that consider body surface area, age, and pubertal development staging.[50]

When treatment decisions are made, pharmacists must not only ensure proper regimen selection and dosing but take active roles in educating children (when appropriate) and caregivers about HIV infection and provide ongoing adherence counseling.[50] Adolescents face multiple barriers that can affect the initiation and maintenance of ART and other aspects of HIV care, including fear, denial, depression, substance abuse, concomitant mental illness, and lack of social and familial support.[51] Healthcare providers, including pharmacists, must work to establish trust and build strong relationships with patients and their caregivers while utilizing patient-care strategies that minimize barriers to adherence. For example, regimen fatigue can occur in young children who have been receiving ART since early childhood and can result in poor adherence, virological resistance, and the need to implement increasingly complex ART regimens.[52] Working with pediatric HIV specialty providers, pharmacists can help to reduce regimen fatigue through the provision of ongoing adherence support as well as the selection or simplification of regimens to minimize the number of required pills, volumes of prescribed liquids, frequency of doses, and presence of drug interactions or adverse effects. Pharmacists are also uniquely aware of the availability of alternative dosage formulations and delivery systems and are equipped to recommend methods to improve the palatability of crushed pills or liquid formulations to minimize treatment aversion due to offending taste.

Finally, pharmacists must be sensitive to the many psychosocial components of care that may be present in the pediatric HIV population. These include the housing status of the child and caregiver; the child's attendance at school or daycare; the presence of substance abuse, mental health issues, or other behavioral issues; and the HIV infection disclosure status of the child.[52-54] When contributing to the care of pediatric HIV patients, pharmacists may be helpful in identifying psychosocial issues that require intervention and possible referral to specialty providers, or to social services and child protective services when appropriate. These interventions can be essential to the overall health and well-being of children as well as their success in managing their HIV infection. Pharmacists may also serve as important information resources as children transition into adolescence and become sexually active. Counseling on contraceptive methods, safe sex, and preventing HIV transmission should occur regularly and should be delivered by members of the healthcare team, including the pharmacist.

Patients with Comorbid Conditions. Comorbidities are common among patients with HIV. Compared with the general population, those with HIV infection are more likely to have cardiovascular disease, hypertension, renal failure, osteoporosis, diabetes, and certain cancers. Not only do these conditions and others appear to occur more commonly in patients with HIV, they also tend to appear earlier in patients with HIV and at times progress more rapidly than in the general population, likely due to complex interactions between host risk factors, HIV infection, and ART exposure.[55] As a result, it is increasingly important for healthcare teams to not only provide effective ART to ensure viral suppression and immune reconstitution but also to provide comprehensive primary care for patients with HIV. Furthermore, due to the success of combination ART regimens in reducing AIDS-related mortality over the years, the HIV-positive population is getting older; it is estimated that more than half of all patients with HIV in the United States are over the age of 50 years.[56]

Effective management of the changing HIV population will require pharmacists and other healthcare providers specializing in HIV care to maintain proficient knowledge and clinical skills in the screening, prevention, diagnosis, treatment, and monitoring of a variety of primary care conditions. Conversely, pharmacists practicing in primary care settings will likely encounter an increasing number of patients with HIV, which will require them to develop the knowledge and skills to be increasingly proficient in the management of this infection.

Regardless of practice setting, pharmacists should be acutely aware of disease management similarities with the general population and potential differences for patients with HIV. They should also understand the potential contributions HIV infection and ART can have in the development of certain primary care disease states. For example, HIV infection and certain antiretroviral agents can contribute to dyslipidemia, insulin resistance, kidney disease, liver disease, and lipodystrophy.[57-60] They also can contribute to bone loss and an increased risk of osteoporosis and fragility fractures.[61-63] Pharmacists can play key roles in understanding the links between HIV, ART, and these disease states; educating patients and other healthcare providers; encouraging disease state screenings; implementing prevention programs; and ensuring proper disease state diagnosis and management according to available treatment guidelines. They can also assist in the selection or adjustment of HIV treatment regimens that account for a patient's baseline risk or current diagnosis of primary care conditions that can be exacerbated by certain antiretroviral agents.

Other comorbidities commonly seen in patients with HIV, such as mental health conditions and substance abuse, may require special attention by pharmacists and other healthcare professionals. Depression is among the most common mental health conditions diagnosed in patients with HIV and is one of the strongest predictors of poor patient adherence and treatment outcomes.[64] Substance abuse, including illicit drug use, and mental health conditions, including major depression, also can affect medication adherence and lead to poor patient outcomes.[65-67] The management of depression and substance abuse problems in patients with HIV is similar to that for the general population, but pharmacists must be aware of the potential for drug interactions between ART and antidepressants as well as agents used in the management of substance abuse.

It is often necessary to properly manage mental health conditions and substance abuse problems before patients are able to initiate and maintain successful ART.[68] As a result, healthcare providers, including pharmacists, need to be active in the screening processes for mental health and substance abuse problems and provide a means of linking patients as necessary to appropriate specialty care and support services. Ongoing and close collaboration with specialty services, particularly in substance abuse treatment settings, is therefore necessary, as pharmacists can identify and prevent possible drug–drug interactions between substance abuse treatment medications and ART.[69] For example, methadone is a common pharmacologic agent used for the management of opioid addiction. Because multiple cytochrome P-450 isozymes are involved in methadone metabolism, methadone is subject to several interactions with antiretroviral agents. These interactions can increase methadone concentrations and therefore toxicity or decrease methadone concentrations and trigger opioid withdrawal. Pharmacists need to educate providers about these potential interactions, assist in ART selection and dosage adjustment, and work in collaboration with substance abuse treatment programs to ensure successful HIV and substance abuse management.

Finally, many recreational drugs, including methylenedioxymethamphetamine, γ-hydroxybutyric acid, ketamine, and methamphetamine, are metabolized in part by cytochrome P-450 isozymes and can therefore interact with certain antiretroviral agents. Overdoses as a result of these interactions have been reported, and pharmacists can educate providers and identify opportunities to counsel patients as a means of prevention.[70]

Patients with Hepatitis B Coinfection. Approximately 10% of patients with HIV in the United States also have chronic hepatitis B virus (HBV) infection.[71] Compared with patients with HBV infection alone, those with HIV coinfection can have a faster progression to end-stage liver disease, cirrhosis, and hepatocellular carcinoma.[72] Pharmacists involved in HIV care should be familiar with the treatment recommendations for both infections and be acutely aware that certain medications have activity against both infections. More specifically, tenofovir, lamivudine, and emtricitabine are active

against both HIV and HBV, which can be important when treatment for either infection is indicated. For example, tenofovir is a preferred agent for treating HBV infection and can be used as a single agent for management of infection. However, in a coinfected patient, initiating tenofovir alone will lead to HIV resistance. As a result, if HBV or HIV treatment is indicated in a coinfected patient, a full ART regimen should be initiated, usually with the combination of tenofovir plus emtricitabine or lamivudine as the nucleoside reverse transcriptase inhibitor backbone.[35] If tenofovir cannot be used, entecavir is often used for the management of HBV. Of note, entecavir is not an effective agent for treating HIV, but it does have some anti-HIV activity and, when used alone in coinfected patients, could lead to HIV resistance.[73] As a result, if entecavir is initiated for the management of HBV infection in an HIV patient, it must be used in addition to a fully suppressive ART regimen.

In addition to concerns regarding the proper selection of antiviral agents, pharmacists should strongly encourage patients to remain adherent to therapies, as acute HBV treatment discontinuations can cause serious hepatocellular damage due to spontaneous HBV reactivation. Pharmacists can also educate patients about avoiding hepatotoxins, such as acetaminophen, encourage patients to abstain from alcohol, and identify patients with alcohol dependence who require referrals to specialty care. Finally, pharmacists should recommend an evaluation of immunity to the hepatitis A virus (HAV) for all coinfected patients. Those not immune to HAV should receive vaccination against it.

