ABSTRACT

The complexities of HIV management present opportunities for pharmacists to become involved in managing multiple-drug therapies, in addition to providing counseling and interventions to enhance medication adherence among patients with HIV infection. There is a range of areas within integrated health systems where pharmacists have become extensively involved in HIV care, including inpatient and outpatient centers. In focusing on the role of the pharmacist in the management of HIV, this article portrays the activities of several HIV pharmacy practices, which include participation in multidisciplinary medical rounds; providing drug information, medication counseling, and compliance education; monitoring of drug therapy; and identification of drug-related problems. The article also reviews common barriers to medication adherence and spotlights medication adherence programs that reach treatment-naive and treatment-experienced patients. In running these programs, pharmacists utilize various adherence tools, such as medication “maps” (organized medication administration schedules), beepers that remind patients to take medications on time, pill planners, and close follow-up. Patients attend several sessions, in which pharmacists develop therapy goals, provide education and counseling on HIV treatment, individualize highly active antiretroviral therapy regimens, assess adherence with ongoing treatment, and suggest ways of managing adverse effects. Also included in the article are practical tips that pharmacists can use in educating patients about HIV medications, in addition to explaining the role of the pharmacist as a liaison between the pharmacy service and other healthcare providers.

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ROLE OF THE PHARMACIST IN A HOSPITAL SETTING

Once perceived as nothing more than distributors of medication, pharmacists have come a long way from the days of count, lick, and pour. This progression is especially evident in the hospital setting, where pharmacists no longer simply enter medication orders and fill carts. They are becoming further removed from physical dispensing and more heavily involved in all aspects of patient care. Just recently, a report published in the Archives of Internal Medicine captured the numerous clinical responsibilities of pharmacists and their impact on patients. Through a systematic review of peer-reviewed literature published between 1985 and 2005, investigators examined the effects of clinical pharmacist-driven interventions on processes and outcomes relating to the care of hospitalized adults. After evaluating 36 studies, the authors concluded that interacting with the healthcare team on patient rounds, interviewing patients, reconciling medications, and providing patient discharge counseling resulted in reductions in adverse drug events, medication errors, and length of stay, in addition to improvements in medication adherence, knowledge, and appropriateness.

In examining the therapeutic areas where a hospital pharmacist would be most useful, few disease states would surpass HIV/AIDS in their requirements for pharmacy support. With the basic pathophysiology and immunology of HIV infection evolving on a regular basis and the US Food and Drug Administration averaging 1 new antiretroviral agent approval per year, it is a challenge for many healthcare providers to keep abreast of the latest strategies for treating HIV infection and its concomitant conditions. The task of managing drug interactions alone requires extensive time and pharmaceutical knowledge because one must consider interactions between antiretroviral agents and drugs used to treat opportunistic infections, between antiretroviral agents and drugs used to treat non–HIV-related comorbidities, and among the antiretroviral agents themselves. Failure to recognize these interac-
tions may result in additional or exacerbated adverse effects, nonadherence, therapeutic failure, or irreversible drug resistance. Patients with HIV infection require extraordinary counseling and education, especially on adherence and ways of recognizing and coping with long-term adverse effects of therapy. These complexities present special challenges and opportunities for pharmacists to become involved in managing multiple-drug therapies and providing counseling and interventions to enhance medication adherence among HIV-infected patients. There is a range of areas within integrated health systems where pharmacists have become extensively involved in HIV care and have made a significant difference.

Coinciding with the advent of highly active antiretroviral therapy (HAART), the treatment of HIV infection has changed considerably over the past 10 years. Essentially, hospitalizations have declined, hospital wards devoted exclusively to patients with HIV infection have closed, and treatment has shifted to the outpatient setting. Consequently, inpatient healthcare providers may not obtain the experience necessary to properly prescribe and manage antiretroviral regimens. Therefore, the pharmacist can be a tremendous asset in properly managing the acute care of hospitalized patients with HIV. In 1 published analysis, a pharmacist at a 400-bed teaching institution was assigned to monitor all adult patients with HIV infection who were admitted during a 5-month period. The pharmacist evaluated the accuracy and appropriateness of these patients’ orders and looked for dosage errors and potential drug interactions. Of the 68 interventions recorded during that time, 93% were accepted by prescribers. Interventions involved drug-drug or drug-food interactions, underdosing, overdosing, ordering the wrong drug, omission of a medication that the patient was taking before admission, therapeutic duplication, inappropriate antiretroviral regimens, and the addition of prophylaxis for Pneumocystis jiroveci pneumonia. Protease inhibitors were associated with 42% of the interventions, with the most frequently intervened drugs being indinavir, saquinavir, and zidovudine. Researchers concluded that the pharmacist had a substantial impact on hospitalized patients with HIV and that a similar program should be possible in most hospitals.