Patients with Hepatitis C Coinfection. Nearly 25% of patients with HIV infection in the United States are also infected with hepatitis C virus (HCV).[74] Like HBV, HCV progresses more rapidly in patients with HIV, resulting in twice the risk of HCV-related death in patients with coinfection compared with patients with HCV infection alone.[75]

The initiation of ART may slow the progression of liver disease in coinfected patients, so current HIV treatment guidelines recommend considering the initiation of ART in this population regardless of CD4+ T-lymphocyte count.[35,75] However, in HIV treatment-naive patients with higher CD4+ T-lymphocyte counts (>500 cells/mm^3), some clinicians may choose to defer ART until HCV therapy is complete in order to avoid the complications of combined HIV and HCV treatment (i.e., large pill burden, drug interactions, and overlapping toxicities).[35] In patients with lower CD4+ T-lymphocyte counts, combined treatment is more likely and pharmacists can play a key role in identifying and managing treatment complications. For instance, currently available direct-acting antiviral agents for HCV have significant drug interactions with multiple antiretroviral agents, including HIV protease inhibitors, elvitegravir/cobicistat, and nonnucleoside reverse transcriptase inhibitors. Pharmacists should contribute to HIV and HCV treatment regimen selection when combined treatment is indicated in order to avoid significant interactions that can lead to treatment failure and drug toxicity. Pharmacists can also recommend self-care strategies for adverse effects and report serious adverse effects back to the prescriber.

Adherence is also essential for optimal HIV and HCV treatment outcomes. As part of an interprofessional team, pharmacists should provide counseling to ensure patients understand what are often complex regimens, including proper administration (e.g., food requirements), the importance of adherence, the benefits and goals of therapy, and the recognition and management of treatment-related adverse effects. This level of pharmacist involvement has been shown to improve overall adherence and response to therapy in patients infected with HIV or HCV and may be particularly beneficial in patients infected with both viruses.[76,77] Furthermore, because the field of HCV medicine is evolving rapidly, it is increasingly essential for pharmacists to maintain a heightened awareness of evolving HCV treatment guidelines (available at www.hcvguidelines.org) and newly available HCV medications, including those in development, and their potential impact on the management of HIV coinfection.[78] Although an increasing number of medicines available for the treatment of HCV will create opportunities to improve patient outcomes, they may also lead to additional challenges in treating coinfected patients that will require pharmacist intervention and management.

Additional roles for pharmacists in treating HIV–HCV coinfection include the evaluation of patient immunity to HAV and HBV infection and the recommendation or provision of HAV and HBV immunizations as necessary. As with patients with HBV, pharmacists should educate patients with HCV infection about avoiding hepatotoxins and encourage patients to abstain from alcohol or pursue specialized care for the treatment of alcohol abuse.

Patients Undergoing Solid Organ Transplantation. Increasing numbers of patients with HIV infection are receiving solid organ transplantation, a practice previously considered controversial or infeasible. The increasing ability to provide transplantation for patients with HIV infection is largely the result of advances in the management of HIV, having a better understanding of the effects of HIV and transplant-associated immune suppression, and accumulating clinical trial data demonstrating the viability of transplantation in the HIV population.[79,80]

Irrespective of concomitant HIV infection, the process of solid organ transplantation is complex and requires interdisciplinary collaboration. The presence of HIV infection only increases the complexity of the process by introducing additional variables to consider during screening and during pretransplantation and posttransplantation management. For example, protocols for liver and kidney transplantation often include thresholds for CD4+ T-lymphocyte count levels and usually require patients to have a sustained undetectable HIV viral load.[81] Pharmacists, in addition to other members of the healthcare team, can contribute to the screening process by reviewing criteria with patients and providing essential adherence counseling to help patients achieve CD4+ T-lymphocyte count and viral load goals.

During pretransplantation management, pharmacists should contribute to the selection and/or adjustment of antiretroviral regimens in anticipation of drug–drug interactions that can occur following transplantation. For instance, nearly all patients will receive proton pump inhibitor medications for stomach acid suppression after transplantation. As a result, ART regimens that contain medications requiring an acidic environment for adequate absorption (e.g., atazanavir and rilpivirine) may need to be avoided. In addition, pharmacists should anticipate antiretroviral drug–drug interactions with posttransplantation immunosuppressing agents. Allograft rejection has been reported to occur at a higher rate

in patients with concurrent HIV infection; one of the causes may be inadequate exposure to immune-suppressing agents as a result of interactions with ART agents.[82,83] Both HIV protease inhibitors and nonnucleoside reverse-transcriptase inhibitors can cause complex interactions with commonly used immunosuppressive agents such as calcineurin inhibitors (e.g., tacrolimus, sirolimus) and cyclosporine. Pharmacists should provide close monitoring of immunosuppressive drug levels and recommend dosing adjustments as necessary to achieve stable therapeutic concentrations. Proper interdisciplinary communication should also occur between HIV specialty pharmacists, transplant pharmacy specialists, and other members of the HIV and transplantation healthcare teams. Communication will help ensure proper awareness and management of potential drug–drug interactions.

The primary indications for solid organ transplantation in patients with HIV are end-stage kidney disease due to HIV-associated nephropathy (HIVAN) and advanced liver disease due to HBV or HCV coinfection.[81] The presence of viral hepatitis adds to the complexity of both pretransplantation and posttransplantation management. Pharmacists should be acutely aware of the differences in managing these infections in transplantation patients, including the differing roles of antiviral therapy. For example, patients with HBV infection should continue to receive antiviral agents after transplantation to prevent a hepatitis flare and should also receive therapy with HBV immune globulin.[84] Patients with HCV may not require antiviral therapy initially, but recurrent infection is common and can adversely impact transplantation outcomes.[81,85,86] As a result, patients should be followed closely following transplantation to identify recurrent HCV infection and the need to initiate therapy.

During the posttransplantation stage, pharmacists should ensure that the use of medications toxic to transplanted organs is limited. They should also work closely with patients to develop strategies to maintain medication adherence to complex drug regimens. At the very least, these posttransplantation regimens will include antiretroviral agents, immunosuppressive agents, and antibiotics for opportunistic infection prophylaxis. The inclusion of the pharmacist on the transplantation team has been shown to improve patient adherence to these complex regimens and may be essential to the overall success of the patient following transplantation.[87]

Finally, pharmacists must be aware of the role of posttransplantation opportunistic infection prophylaxis. Although patients generally receive prophylaxis against *Pneumocystis jirovecii*, opportunistic infections and other AIDS-defining conditions are uncommonly reported following transplantation.[83,88] Importantly, the risk of infection may change following the administration of thymoglobulin for the treatment of acute rejection. Thymoglobulin has been associated with prolonged CD4+ T-lymphocyte declines, loss of cytotoxic antiviral T-cell responses, and development of severe bacterial infections.[89,90] To address these risks, pharmacists must have a thorough understanding of antirejection medications, their impact on CD4+ T-lymphocytes, and the need for increased monitoring and/or additional prophylaxis to reduce a patient's risk of severe infection.

Immigrant and Refugee Populations. In January 2010, the restriction on immigration to the United States for non-U.S. citizens living with HIV was lifted.[91] The restriction had been in place for more than 20 years, and its removal not only helped to reduce social barriers, discrimination, and stigma for immigrants and refugees with HIV, it also aligned the domestic position of the United States with its increasing efforts to combat HIV and AIDS internationally.

While there are many positive implications from the removal of the immigration restriction, there are now also challenges for U.S. healthcare professionals to ensure that immigrants and refugees living with HIV consistently receive proper care. For example, the removal of the immigration restriction also removed mandatory HIV testing as a part of the immigration process. CDC estimates that lifting the ban will allow an additional 4275 persons with HIV to enter the United States each year.[91,92] At least some of these immigrants will have missed opportunities for early HIV diagnosis and entry into care. Furthermore, although CDC recommends HIV screening for all immigrants and refugees, these patients will encounter barriers to healthcare as they enter the United States (e.g., lack of familiarity with the U.S. healthcare system) that limit not only their opportunities to receive HIV testing but also proper primary care services.[93] Pharmacists can assist in overcoming these barriers by being knowledgeable of the local medical clinics and organizations serving immigrant and refugee populations and helping to link patients into care as necessary.

As patients enter into care, additional barriers may need to be addressed before performing HIV testing. These include language differences, cultural beliefs regarding HIV and healthcare in general, and mistrust regarding confidentiality and disclosure of HIV status.[94] Pharmacists must be sensitive to these issues and help reduce barriers whenever possible. Language barriers can be addressed through the use of interpreters. Patients should receive HIV education and counseling in their primary spoken language, and interpreters should be medically knowledgeable so they can explain the complexities of HIV infection and the importance of HIV testing. Pharmacists should be sensitive to situations in which a patient declines the use of an interpreter for fear of disclosure within his or her community and seek alternative translation methods if available (family member or close friend). The delivery of information to the patient in his or her primary language and in a safe environment is paramount, as it not only helps to ensure patient understanding but can also be helpful in developing a trusting patient–provider relationship.

When providing HIV education and prevention counseling, pharmacists should also be particularly sensitive to the HIV risk profiles that may be present in immigrant populations. Specifically, foreign-born persons with HIV are more likely than patients born in the United States to be women who have acquired HIV through heterosexual contact.[95] Pharmacists should also be aware of conditions heightening HIV risk for refugees, such as sexual abuse, violence, and gender inequality.[93,96] Failure to recognize these issues may limit the patient's engagement in care as well as the pharmacist's ability to provide proper counseling and referral to social services.

When testing is performed, it is important for pharmacists and other healthcare providers to follow CDC recommendations specific to the refugee population.[93] These include specific recommendations for screening adults and adolescents as well as pregnant women and children from endemic areas. Also included are recommendations for

screening patients at risk for HIV-2. Pharmacists should have an understanding of the testing for HIV-2 infection as well as groups of HIV-1 infection that are endemic in certain countries and may not be detected with assays commonly used in the United States

Finally, pharmacists, as part of an interprofessional team, should be involved in the ART selection process for HIV-positive refugees and immigrants. They should provide ongoing HIV education and adherence counseling using an interpreter as well as ongoing evaluations for potential drug–drug interactions. Patients should be assessed for coinfections endemic to their home countries and receive proper treatment, including prophylaxis therapy for opportunistic infections when necessary. Patients may encounter financial difficulty, and pharmacists should pursue available services that can assist patients in paying for their medications.

Pharmacist Involvement in the Management of HIV Treatment Failure

Once an ART regimen is initiated, it is critical to monitor the success of therapy via routine assessment of the CD4+ T-lymphocyte count and HIV RNA viral load. Pharmacists can play a key role in interpreting test results to detect possible treatment failure. Treatment failure may be defined immunologically by identifying a significant decline in CD4+ T-lymphocyte count or virologically by finding a significant quantity of virus when full viral load suppression is expected. In identifying potential treatment failure, monitoring trends in viral load is essential, as a single detectable viral load is not generally sufficient to diagnose treatment failure. These viral "blips" occur when a previously undetectable viral load becomes detectable but does not exceed 200 copies/mL and generally decreases to undetectable levels again with subsequent testing. Increasing viral loads over time or a viral load of >200 copies/mL is suggestive of treatment failure. Pharmacists can reduce the chances of unnecessary ART regimen changes in response to viral load blips by monitoring the viral load trend and understanding the definitions of virological failure. If true failure is identified, pharmacists should work with other members of the healthcare team to identify the cause of the regimen failure.

Most treatment failures are the result of nonadherence, pharmacokinetic complications, and ART resistance. Pharmacists, especially those with specialized training in adherence assessment, interventions, and motivational interviewing, can help determine which of these reasons may have contributed to valid ART failure. Many factors lead to nonadherence, including medication intolerance and adverse effects, depression, substance use, psychosocial factors, lack of social support, housing insecurity or homelessness, and patient beliefs. The pharmacist should work with the patient to assess and resolve any barriers to ART adherence. Strategies for improving adherence include utilizing an interprofessional team approach, establishing a rapport with the patient, proactively identifying adherence barriers prior to regimen initiation, assessing patients for medication intolerance and adverse effects, providing mental health and social resources for the patient, assessing adherence at every pharmacy visit, involving the patient in regimen selection, providing adherence aids such as pillboxes and calendars, and assisting the patient in setting reminders through cell phone alerts or text messages.[97] Literature has shown that virological failure has been reduced and the initial ART regimen preserved with pharmacist involvement and adherence interventions.[35]

Pharmacokinetic complications may also contribute to HIV treatment failure. Malabsorption, alterations in drug distribution, and drug–drug and drug–herbal supplement interactions may all cause subtherapeutic antiretroviral concentrations and lead to HIV resistance and ART failure. Pharmacists should be aware of and monitor for these factors and suggest treatment alternatives. Although not routinely recommended, therapeutic drug monitoring may be obtained in specific clinical situations and pharmacists may assist in the interpretation of antiretroviral drug levels.[35,98]

Once ART adherence and pharmacokinetic complications have been assessed, attention should then focus on ART resistance testing. An HIV genotype and other specific medication tests (as needed) should be obtained to determine the presence of viral mutations. Specialized pharmacists involved in HIV care should be fully versed in ordering appropriate resistance tests, including the appropriate timing of particular tests, as well as in interpreting test results. Pharmacists thus serve an important role in the review and interpretation of viral genotypes. This role requires an understanding of primary and secondary mutations, polymorphisms, and the accumulation of mutations to a critical number that will contribute to ART failure. Pharmacists should be familiar with resources available to assist with HIV resistance mutation assessment including the Stanford University HIV Drug Database and International AIDS Society-USA online repository (appendix).[99] With knowledge of the viral genotype, mutation patterns, and associated antiretroviral medications, pharmacists can be a resource for the healthcare team in determining treatment options. Pharmacists should apply the results of genotype testing as well as consider clinical guideline recommendations, ART regimen history, adverse effects, pill burden, and patient preference to provide a new ART regimen for a patient. Pharmacists should be involved in any ART regimen change, with the goals of reestablishing viral suppression and improving the CD4+ T-lymphocyte count.

Pharmacist Involvement in the Management of HIV Disease State Complications

Long-term complications of HIV infection have become an area of focus as patients with HIV live longer. Historically, research and treatment efforts have revolved around antiretroviral-related medication toxicities, and little has been known about the long-term consequences of being infected with HIV. However, recent literature has identified that chronic HIV infection can lead to end-organ toxicities, thrombotic complications, non-AIDS-defining cancers, and metabolic abnormalities.[100] Pharmacists can play a key role in the identification and treatment of these emerging complications.

The mechanism by which HIV infection causes organ toxicity remains unclear. One theory is that the virus causes a prolonged state of immune system activation that can lead to inflammation, endothelial dysfunction, and accelerated atherosclerosis, resulting in organ damage.[101] This prolonged inflammatory state may lead to the generation of free

radicals and oxidative stress in various organs.[102] Another possible mechanism is via a hypercoagulable state that is seen in patients with HIV. Evidence supports a depletion of proteins C and S, leading to enhanced thrombosis and subsequent disease complications.[101,103] The extent of the contribution of the virus itself in these conditions is unknown, and the increased disease incidence may be a combination of the effects of the virus, ART, and the longevity of HIV-infected patients. Organ toxicity, via a variety of mechanisms, may be seen in virtually all organ systems, but most research has been in HIV-associated cardiovascular, renal, hepatic, and neurologic toxicities.

HIV and Cardiovascular Disease. In the cardiovascular system, HIV infection has been linked to coronary artery disease and cardiomyopathy. Cardiovascular disease is now the third-most common cause of death in HIV-infected patients in the United States, and literature has shown that patients with HIV have a greater incidence of myocardial infarction than noninfected patients.[104,105] In addition to myocardial infarction, cardiomyopathy in the form of systolic dysfunction has been seen in 10–20% and diastolic dysfunction in 48% of HIV-infected individuals.[106,107] The mechanism underlying this increase in cardiovascular disease is thought to be a combination of HIV infection, treatment with ART, and the increased lifespan of HIV-infected patients.[105] Known inflammatory markers associated with cardiovascular risk are elevated in HIV disease, leading to chronic inflammation, endothelial dysfunction, and accelerated atherosclerosis and thrombosis.[108] Additionally, adverse effects of ART, specifically protease inhibitors, include metabolic abnormalities such as hyperlipidemia and hyperglycemia that heighten the risk of cardiovascular complications.[109] Pharmacists are vitally important in assisting with the control of risk factors and improving the cardiovascular risk of patients living with HIV.