With the dramatic decrease in opportunistic infections brought about with HAART, the care of patients with HIV has largely been transferred to the outpatient setting. As a result, many hospital pharmacists who received much of their training and experience in HIV care on the inpatient side have followed their patients to hospital-run ambulatory centers, many of which have incorporated pharmacy clinics. Pharmacists in HIV clinics are frequently part of a multidisciplinary team consisting of physicians, nurses, social workers, and other health professionals. They often provide drug information, medication counseling, and compliance education; monitor patients’ response to therapies; identify drug-related problems; and document interventions. For example, at the Veterans Affairs Medical Center in Providence (VAP), the pharmacy and therapeutics committee realized the need for controlling the prescribing and dispensing of antiretroviral agents, in addition to the necessity for detailed patient counseling. Therefore, a pharmacy clinic was added to VAP’s physician-directed infectious diseases clinic, and the pharmacy-driven interventions were recorded and analyzed. A total of 70 patients received pharmaceutical services during the 4-year period, with each patient receiving an average of 7 medications and 2 interventions. The most common interventions were medication counseling, recommendations for monitoring parameters, and prescription processing. It was concluded that pharmacists’ interventions and direct patient care at an HIV clinic effectively ensured patient adherence to treatment and provided clinical benefits for patients.

In attempting to standardize the care that pharmacists provide in HIV clinics, one practice devised a pharmacy progress note that is filled out every time a pharmacist sees a patient on a triple-antiretroviral cocktail. In completing this form, the pharmacist is prompted to gather specific information, including all medication and homeopathic preparations, new therapies, new opportunistic infections, daily fluid intake if the patient is taking indinavir, adherence, and patient satisfaction with therapy. There are also sections that prompt the pharmacist to consider ordering routine laboratory tests such as viral load, CD4+ lymphocytes, complete blood count, liver function tests, and blood glucose. After collecting and analyzing the data, the pharmacist formulates and records a patient assessment and plan, which he discusses with the patient and the physician. Because the pharmacist’s progress note becomes a permanent part of the medical record, other caregivers in the hospital and clinics can also access the information.
IDENTIFICATION AND ASSESSMENT OF BARRIERS TO ADHERENCE

At this point, the association between the lack of adherence and drug resistance or therapeutic failure is well known. Suboptimal administration of antiretroviral agents allows HIV to replicate at an accelerated rate, selecting for viral mutations, which leads to drug resistance and therapeutic failure. Once resistance develops to 1 antiretroviral agent, extensive cross-resistance to other agents within the same class can develop rapidly, severely limiting therapy for compliant and noncompliant patients. Although the exact degree of adherence needed to ensure successful outcomes from drug therapy is not fully known, a landmark study by Paterson et al found that patients must take 95% of their doses to maintain drug levels that will achieve viral suppression, prevent drug resistance, and avert treatment failure. This adherence rate is considerably higher than that required for other chronic diseases, such as hypertension, in which approximately 80% adherence is sufficient to achieve therapeutic goals. Complicating the matter further is the perception among physicians that patients are more adherent than they actually are. A healthcare professional's assessment of a patient's ability to adhere to a medication regimen is a notoriously poor predictor of actual adherence. In a study examining the rate of discordance between patient-reported and physician-estimated adherence with antiretroviral therapy, investigators found that of the 111 studied patients, physicians did not correctly estimate patient-reported adherence to HAART in more than one-third of patients.

Causes of nonadherence are multifactorial and commonly include mental illness (particularly untreated depression), unstable housing, active substance abuse, and major life crises. One study found a direct correlation between the number of lifetime traumatic events, including physical and sexual abuse, and antiretroviral nonadherence. Considering the many adverse effects associated with antiretroviral therapy and the necessity for lifelong treatment, it is not surprising that many patients with HIV infection stop or reduce the dose of medication because of adverse effects. A study looking at the types of reported side effects that are predictive of nonadherence found that nausea, anxiety, confusion, vision problems, anorexia, insomnia, taste perversion, and abnormal fat distribution were significantly associated with nonadherence.