Pharmacists should be actively involved in controlling the cardiovascular risk factors of patients living with HIV. Pharmacists should recommend annual cardiovascular risk assessments that include a lipid profile, fasting glucose, glycosylated hemoglobin (HbA_{1c}), and blood pressure. Specifically, pharmacists who practice in the ambulatory care setting may advocate for complete care via pharmacist-directed outpatient clinics based on physician collaborative practice agreements. Most research on pharmacist impact has been conducted in pharmacist-managed outpatient lipid, hypertension, diabetes, and heart failure clinics. Within a collaborative practice agreement, pharmacists may conduct risk assessment screening, limited physical examinations, laboratory monitoring, medication adjustments, and patient education. While not specific to the HIV disease state, incorporation of a pharmacist into outpatient clinics has been shown to significantly reduce cardiovascular events, low-density lipoprotein cholesterol, blood pressure, and HbA and improve utilization of mortality-reducing heart failure medications.[110-114] Pharmacist patient care may be conducted by facilitating in-person clinic visits or via telephone consultations.[115] In addition, the benefits of pharmacist management of cardiovascular risk factors in the patient-centered medical home model have been demonstrated.[116,117] Pharmacists practicing in the community setting should recommend routine blood pressure monitoring at all pharmacy visits and assist in appropriate selection and training of diabetes supplies such as glucose meters and test strips.[33] Community pharmacists should perform routine medication profile review and recommend selection of safe and effective over-the-counter medications and herbal products. Pharmacists may also be proactive by recommending and overseeing the use of patient self-monitoring treatment journals documenting changes in blood pressure and glucose control. Finally, inpatient pharmacists may facilitate the increased use of medication prescriptions for cardiovascular risk reduction at hospital discharge. In all practice settings, pharmacists should be familiar with lipid, blood pressure, and blood glucose treatment goals and guidelines and should directly apply those guidelines to assist in decreasing the cardiovascular risk in HIV-infected patients. In addition, pharmacists should routinely monitor and recommend lifestyle modifications, including smoking cessation, diet modification, and exercise adherence, as these have also been shown to decrease cardiovascular risk in patients with HIV.[118-120]

In addition to controlling risk factors, pharmacists should collaborate with the healthcare team to minimize patients' exposure to direct cardiotoxic medications and other medications that have adverse effects on the lipid profile. The use of abacavir, a nucleoside reverse-transcriptase inhibitor, has been linked to a possible increased risk of myocardial infarction.[121,122] While the literature is conflicting regarding this adverse effect, pharmacists should be cognizant of this possibility and recommend alternative antiretroviral therapies as appropriate. In addition, pharmacists involved in HIV management may recommend an ART regimen that may have a less detrimental effect on the patient's lipid profile.[123]

HIV and Renal Disease. HIV infection is associated with nephropathy in the form of acute kidney injury and chronic renal failure.[124] Acute kidney injury has been found to be more common among HIV-infected patients than the general patient population and is associated with poor outcomes.[125] Acute kidney injury presents in many forms, but prerenal failure and acute tubular necrosis are the most common. Postulated mechanisms of HIV-induced acute renal failure include medication-induced toxicities, specifically nephrolithiasis with atazanavir and indinavir, Fanconi's syndrome with tenofovir, and dehydration from opportunistic infections.[125] Pharmacists are vital in the management of HIV-induced renal toxicities and should review the patient's serum creatinine level and urinary analysis results for the development of acute renal toxicity.[33] Pharmacists should readily identify contributing nephrotoxic medications that may compound nephrotoxicity and recommend possible discontinuation and therapeutic alternatives. In addition, pharmacists should be familiar with common medications used in the treatment of HIV that interfere with the tubular secretion of creatinine, such as cobicistat, rilpivirine, dolutegravir, ritonavir, and trimethoprim–sulfamethoxazole.[126] These medications, although not inherently nephrotoxic, may increase the serum creatinine level and complicate the renal assessment of patients taking these antiretroviral medications.

Patients with HIV may also have chronic forms of nephrotoxicity. Perhaps the most widely recognized form of renal failure in HIV disease is HIV-associated nephropathy (HIVAN). HIVAN is most common among patients of African descent and is a significant contributor to chronic renal failure. ART has been shown to aid in the reversal of HIV

nephropathy by suppressing viral replication in the kidneys, and pharmacists should advocate for prompt initiation of ART in these circumstances.[127,128] HIV infection may also enhance other common risk factors for chronic kidney disease, such as diabetes and hypertension. As with cardiovascular toxicity, pharmacists should assist in the management of patients' glucose and blood pressure control and recommend therapies such as angiotensin-converting enzyme inhibitors or angiotensin receptor blockers that are thought to delay the progression of kidney failure.[129,130]

For patients with renal failure, pharmacists should recommend appropriate dosage adjustments of renally eliminated medications, including antiretroviral medications and other medications on a patient's profile (appendix).[35] Active pharmacist involvement in ensuring proper doses of renally eliminated medications has been demonstrated to decrease adverse effects and result in cost savings.[131] Such dosage adjustments are especially important in patients with advanced nephropathy requiring dialysis. Pharmacists should be familiar with various dialysis modalities and their effects on medication removal. Pharmacists should then pair this knowledge with their understanding of the clearance of specific medications by renal elimination to ensure safe and effective medication regimens.

Finally, pharmacists knowledgeable about HIV may recommend ART that minimizes nephrotoxicity, taking into consideration the HIV genotype and laboratory markers of HIV disease. Alteration of a patient's ART to minimize renal involvement can lead to enhanced safety and simplification of the ART regimen. In addition, pharmacists should aim to minimize the renal toxicity of all medications prescribed, with the goal of providing a safe and effective medication profile.

HIV and Hepatic Disease. As with HIV-associated nephrotoxicity, pharmacists should be cognizant of HIV-induced hepatotoxicity. Although the majority of literature revolves around mechanisms such as medication-induced hepatotoxicity, coinfection with viral hepatitis, and alcohol injury, there is some evidence that HIV infection alone may contribute to accelerated liver damage.[132] Pharmacists should routinely monitor liver function tests to detect the presence of hepatic toxicity. If clinically significant elevations in hepatic function tests are detected, pharmacists should identify and assist in limiting all medications that may induce hepatic injury. Many classes of antiretroviral medications have been linked to hepatotoxicity, including nonnucleoside reverse-transcriptase inhibitors and protease inhibitors. Specifically, nevirapine, maraviroc, and tipranavir have boxed warnings for hepatotoxicity, and ART regimens may need to be altered for patients being treated with those medications. If toxicity progresses to advanced liver failure and cirrhosis, pharmacists need to recognize that altered drug metabolism may occur and monitor these patients for medication toxicities and possible treatment failure.[133] Pharmacists should also recommend testing for viral hepatitis, as coinfection has been known to accelerate the decline in hepatic function.[130] Pharmacists may also recognize current alcohol and illicit drug use in patients and facilitate their admission into treatment programs, if necessary.[133] In addition, recognizing that alcohol and illicit drug consumption may alter medication adherence, pharmacists should reinforce the importance of medication adherence and adopt adherence strategies that are acceptable to patients. Finally, pharmacists should recommend hepatic dosage adjustments of medications for which a need for adjustment has been identified (appendix).

HIV and Neurologic Disease. Neurotoxicity and central nervous system disorders are recognized complications of HIV infection. HIV-associated neurocognitive disorders (HAND) include certain neurologic complications of HIV infection, such as mental slowing, memory loss, motor disorders, and behavioral abnormalities.[134] These progressive symptoms lead to a decline in cognitive function that may eventually develop into HIV dementia. HAND complications occur in approximately half of patients diagnosed with HIV and represent a substantial cause of morbidity and mortality.[134-136] Although the known incidence of HAND is high, this estimate may be conservative, as HAND is often unrecognized and may be underdiagnosed. Pharmacists should be alert to symptoms of possible cognitive decline. If such symptoms are recognized, communication and facilitation with the patient's provider are recommended.

Several theories about the mechanism of HAND have been postulated, with most suggesting that the chronic inflammation state caused by HIV infection generates free radicals that inflict neuronal damage. There is no correlation between the development of HAND and HIV plasma concentration, current CD4+ T-lymphocyte count, or the presence of effective ART[134,136]; however, the development of HAND has been associated with a low CD4+ T-lymphocyte nadir.[137] This association reinforces the need for early initiation of ART to prevent low CD4+ T-lymphocyte counts and protect against the development of neurotoxicity. No other therapy has been shown to prevent or improve HAND, so pharmacists can contribute to the care of these patients by focusing on the early and effective utilization of ART.[102,138]

HAND and its complications have serious ramifications on other aspects of HIV care. Decreased neurologic function has been linked to poor patient adherence to ART and other therapies, unemployment, lack of transportation, and increased reliance on financial assistance for medications.[139] Pharmacists should work closely with their patients to create personalized medication adherence programs and provide access to medication assistance programs. Ensuring safe and effective use of medications is the pharmacists' highest priority in caring for these patients.

Other HIV-associated neurologic complications include peripheral neuropathy and ischemic stroke. Peripheral neuropathy is the most frequently reported neurologic diagnosis in HIV-positive patients and usually responds to medications typically used to treat neuropathic pain.[136] Common causes of peripheral neuropathy in HIV-infected patients include neurotoxic medications (such as didanosine), diabetes, alcohol use, and nutritional deficiencies (e.g., low vitamin B_{12} levels). Pharmacists should help to assess patients for the development and progression of peripheral neuropathy and recommend appropriate treatment options.