The frequency of moderate/severe side effects in nonadherent patients ranged from 3.6% to 30%. Another study examining nonadherence among patients with HIV found that those who experienced at least 1 severe medication-related symptom were more than twice as likely to report intentional nonadherence. Similarly, each additional symptom that required clinical action was associated with a 25% increase in the risk of intentional nonadherence. Other factors that negatively affect adherence include increased frequency of drug administration, dietary restrictions, and increased pill burden.

Sometimes, the barrier to adherence is the hospital itself, particularly places that allow clinicians to initiate antiretroviral therapy in newly diagnosed, treatment-naive inpatients. Although their intentions are commendable, these acute care physicians do not always consider critical factors required for continuity of care, such as how the patient will pay for medication after discharge and who will follow clinical progress to ensure appropriate therapy and medication adherence. Because hospitals cannot provide the intense follow-up required for newly diagnosed HIV-infected patients, many institutions have developed policies against initiating antiretroviral therapy in inpatients. Instead, hospitals will often refer patients to dedicated outpatient HIV clinics. Many hospitals will also withhold antiretroviral agents in newly admitted patients for various reasons (Table 1).

HOSPITAL PHARMACISTS LEND STRUCTURE AND SUPPORT TO PATIENT ADHERENCE

Given the rigors of near-perfect adherence with antiretroviral therapy, there is limited room for error in

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Table 1. Reasons to Stop HIV Medications in Hospitalized Patients

- Unable to tolerate oral medications
- Adverse reactions
- Elective surgery—especially if medications should be taken with food
- Not taking HIV medications regularly prior to admission
- Patient refusing HIV medications
- Drug interactions with needed acute medications
- Hospital does not have the entire regimen available—NEVER GIVE PARTIAL REGIMENS
ensuring that patients take all their prescribed doses appropriately. Therefore, most HIV pharmacy services have an organized and standardized program that reaches treatment-naïve and treatment-experienced patients. At the VAP, pharmacists counsel patients on their new therapies, call them 1 week after their therapy has begun to assess tolerance and adherence, and see patients at the clinic regularly for follow-up. Adherence is continually assessed by conducting patient interviews, using permissive language to encourage an honest report, and reviewing refill records in the pharmacy computer database.9

At the Christiana Care Health Services HIV program, a clinical pharmacy specialist runs a medication adherence program that provides education and counseling for patients beginning HIV therapy, patients requiring changes in HAART, and patients with long-standing adherence problems.25 Table 2 outlines the protocol for patients referred to this program. Time is taken to fully educate a newly diagnosed patient about HIV, including the benefits and adverse effects of HAART. Adherence tools, such as medication “maps” (organized medication administration schedules), beepers that remind patients to take medications on time, pill planners, and close follow-up, can improve patients’ adherence with complicated medication regimens.25

Patients who have never taken antiretroviral agents initially attend medication readiness assessment visits, where pharmacists develop therapy goals, in addition to providing education and counseling on HIV treatment. Patients are evaluated for the presence of psychosocial barriers to medication adherence and HAART is individualized based on factors such as total number of pills, food restrictions, confidentiality in taking pills, and tolerance for potential adverse effects.25 Once deemed candidates for HAART, patients are scheduled for a “medication start” session, in which a pharmacist offers adherence tools and discusses dosages, precautions, and adverse effects of antiretroviral therapy. Two weeks after the initiation of antiretroviral therapy, patients return for a “medication check” session at which adherence is assessed by pill counts and patient self-report.25 This visit gives pharmacists the opportunity to detect any problems in adherence and to suggest ways of managing adverse effects or other problems before the drugs must be discontinued. The pharmacy team then monitors adherence on an ongoing basis with follow-up telephone calls, additional medication checks (if needed), and the tracking of prescription refills. More intensive weekly pill planner visits are useful for patients recently diagnosed with opportunistic infections and those