Hospital admissions for ischemic stroke in HIV-infected patients have increased 43% over the past decade in the United States. The higher incidence of ischemic stroke is thought to be caused by a combination of accelerated atherosclerosis and thrombosis.[101] Pharmacists should play an active role in assisting in the medication selection of acute stroke treatment. Because stroke patients often suffer from dysphagia, necessitating the use of short- and long-term enteral feeding tubes, pharmacists should be familiar with

guidelines for proper administration of medications via enteral tubes (e.g., determining whether a medication may be crushed, the implications of the site of enteral medication absorption) (appendix).[140,141] After patients suffer an acute stroke episode, pharmacists should be involved in assisting in the selection of secondary prevention medications (e.g., antiplatelet and antihyperlipidemic agents) to minimize drug interactions and maximize the safety and efficacy of the patient's entire medication regimen. Pharmacists should also be aggressive in helping manage modifiable risk factors, such as hypertension, diabetes, and hyperlipidemia. The literature demonstrates that interdisciplinary teams including active pharmacist intervention improve management of ischemic stroke risk factors.[142] Pharmacists should encourage intensive management of these risk factors and other lifestyle modifications, such as smoking cessation, exercise regimens, and weight management programs.

In addition to physiological factors, medications are another important consideration in the neurologic state of the patient with HIV. Pharmacists should review the medication profile for all medications that may affect cognitive function, such as opioid narcotics and benzodiazepines. Certain antiretroviral medications, including efavirenz, have also been associated with central nervous system abnormalities. The pharmacist should be alert to and work with the healthcare team to minimize the neurologic adverse effects of medications in patients experiencing HIV-associated neurotoxicity and recommend appropriate therapeutic alternatives.

HIV and Malignancy. AIDS-associated malignancies are a well-documented complication of HIV, but HIV-infected patients also face increased incidence of other cancer types.[143] Collectively, these cancers are termed *non-AIDS-defining cancers* and include cancers such as Hodgkin's lymphoma and malignancies of the lung, kidney, anus, liver, and skin.[144,145] Guidelines for identification of these cancers overall mimic recommendations for the general population; however, some, such as cervical cancer, require more frequent monitoring, and pharmacists should recommend routine cancer screening when appropriate.

Cancer treatment in patients with HIV presents a challenge to pharmacists and practitioners, as the need to balance cancer cure must be weighed against the risk of chemotherapy-enhanced immunosuppression and resulting opportunistic infections. Given their expertise in drug–drug interaction and toxicity management, pharmacists are uniquely qualified to assist in chemotherapy and ART selection. Pharmacists should be knowledgeable in drug interactions between ART and chemotherapy agents and assist with regimen selections for both disease states that minimize toxicity while ensuring efficacy (appendix). In addition, pharmacists can aid in the initiation of appropriate opportunistic infection prophylaxis. Finally, more research is needed on the interaction between cancer, chemotherapy, HIV disease, and ART. Pharmacists should be a key component in future research teams where research is desperately needed to ensure safe and appropriate patient care.

HIV and Endocrine Disease. Patients living with HIV are also at risk for the development of traditional endocrine disorders related to HIV disease, including lipodystrophy, hypogonadism, and HIV wasting syndrome. These conditions are thought to be caused by mitochondrial toxicity and alterations in levels of growth hormone accelerated by adverse effects of antiretroviral medications, specifically protease inhibitors.[146,147] Lipodystrophy consists of an increase in visceral fat and a decrease in subcutaneous fat stores, particularly in the face and extremities.[147] Low levels of testosterone may lead to hypogonadism, sexual dysfunction, and muscle wasting in HIV-infected individuals.[148] Some patients with HIV suffer from HIV wasting syndrome due in part to increased energy expenditure that leads to a decrease in lean body mass and the total body mass index.[149] New agents are being investigated for the treatment of these disorders, and pharmacists caring for patients living with HIV should be knowledgeable about available recommended therapies.[150,151] Specifically, pharmacists may assist in testosterone formulation selection, contraindication assessment, laboratory test monitoring, and counseling on proper testosterone administration and adverse effects.[152-154] Pharmacists should also minimize ART agents that have adverse metabolic effects and recommend appropriate alternatives.[147] In addition, pharmacists should work closely with dietitians to ensure appropriate nutrition support for the complete care of the HIV-infected patient.[154] Morphological complications may have detrimental physical and psychological effects on patients, which may decrease adherence to ART. Pharmacists should be cognizant of morphological complications, recommend medical and lifestyle modifications as appropriate, and work with patients and providers to maximize treatment and adherence to HIV therapies.

In addition to traditional endocrine complications, alterations in bone metabolism have become a significant endocrine complication of HIV. HIV infection leads to earlier and more frequent loss of bone density, leading to increased incidence of osteopenia, osteoporosis, and fractures.[155] Like other chronic HIV complications, this is due to traditional risk factors, the effects of the virus itself, and the use of certain ART agents, specifically tenofovir.[156] Specific screening recommendations have been developed for patients with HIV, and pharmacists should be informed of these recommendations and take an active role in screening patients for this complication.[157] Pharmacists should also be versed on appropriate osteoporosis treatments and recommend vitamin supplementation and pharmacologic therapy when warranted. In addition, pharmacists should aid in recommending nonpharmacologic strategies for prevention of bone loss, including reducing alcohol intake, smoking cessation, and a healthy body weight.

As patients with HIV live longer, more information will emerge regarding the role of chronic HIV disease state complications. What is already evident is that proper recognition and treatment of cardiovascular, renal, hepatic, neurologic, malignant, and endocrine complications are desperately needed to fully care for HIV-infected patients. Pharmacists are integral to the medical team that must care for the whole patient, including the HIV infection itself and long-term complications of HIV disease.

Pharmacist Involvement in Management of Opportunistic Infections

Opportunistic infections contribute significantly to the morbidity and mortality of HIV-infected individuals. Although effective ART has reduced the incidence of opportunistic infections, prevention, recognition, and treatment of those

infections continue to be of utmost importance in this patient population.[158] The complexity of prophylaxis and treatment of opportunistic infections in HIV-infected patients requires an interdisciplinary approach. Pharmacists can be involved in the prevention and treatment of HIV-associated opportunistic infections by providing recommendations on the initiation or discontinuation of opportunistic infection prophylaxis, the recognition and diagnosis of active opportunistic infections, treatment and dosing recommendations for active opportunistic infections, and the timing of ART initiation. Through these interventions, pharmacists play a key role in improving the medication management of individuals with HIV disease.

Pharmacists may first intervene with recommendations for when to initiate opportunistic infection prophylaxis. Medication prophylaxis for various opportunistic infections is offered to individuals with advanced HIV disease. Primary prophylaxis aims to prevent the first occurrence of an opportunistic infection; secondary prophylaxis is geared toward preventing disease recurrence.[159] The decision to initiate prophylaxis is therefore dependent on the patient's CD4+ T-lymphocyte count and the patient's history of an active opportunistic infection. Pharmacists should be familiar with and recommend specific prophylactic agents and alternative regimens for patients with medication allergies. Published guidelines are available that can help pharmacists in making recommendations regarding appropriate prophylactic medications and when to initiate primary and secondary opportunistic infection prophylaxis (appendix).[160]

The recognition of when to discontinue prophylaxis is as important as its initiation. Literature supports the safety of discontinuation of opportunistic infection prophylaxis when the CD4+ T-lymphocyte count rises above a threshold for a defined period of time while on effective ART.[159-161] Pharmacists familiar with discontinuation recommendations may intervene to discourage inappropriate continuation of drug therapy. Discontinuation of opportunistic infection prophylaxis may lead to a decrease in adverse effects and drug–drug interactions, limit drug resistance, lower pill burden, increase rates of adherence, and provide cost savings.[159]

Pharmacists also play a vital role in the recognition and treatment of active opportunistic infections. Pharmacists aid in the diagnosis of opportunistic infections via symptom recognition and testing recommendations. Once a patient is diagnosed, pharmacists can contribute to the treatment of opportunistic infections by offering evidence-based recommendations on antiinfective drug selection and dosing, monitoring medication efficacy and toxicity, preventing and recognizing drug–drug and drug–nutrient interactions, and making literature-based recommendations on total treatment duration.[160]

After an opportunistic infection has been diagnosed and treatment initiated, pharmacists should be active in determining the optimal timing of ART initiation. The decision regarding ART initiation is complex and must weigh the benefits of ART against the possibility of the complication of immune reconstitution inflammatory syndrome. Although some literature has shown that early ART initiation is paramount in improving survival and decreasing AIDS progression by improved immune functioning, other studies have demonstrated that ART may not improve or may perhaps be detrimental in patients with certain types of opportunistic infections.[162-164] Current guidelines provide recommendations on when to initiate ART in patients with specific types of opportunistic infections and can help guide patients, pharmacists, and other healthcare providers in this decision-making process.[160,165] Pharmacists can assist other HIV care practitioners by providing evidence-based recommendations regarding the initiation of ART in the setting of an active opportunistic infection and contributing to the selection of an ART treatment regimen that avoids interactions with the antiinfective medication regimen.

Patients with opportunistic infections are on complex medication regimens and often require hospitalization. Pharmacists practicing in the inpatient setting play a key role in the appropriate care of these patients by preventing and resolving medication-related errors. Patients with HIV experience a high rate of medication errors due to the complexity and alteration of medication regimens, the necessity of transitions of care, and the need for their care to be provided by practitioners who may be unfamiliar with ART and HIV complications.[166] The inpatient setting provides pharmacists a unique venue to make an impact in the care of HIV-infected patients, and the literature has shown that pharmacist involvement specifically in this patient population decreases medication-related errors.[167] Pharmacists should be involved in admission and discharge medication reconciliation, provide patient discharge medication education, and assist with the transition of the patient to outpatient care.

HIV and Immunization. Immunization, as disease prevention, is important in the care of patients with HIV, as immunodeficiency creates enhanced susceptibility to infection acquisition. Pharmacists should be aware of current immunization recommendations for HIV-infected patients and work to ensure appropriate and timely routine immunization (appendix). In addition, pharmacists should be active immunization advocates by facilitating pharmacist-administered immunization programs.

The Advisory Committee on Immunization Practices publishes annual immunization recommendations for all patients, including specific recommendations for those with HIV infection. It is generally accepted that inactivated vaccines are considered safe for HIV-infected patients; some live vaccines may be administered based on a patient's CD4+ T-lymphocyte count. Patients with HIV should be immunized against infections such as influenza, pneumococcus, HAV, HBV, and tetanus/diphtheria.[168] In addition, certain immunizations may require different dosages in HIV-infected patients. Pharmacists should be aware of the immunization status of their patients and provide recommendations regarding safe and effective vaccine administration.

Effective seroprotective antibody levels after immunization are a concern in patients with HIV. Immunization is most effective at high CD4+ T-lymphocyte counts and may be delayed until the CD4+ T-lymphocyte count is above 200 cells/mm^3. There are situations, however, in which delay is not feasible, as patients with HIV may receive pneumococcal vaccination upon HIV diagnosis and an annual influenza vaccination regardless of the CD4+ T-lymphocyte count.[169] In addition, certain live vaccines are now being safely administered if the CD4+ T-lymphocyte count is near normal levels. Pharmacists should aid HIV care providers in the appropriate timing of immunizations to enhance adequate immune response while balancing the safety of vaccine administration.

After determining immunization needs and timing, pharmacists in community and clinic settings may also directly administer immunizations. Pharmacist-managed immunization programs improve access to vaccine administration and corresponding immunization rates.[170] Pharmacist vaccine administration privileges vary by type of vaccine, patient age, and immunization training requirements, so pharmacists should practice in accordance with state and local regulations. Pharmacists certified or licensed in immunization administration should take an active role in immunizing patients with HIV. Documentation of vaccine administration and communication of immunization status to prescribers and other practitioners should be completed to bridge the continuum of HIV patient care.[171]

Pharmacist Involvement in HIV Prevention

HIV prevention requires an interdisciplinary approach involving pharmacists as active members of the healthcare team. Active pharmacist participation in prevention initiatives can help prevent transmission and reduce the rate of HIV infection. Pharmacists play a key role in HIV prevention through both pharmacologic and behavioral interventions.

High viral load is a risk factor for HIV transmission.[35] By reinforcing ART adherence and subsequently lowering a patient's HIV viral load, the risk of HIV transmission can be reduced. The benefits of ART for prevention have been demonstrated in various populations, including pregnant women, HIV-serodiscordant partners, and geographic communities. Because the risk of mother-to-child transmission is strongly associated with a higher HIV viral load, the use of ART in pregnancy has dramatically reduced the incidence of perinatally transmitted HIV infections and is recommended by DHHS guidelines.[42] Decreases in HIV viral load via ART are also associated with decreased heterosexual transmission, as demonstrated in observational studies and randomized trials.[172-175] Based on these results, DHHS guidelines recommend that ART be offered to those at risk of transmitting HIV to sexual partners, including heterosexuals and other risk groups.[35] In addition to the benefits of ART for preventing HIV transmission in serodiscordant couples, data have shown that widespread use of ART may benefit entire communities via reductions in community viral load and decreased numbers of new infections.[176,177]

Medication adherence is the key to maximizing the full benefits of ART. Pharmacist involvement in improving antiretroviral medication adherence is perhaps the most well-documented preventive intervention and, as shown in a systematic review, is associated with statistically significant improvements in adherence and a positive impact on viral suppression.[178] Pharmacist involvement in direct patient care efforts focused on adherence extend well beyond required prescription counseling and may include providing practical and social support to motivate adherence, educating to enhance patient self-efficacy, regularly monitoring adherence, collaborating with other healthcare professionals, recognizing and helping to manage adverse effects, making recommendations regarding self-management, advocating for patients with insurance issues, and instructing on the use of adherence-enhancing tools.[178-180] The DHHS adult HIV guidelines provide evidence-based recommendations on assessing and monitoring adherence and outline strategies to help patients maintain high levels of adherence.[35] Identifying patients with adherence challenges requiring attention and implementing methods to enhance adherence are essential roles for all members of the treatment team, including pharmacists.

Although ART adherence is an essential component of HIV transmission prevention among HIV-infected individuals, it is also a necessary factor for prevention among HIV-exposed individuals taking PrEP or postexposure prophylaxis (PEP). PrEP is the use of antiretroviral medications by higher-risk, uninfected individuals before and during periods of risk to prevent HIV acquisition. Currently, the fixed-dose combination oral tablet of tenofovir–emtricitabine is the only FDA-approved product for PrEP; however, ongoing studies are examining the use of other antiretroviral agents in various dosage forms. When responding to patient inquiries regarding PrEP, pharmacists should be familiar with clinical practice guidelines published by CDC on the use of PrEP in high-risk populations and make informed and appropriate recommendations about PrEP safety, efficacy, acquisition, and need for routine follow-up HIV testing.[181] Pharmacists practicing in community settings that sell barrier methods or who fill prescriptions for PrEP or medications used to treat sexually transmitted infections can help identify patients who may benefit from PrEP and link them to PrEP prescribers in the community. The success of PrEP is largely dependent on high levels of medication adherence. To date, five clinical trials have demonstrated the efficacy of PrEP for HIV prevention in various patient populations, with improved efficacy for adherent individuals.[182-186] Notably, other PrEP studies have been halted early due to futility, primarily attributed to lower medication adherence.[187,188] Pharmacists have the opportunity to assist with developing PrEP protocols for newer prevention modalities, and, with appropriate training and resources, pharmacists can improve patient understanding, promote medication adherence, and enhance PrEP efficacy.[189,190] Pharmacists are well positioned to play a key role in helping patients make choices about PrEP, collaborate with prescribers to manage a patient's therapy, and advocate with other healthcare professionals regarding policy development.

PEP is the short-term use of antiretroviral medications by uninfected individuals after exposure to HIV. CDC has published guidelines for the implementation of HIV PEP after occupational and nonoccupational exposures.[191,192] Effective perinatal ART is also thought of as a form of PEP, and pharmacists are involved in the prevention of mother-to-child transmission of HIV.[193] Opportunities for pharmacist involvement in PEP vary by setting and may include developing institutional protocols, dispensing initial PEP doses, counseling patients on PEP medications, identifying drug interactions, and recommending follow-up testing. An important resource for pharmacists and other healthcare providers is the Clinician Consultation Center, which provides national expert telephone consultation, free of charge, surrounding PrEP, PEP, and perinatal HIV infection (www.nccc.ucsf.edu). The use of antiretroviral chemoprophylaxis for preventing HIV after accidental or occupational exposure and in maternal-to-fetal HIV transmission has become a widely accepted method to combat HIV, and pharmacists can effectively contribute to these initiatives.