<table>
<thead>
<tr>
<th>Visit</th>
<th>Goals</th>
<th>Follow-up</th>
<th>Laboratory Tests Ordered</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial nurse interview and office visit</td>
<td>Assess patient’s ability to comply with complex medication regimen, evaluate psychosocial and insurance issues</td>
<td>Next available appointment</td>
<td>Baseline per clinic standard</td>
</tr>
<tr>
<td>Office visit and initial adherence visit</td>
<td>Begin all agents simultaneously, educate patient about medication and treatment goals</td>
<td>2-week follow-up appointment at medication adherence clinic</td>
<td>—</td>
</tr>
<tr>
<td>Medication adherence clinic with pharmacist</td>
<td>Assess patient adherence to regimen and use of adherence tools, educate patient about medication and treatment goals</td>
<td>2-week follow-up appointment at office visit</td>
<td>—</td>
</tr>
<tr>
<td>Office visit</td>
<td>Assess patient adherence to regimen, follow up as needed for additional adherence issues</td>
<td>1–3 months, based on patient needs</td>
<td>CD4+ T-lymphocyte counts and HIV PCR quantitation, any baseline values not previously ordered</td>
</tr>
</tbody>
</table>

PCR = polymerase chain reaction.
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with long-standing difficulties with adherence. In demonstrating effectiveness of the adherence program, a retrospective chart review of 80 patients found that patients receiving at least 1 educational session from clinical pharmacists refilled their medications in a more timely manner than those who did not attend (31 vs 50 days). A more extensive 12-month retrospective review showed that the group of patients attending the medication adherence clinic had a statistically significant decrease in viral load within 6 and 12 months after initiating therapy, compared with those who did not attend the clinic.

The impact of an HIV clinical pharmacist on antiretroviral adherence in treatment-experienced patients was recently evaluated in a retrospective study conducted at Kaiser Permanente in Northern California. In comparing patients who had exposure to an HIV clinical pharmacist (n = 1049) with those who had not (918), researchers found that the exposed group had better medication adherence, greater declines in viral load, and less hospital days and office visits. They concluded that an HIV clinical pharmacist is associated with improved adherence, virologic control, and utilization measures in antiretroviral-experienced patients.

In looking at the types of intervention strategies that have been known to improve antiretroviral adherence, a systematic review of the literature and ongoing studies have identified several innovative aids, such as handheld devices, 2-way pagers, and alarmed medication vials. Medication refill tools can have a significant impact on antiretroviral refill adherence. In a retrospective study of 110 HIV-infected patients receiving standard antiretroviral regimens for 3 or more months, patients who obtained refills via pill organizers dispensed by a pharmacist had higher adherence rates compared with those obtaining ordinary refills (80% vs 91%). Specific steps that pharmacists can take to promote adherence include developing a daily medication administration schedule that accommodates the patient’s sleep, work, and meal schedules; providing memory aids for medication taking; recruiting an adherence coach; and educating and motivating patients and caregivers. To ensure a consistent supply of antiretroviral medications, patients must be counseled to plan for medication refills so that they are never without these medications.

**Pharmacists Educate Patients About the Safety and Appropriate Use of Medication**

To improve the education of patients with HIV about the many aspects of their treatment, the AIDS institute at the New York State Department of Health and Johns Hopkins University have collaborated to develop an HIV clinical resource Web site that offers pharmacists practical tips for counseling patients. To ensure appropriate use of antiretroviral therapy, pharmacists are encouraged to discuss HIV management with patients, even if it duplicates the prescribers’ discussions. Additionally, visual aids can be used to demonstrate the relationship between poor medication adherence and antiretroviral resistance to help patients understand the importance of taking their HAART regimens as prescribed. This Web resource underscores the fact that patients may not adhere to their regimen if adverse effects are not adequately managed or alleviated. Therefore, pharmacists must take the time to thoroughly educate patients about potential drug toxicities, assess for the presence of any adverse effects, and assure patients that these toxicities are being monitored and addressed by their prescribers. Patients may see their pharmacists more often than they see their healthcare provider; thus, some patients may initially report problems with adverse effects to their pharmacists and not to their prescriber. This provides pharmacists with the opportunity to contact prescribers and advise them on the management of these ill effects. In an effort to avoid premature discontinuation of an antiretroviral agent, the patient should be informed that many toxicities subside a few weeks after initiating therapy.