HIV testing, in addition to ensuring early entry into care for HIV-infected individuals, is also an effective HIV

prevention strategy. Pharmacists should be an entry point for early testing for HIV; they should recognize HIV risk factors and signs and symptoms of HIV/AIDS and recommend testing, whether it is provided onsite in community pharmacies or as an inhome test. Pharmacists should link individuals who test negative with effective prevention measures, including PrEP. Pharmacists should ensure that patients who test positive have access to medical care.

Decreasing circulation of contaminated syringes in and beyond the intravenous drug user (IDU) community is a central HIV prevention strategy.[194] Pharmacists can play an integral role in HIV prevention and the provision of health services to IDU populations by counseling IDUs regarding syringe access and disposal and addiction treatment programs. The literature documents pharmacist participation in providing and encouraging use of sterile syringes and injection equipment, providing patient counseling on harm-reduction strategies (e.g., substance abuse treatment, safe injection and disposal practices, safe sex practices), and supporting local syringe exchange programs.[194,195] In some areas, IDUs have the option of purchasing syringes from a pharmacy without a prescription. Such policies are controversial, however, and ultimately the decision to sell syringes without a prescription belongs to the individual pharmacist. Pharmacists should be aware of syringe replacement programs in their community and provide appropriate information to IDUs when requested. Providing HIV-related services to IDUs may not only limit HIV transmission but may also present an opportunity to expand healthcare services to a population that is historically underserved and may have limited access to other healthcare services.

Pharmacists should be knowledgeable about behavioral interventions to reduce HIV transmission, though documentation of pharmacists' delivery of behavioral interventions is still nascent. Pharmacists should provide educational messages and materials, advise patients on prevention methods (e.g., condom promotion, safer sex practices, drug-use counseling), and deliver behavioral risk-reduction counseling.

Pharmacists' unique position in society allows them to contribute to HIV prevention efforts. Pharmacist involvement includes both traditional roles (providing ART education and ensuring legal access to sterile needles and syringes) and innovative roles (developing PrEP protocols and delivering behavioral interventions). As HIV prevention becomes increasingly emphasized, pharmacists will play an important role on the healthcare team.

Pharmacist Involvement in HIV Education

Pharmacists are extensively involved in providing education to patients and providers about medication-related care, assessing the patient's readiness and ability to adhere to ART, providing initial or follow-up education on HIV-related disease and complications as well as antiretroviral medications, and evaluating adherence to a therapeutic regimen. Pharmacists perform these tasks within an interprofessional healthcare environment. As medication experts, pharmacists play a role in the education of patients, communities, and healthcare workers.

Central pharmacist roles are patient education and the provision of medication counseling to patients and communities. A recent systematic review documented the positive impact of pharmacist-conducted medication adherence education on clinical patient outcomes.[38] Education about medication indication, dose, route, frequency, potential adverse effects, and the importance of adherence should occur at every patient encounter. For returning patients, medication understanding and adherence should be reassessed not just for antiretroviral medications but for all medications. Through patient educational initiatives, pharmacists can help to ensure optimal pharmacotherapy, adherence, and successful outcomes.

Pharmacists often act as an educational liaison between the patient and the medical provider. The pharmacist's tasks can include helping with the selection of the optimal ART regimen, assisting patients in overcoming adherence issues, counseling patients, identifying and advising on potential drug–drug interactions, recognizing and managing medication adverse effects, and providing information on clinically oriented questions. Because HIV management is complex and involves coordination of multidrug therapies, pharmacists should support providers and assist prescribers and patients in attaining specific disease state goals. Pharmacists have expertise in medication dosing, adverse effects, drug–drug interactions, and medication adherence, and they serve as useful drug information sources for provider and patient inquiries.

Pharmacists practicing in HIV medicine should educate healthcare team members, provide in-service training to healthcare staff, and conduct community seminars for patients, caregivers, and the public on HIV, ART, drug interactions, and adherence. As a leader in HIV medication use, the pharmacist should train colleagues and the next generation of providers by teaching pharmacy students and residents. Trainee education could expand to other health professions, including medical students and residents; nursing students, especially those in advanced-degree programs; midlevel provider students; and allied health professions students as well as those receiving advanced training in the field of infectious diseases. Teaching may be clinical in nature (e.g., experiential rotations) or didactic training in a classroom setting.

Emphasis on the importance of keeping current with the rapidly evolving HIV field is vital for both practicing clinicians and future providers. Whatever the setting, pharmacists should continue to serve as a liaison between patients and providers to remain knowledgeable and credible within the field and to interact with colleagues in the HIV field at an interprofessional level. It is important to stay active and to be part of the exchange of information and clinical experience with other connected providers and trainees.

Pharmacist Social Services Involvement

Access to healthcare, including prescription medications, is a growing problem as the cost of healthcare rises. The cost of medications and copayments are major predictors of adherence to medication therapy regimens.[196-198] Many programs are available to assist with healthcare costs, but eligibility guidelines and application processes can be complicated. Pharmacists are well positioned to assist patients in overcoming these obstacles, making medications more accessible and reducing costs to individuals and healthcare entities.

Pharmacists are in an ideal position to educate patients, monitor adherence with therapy, and help patients work through drug-related problems. Pharmacists should monitor refills—both for availability and for timeliness—and notify the prescriber of any concerns. Pharmacists should know when prior-authorization requirements exist for medications and be able to facilitate approval to prevent delays in medication access for patients.[199] Pharmacists should ensure all antiretroviral medications and medications for opportunistic infection treatment and prophylaxis can be ordered for stock quickly and easily to minimize delays in medication access. Pharmacists can also ensure an adequate stock is available for the most common regimens. Likewise, pharmacists in all settings can play a significant role in medication reconciliation during care transitions.[200] Pharmacists should assist other healthcare providers in providing seamless care transitions (from outpatient care to institutional care, during hospitalization, and at the time of discharge) to prevent medication errors.[201] Pill burden, adverse effects, and demands on time and attention pose considerable obstacles to adherence; helping patients obtain their medications in a timely manner removes one major obstacle.

Pharmacists should assist patients at risk of nonadherence due to limited financial means. Patients often misunderstand available insurance benefits, and pharmacists can support patients by reviewing drug formularies, suggesting cost-effective options, and relaying this information to the prescriber. Pharmacists must know how to access national, state, and local resources. For patients with prescription drug insurance but difficulty affording copayments, or for patients lacking insurance, the pharmacist should confirm all medications are necessary and identify less-expensive alternatives. Many antiretroviral medication manufacturers offer prescription copayment cards that reduce a patient's out-of-pocket costs. Pharmaceutical manufacturers also offer patient assistance programs (PAPs) to ease the financial burden of medications. Eligibility criteria and enrollment requirements for PAPs vary, but they generally include documentation of limited income, lack of prescription drug coverage, and ineligibility for public assistance. Although PAP applications usually require both the prescriber's and the patient's signatures, pharmacists can assist in the application process.[197,198] Pharmacists should also be aware of pharmacies—local or mail order—that offer special generic retail pricing, which is sometimes less expensive than insurance copayments.

Pharmacists should have the knowledge to effectively help low-income patients gain access to national and state-level prescription drug programs for which they may be eligible, including Medicare Part D, Ryan White AIDS Drug Assistance Programs (ADAPs), and Medicaid. Medicare Part D is designed to offer the beneficiary a choice between prescription drug plans, and many pharmacists offer Part D plan selection assistance to help beneficiaries obtain optimal drug coverage.[202] ADAPs are available in each state, guaranteeing antiretroviral medication prescription assistance to low-income, underinsured, and uninsured HIV-infected patients. The Patient Protection and Affordable Care Act will expand health insurance program eligibility and provide opportunities for pharmacists to assist with care coordination and expand their scopes of practice.[203] Although pharmacists cannot choose prescription drug plans for patients, pharmacists should serve as a resource to help patients understand their options to ensure continued access to antiretroviral medications.

Pharmacist Professional Involvement

Although pharmacists have a role in direct HIV patient care, there are other ways pharmacists can assist the HIV patient population. Pharmacists should be active in extracurricular professional involvement, which can be achieved via organizational membership, HIV pharmacist certification, advocacy initiatives, volunteer positions, and participation in clinical research. These areas represent possible opportunities for pharmacists to supplement clinical roles.

In recent years, HIV-focused professional organizations have expanded to include pharmacist membership. State and regional AIDS education and training centers have embraced pharmacist involvement and many provide education, networking, and faculty appointments for pharmacists involved in HIV care. On a national scale, the American Academy of HIV Medicine encourages pharmacist membership and invites pharmacists to serve as active members in organizational leadership and committees. Several national HIV organizations also have pharmacist-specific registration, programming, and continuing-education credit opportunities at their educational conventions. Internationally, the Canadian HIV/AIDS Pharmacist Network strives to connect pharmacists involved in HIV care and provides educational information to its members. In addition, the International Association of Providers of AIDS Care has expanded to recognize pharmacists as part of the HIV treatment team. Pharmacists involved in HIV care should strive to be active members of professional organizations, attend organizational meetings, provide meeting lectures on HIV clinical updates, participate in the sharing of HIV information via pharmacist networks, and support enhanced pharmacist membership in these organizations (appendix).

The creation of pharmacist HIV credentialing programs highlights the importance of having pharmacists knowledgeable about and trained in the treatment of HIV disease. The American Academy of HIV Medicine HIV Pharmacist credential (AAHIVP) is offered to pharmacists who have completed certain requirements, such as evidence of direct HIV patient care, HIV continuing education, and successful completion of the AAHIVP credentialing exam.[204] Other institutions also offer specific pharmacist HIV certificate programs. Pharmacists should investigate certification opportunities, seek the knowledge and skills necessary to be certified HIV pharmacists, and lead the pharmacy profession in the care of HIV-positive patients (appendix).

Pharmacists should also be aware of local and national policy issues surrounding HIV care. The world of HIV changes rapidly, and many challenges require legislative or regulatory action. Pharmacists should be advocates for HIV patients by being familiar with current HIV legislation and national HIV programs such as the Ryan White Program. Pharmacists should also contact local and national policymakers to ensure proper education about HIV issues, be involved in HIV advisory panels, provide expert testimony, and participate in advocacy initiatives to assist in the development of laws that best serve HIV patients. Through these opportunities, pharmacists can steer policy development and actively advocate for HIV patients.

There are also many opportunities for pharmacists to volunteer for HIV-related activities. Locally, pharmacists can volunteer in their communities by participating in fundraising events such as AIDS walks, auctions, and other functions in which proceeds go to fund local HIV programs. Many communities are in need of pharmacists to serve in free medical and dental clinics, where underserved patients receive access to much-needed HIV care. Pharmacists can also choose to volunteer outside of their communities through programs such as Doctors Without Borders that focus on delivering HIV care and medications to developing countries.[205] There are numerous volunteer opportunities that benefit HIV patients outside of medical settings, and pharmacists should dedicate time to serving in these capacities.

Finally, pharmacists should play an active role in HIV clinical research. Pharmacists should be knowledgeable about ongoing clinical research trials on topic areas such as new antiretroviral medications, disease state complications, and prevention strategies that will shape the future of HIV care. Pharmacists can serve in a variety of capacities as part of HIV clinical research teams, as principal or coinvestigators, in the recruitment and obtaining the consent of trial participants, and in facilitation of clinical research trials within their practice settings.[206] Permissible scope-of-pharmacist involvement in clinical research varies by state, and pharmacists should be familiar with laws that define pharmacist activity. Pharmacists may also be involved in research by publishing case reports, serving on institutional review boards, acting as consultants in HIV clinical research trials, and serving as research mentors to other practitioners caring for patients with HIV. With over 30 antiretroviral medications available and more in the investigational pipeline, pharmacists can have an integral role in facilitating the introduction of safe and effective HIV medications and clinical research.

Pharmacist involvement in the care of the HIV patient extends beyond the bedside to include other types of professional activity. Through organizational membership, HIV pharmacist certification, advocacy initiatives, volunteer positions, and participation in clinical research, pharmacists should be true advocates in all aspects of HIV patient care. Pharmacists are a tremendous resource that should be mobilized, and each pharmacist has a responsibility to be an active proponent for the advancement of HIV care.

Conclusion

HIV medicine is a dynamic field that has evolved dramatically since its inception. It continues to evolve today, providing both opportunities for and challenges to delivering optimal patient care. These challenges and opportunities should be met with interprofessional efforts that identify and optimize the roles of all healthcare team members, including pharmacists, as a means to provide comprehensive care and improve patient outcomes. Pharmacists in particular are uniquely capable of contributing to all components of HIV care by being highly accessible to both patients and providers in a variety of healthcare settings. Their expert drug therapy knowledge and clinical skills provide an avenue for proficient clinical consultation with other healthcare providers as well as effective patient interactions through counseling and education. Furthermore, given their training and skills set, pharmacists are well positioned within the interdisciplinary healthcare team to help meet the current and future challenges of HIV medicine, including helping to deliver comprehensive primary care to an aging HIV patient population as well as working with others to identify and manage the long-term complications of HIV infection and ART. Given the ongoing evolution of HIV medicine, pharmacists must continue to evolve their roles as a part of the healthcare team to identify and meet the future needs of HIV-positive patients. This goal can be achieved through continuous assessment of the role of the HIV pharmacist, the development and maintenance of HIV specialty pharmacist training programs and expert certification, and the continued collaboration with other healthcare providers, patients, activist groups, and professional HIV medicine and pharmacy organizations.

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Appendix—Additional Sources of Information

Website Resources

General HIV Care and Treatment Information

- U.S. Department of Health and Human Services AIDSinfo website (www.aidsinfo.nih.gov)
- Clinical Care Options HIV – in Practice (www.inpractice.com/Textbooks/HIV.aspx)

Clinical Practice Guidelines and Recommendations

- U.S. Department of Health and Human Services AIDSinfo website (www.aidsinfo.nih.gov)
- International Antiviral Society- USA (www.iasusa.org/guidelines)
- World Health Organization (www.who.int/hiv/pub/guidelines/en/)
- European AIDS Clinical Society (eacsociety.org/Guidelines.aspx)

Antiretroviral Information (Drug Interactions, Renal/Hepatic Dose Adjustments, and Crushing/Liquid Formulations)

- U.S. Department of Health and Human Services AIDSinfo website (www.aidsinfo.nih.gov)
- University of Liverpool Drug Interaction Database and Mobile Application (www.hiv-druginteractions.org/)
- Toronto General Hospital Immunodeficiency Clinic website (www.hivclinic.ca/main/drugs_interact.html and www.hivclinic.ca/main/drugs_extra.html)
- HIV Insite (hivinsite.ucsf.edu)
- Clinician Consultation Center, Antiretroviral Drug Tables (nccc.ucsf.edu/clinical-resources/hiv-aids-resources/pharmacy)
- Florida/Caribbean AIDS Education and Training Center Antiretroviral Therapy Pocket Cards (www.fcaetc.org/treatment-guidelines.php)

HIV Resistance Testing and Mutations

- HIV Drug Resistance Database – Stanford University (www.hivdb.stanford.edu)
- International Antiviral Society – USA (www.iasusa.org/resistance_mutations/mutations_figures.pdf)

Immunizations

- Centers for Disease Control and Prevention (www.cdc.gov/vaccines/schedules/hcp/index.html)

Professional Organizations

- American Academy of HIV Medicine (www.aahivm.org)
- British HIV Association (www.bhiva.org)
- HIV Medicine Association (www.hivma.org)
- International Association of Providers of AIDS Care (www.iapac.org)
- International AIDS Society (www.iasociety.org)

Information Exchange

- The Canadian HIV/AIDS Pharmacists Network (hivclinic.ca/chap)
- National AIDS Treatment Advocacy Project (natap.org)
- American College of Clinical Pharmacy, HIV Practice and Research Network (www.accp.com/about/prns.aspx)

Clinical Trials

- U.S. Department of Health and Human Services AIDSinfo website (www.aidsinfo.nih.gov)

Hotlines and Clinical Consultation

- Clinicians Consultation Center (nccc.usf.edu)
- Pre-Exposure Prophylaxis (855) 448-7737
- Post-Exposure Prophylaxis (888) 448-4911
- HIV/AIDS Management (800) 933-3413
- Perinatal HIV/AIDS (888) 448-8765

HIV Certificate and Credentialing Programs

- American Academy of HIV Medicine, HIV Pharmacist Credentialing (www.aahivm.org/about)

- University of Buffalo School of Pharmacy and Pharmaceutical Sciences (tdm.pharm.buffalo.edu/hiv_cert_main)

Continuing Education for Pharmacists

- Clinical Care Options – HIV (www.clinicaloptions.com/HIV.aspx)
- International Antiviral Society – USA (iasusa.org)
- American Academy of HIV Medicine (aahivm.org)
- AIDS Education and Training Centers (aidsetc.org)

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