Reviewing the medication profile and asking patients insightful questions are essential in ensuring that antiretroviral therapy is used appropriately. At every visit to the pharmacy, the patient’s medication profile should be reviewed for new drugs (including over-the-counter medications and herbal/alternative therapies), medication changes, missed refills, and medication-related problems. If the pharmacist has questions about a patient’s medication profile that the patient cannot explain, he should contact the prescriber for clarification. Table 3 includes a list of essential counseling points for patients receiving new prescriptions and some open-ended questions that can be used to determine areas where more education is needed for patients who have been taking the same regimen for some time. Another way to help patients
take their antiretroviral regimens appropriately is to offer a written medication schedule tailored to their particular regimen. The pharmacist can help patients determine the most appropriate times to take medication while considering individual daily routines, drug-food interactions, and potential drug-drug absorption-related interactions. Stickers with pictures of antiretroviral agents may help patients who have difficulty remembering drug names and distinguishing between drugs to remember to take their medications correctly and on schedule. Using multilingual staff and providing written materials in the language that is most prevalent in the patient population will help ensure appropriate use of antiretroviral regimens in many HIV-infected people who speak English as a second language or do not speak English at all.31

**HOSPITAL PHARMACIST AS A LIAISON BETWEEN THE PHARMACY SERVICE AND OTHER HEALTHCARE PROVIDERS**

One study estimated that 20,000 to 100,000 physicians, nurses, pharmacists and other core clinical staff were needed to meet the World Health Organization’s target of treating 3 million people with HIV infection by the end of 2005.32 Besides offering an indication of the girth of workforce required to manage the HIV population, this statistic underscores the essential need for a conglomerate of healthcare providers to deliver the wide scope of required HIV services. In meeting the complex goals of HIV therapy, pharmacists have a professional obligation to work collaboratively with patients, family members, physicians, nurses, case managers, and social workers. The pharmacist can play a pivotal role in bringing everyone together to manage not just the patient’s principal diagnosis of HIV, but also many other associated needs including nutrition support, diarrhea, electrolyte imbalances, pain, depression, other quality-of-life needs, and even socioeconomic issues. In addition to collaborating with physicians on patient rounds, pharmacists also work together with hospice caregivers and volunteer community service organizations to improve overall patient care. They also communicate with payers to resolve issues that may impede access to medication therapies.2 Pharmacists can be instrumental in referring patients to psychologists, psychiatrists, social workers, case managers, and chemical-dependency providers or support groups (e.g., Alcoholics Anonymous or Narcotics Anonymous). Educating the community about HIV transmission and prevention are other ways of collaborating with providers.

Having a centralized pharmacy satellite can substantially improve communication between pharmacists and other healthcare providers. A study evaluating whether decentralization of pharmaceutical services to the HIV clinic would lead to improved collaboration between pharmacists and other healthcare professionals found that a pharmacy satellite enabled healthcare professionals to understand the pharmacy’s way of working and increased trust in the pharmacy staff. Hence, collaboration was developed between the professions, leading to a consistent way of informing patients about their HIV drugs.33

**CONCLUSIONS**

By providing comprehensive pharmaceutical care and ensuring adherence to complex treatment regimens, pharmacists play a critical role in the direct and indirect care of HIV-infected patients. In the hospital setting and the outpatient setting, pharmacists are actively involved in the day-to-day management of HIV-infected patients through identification of problems, including incorrect dosing and drug interac-

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Table 3. Essential Counseling Points for Patients Receiving New Prescriptions

<table>
<thead>
<tr>
<th>Topics to cover:</th>
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<tbody>
<tr>
<td>• Name of medication (brand name and generic name)</td>
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<tr>
<td>• Purpose of medication</td>
</tr>
<tr>
<td>• Strength of medication</td>
</tr>
<tr>
<td>• Dose (number of tablets, capsules, etc)</td>
</tr>
<tr>
<td>• Frequency</td>
</tr>
<tr>
<td>• Food requirements/restrictions</td>
</tr>
<tr>
<td>• Common side effects/toxicities</td>
</tr>
<tr>
<td>• Storage</td>
</tr>
<tr>
<td>• Missed dose instructions</td>
</tr>
<tr>
<td>• Special instructions (including potential for drug interactions)</td>
</tr>
<tr>
<td>• Under what circumstances to call patient’s prescriber</td>
</tr>
</tbody>
</table>

Questions for patients who have been taking the same regimen for some time:

• What medications and doses are you taking?
• What time of the day do you take your medication?
• What do you do when you miss a dose?
• What kinds of problems are you having with your medication?

tions. They provide extensive education for patients and prescribers. Additionally, pharmacists serve as effective liaisons between other healthcare providers in the multidisciplinary treatment of HIV/AIDS.

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