Medical Assessment and Treatment for Persons with HIV/AIDS

Treating HIV/AIDS is extremely complex. It can be difficult to keep abreast of the latest recommendations for the care of HIV-infected individuals at a time when knowledge of the nature and course of HIV infection is changing quickly. Therefore, it is important to seek out qualified physicians who have a history of providing services to HIV-infected individuals. This chapter is designed to assist clinicians and medical staff in providing effective medical assessment and treatment of their HIV-infected substance-abusing clients.

It is important that the medical care team have experience with substance-abusing clients because the combination of substance abuse and HIV/AIDS poses special challenges. Practitioners who do not understand the nature of substance abuse may be hesitant to prescribe potent antiretroviral therapy, fearing that substance abusers will not take the medications correctly. There are also special physical considerations for substance abusers. For example, injection drug use (IDU) is associated with very high rates of hepatitis B and C, which can damage the liver. Some medications used to treat HIV/AIDS and its complications can affect treatment for hepatitis, and their use should be planned carefully. Many HIV/AIDS treatment drugs are processed through the liver, and their effects can be either increased or decreased because of hepatitis or chronic alcohol use.

If there is no specialized practice available to the client, alcohol and drug counselors should establish a relationship with a specialty group that can be consulted by the medical care team. The most crucial time for consulting a specialist is when the client is starting, stopping, or changing HIV/AIDS treatment.

Adherence to Medical Care

There is little doubt that adherence to antiretrovirals plays a more important role in long-term outcome than does choice of antiretroviral medications. A client who adheres to the medications will likely have a better outcome, and adherence also is important for preventing the development of drug resistance. Many barriers prevent HIV-infected substance abusers from receiving appropriate, timely medical care (see the section, "Barriers to Care for HIV-Infected Substance Abuse Disorder Clients"). However, once in treatment, their compliance may not be worse than that of other HIV-infected clients (Broers et al., 1994). A client's belief in the effectiveness of anti-retroviral therapy is positively associated with adherence to treatment (Samet et al., 1992). This shows how important it is to educate clients and include them in all aspects of the treatment process. Although a long-term relationship with a provider is based on trust, continuity and availability will also make it more likely that clients take their medications properly.

Health care providers seldom can predict which clients will comply with complex medication schedules. Primary care providers should be aware, however, that a client's relapse into substance abuse is likely to result in noncompliance with medical care. It is important that linkages be maintained between primary care and substance abuse treatment providers so that primary care providers are aware of relapses when they occur; however, it is also important to remember

confidentiality rules (see Chapter 9 for more information). Other factors may prevent clients from taking medications as prescribed, such as living in an institution (e.g., a halfway house, homeless shelter, or prison). Psychiatric disorders among drug abusers may also hamper adherence (Ferrando et al., 1996).

Techniques to achieve optimal compliance among HIV-infected clients include the following:

- Simplify drug regimens--twice a day should be the goal.
- Repeat instructions.
- Use written protocols where doses coincide with habits or normal schedule.
- Use a timing device to ensure that medications are taken at the proper time.
- Use lists that clients can post in highly visible places.
- Give positive feedback: provide evidence of effectiveness, such as declining viral load.

Have support persons (e.g., case managers, family members) reinforce the importance of keeping appointments and adhering to medication regimens.

- Use visual tools, such as pictures of clocks and pills, to help visual learners and those who are illiterate or non-English speaking.
- Encourage attendance at an outpatient HIV/AIDS support group. Hearing from others who have successfully weathered the uncomfortable side effects and can give support when discouragement or relapse occurs can be highly reinforcing.

The key to encouraging client adherence is education, not only of the clients themselves but also of their families and peers. The client and those who surround her must understand why she is taking these drugs, what they do, and what side effects she may experience. The client should also understand that she may have to take additional medications or use nonmedicinal methods to alleviate the side effects, which can include nausea, vomiting, headaches, rashes, muscle pain, and diarrhea.

The clinician should familiarize the client with the names of all the medications she will be taking, including generic names, brand names, and common abbreviations. It is also important that the medical staff discuss with the client why the timing of the doses is important and how food can affect the ability of the medication to work properly. Staff members should fill out a weekly medication timetable for the client so she can easily see and remember when and how to take her medications.

Because the HIV-infected individual must take antiretroviral medications several times a day for the rest of his life, the drugs must be chosen with care. The choice should be based on the client's daily patterns and on any other medical conditions besides HIV/AIDS. Generally, the fewer doses per day and the fewer restrictions for taking the drugs, the better. (Currently, there is one once-a-day medication available--efavirenz [Sustiva]. Another drug, adefovir dipivoxil [Preveon], has been in development but is not now available.) For example, a person who is using opiates, amphetamines, or cocaine is not likely to be eating regularly, so a medicine that must be taken with food may not be the best option. Before prescribing medications, the medical care team could consult the substance abuse counselor about the client's living patterns. If the

therapy is effective, clients who are well will remain so, possibly indefinitely, and those who are ill will generally improve, sometimes becoming well enough to return to or stay at work or begin seeking employment.

Side effects from medications can be difficult or frightening, but the client should not stop taking the medications without first contacting her medical practitioner. Substance-abusing clients are particularly intolerant of unexpected effects such as diarrhea or nausea but usually will continue the medication if they have been informed about such possibilities. Given the tradeoff for a healthier life, most will continue their medications as long as they know that this is less dangerous to them than the HIV itself.

Although injection drug users are one of the groups at high risk for contracting HIV, the majority of them are not in drug treatment. People who provide medical care to HIV-infected substance abusers must work to overcome the barriers that keep many of these clients out of the health care and substance abuse treatment systems and enlist clients who are in these systems to actively participate in their own care.

Supervised Therapy

Substance abuse treatment programs, because of their relatively intense interaction with clients, are in a unique position to help deliver such medication-related services as supervised therapy. Different models for supervised therapy can be effective and should be developed for specific substance abuse treatment settings.

Daily dispensing has been shown to improve adherence to zidovudine (Retrovir--abbreviated as AZT), but its applicability may be limited (Wall et al., 1995). If supervised therapy is already part of a client's substance abuse treatment, it need not be changed because of HIV infection. While important for clients with tuberculosis (TB), supervised therapy also is a significant issue for clients who have difficulty following antiretroviral and *Pneumocystis carinii* pneumonia (PCP) prophylactic regimens because of homelessness, cognitive impairment, or lack of health insurance or money to obtain medications. This kind of supervision is particularly useful for medications that can be given only once daily or less (e.g., trimethoprim-sulfamethoxazole [abbreviated as TMP-SMX] [Bactrim DS, Septra], fluconazole [Diflucan], dapsone [Dapsone]). A potent once-a-day combination antiretroviral therapy that can be easily administered may soon be available.

Client Empowerment

Adherence to medical care means more than simply taking medications as prescribed. The foremost challenge in providing HIV/AIDS and substance abuse treatment is engaging clients and encouraging them to be active participants in their own care.

Many HIV-infected substance abuse clients may be deeply distrustful of medical providers, and some will refuse or resist treatment for fear that their HIV status will be disclosed. Strict observance of client confidentiality is an essential element of creating an atmosphere of trust in which clients can make the choices that are best for them. Encouraging clients to discuss their

fears can help build trust between clients and providers. Client education facilitates client engagement and empowerment, and empowerment results in better adherence to medical care.

The client may also receive help from social support systems that can involve family members, partners, peer support groups, and local AIDS service organizations, which often provide "check-in" telephone calls. It is also likely that the client will respond well to continued positive feedback about her improving condition. For instance, knowing that her viral load has declined while her CD4+ T cell count has increased can help the client continue to tolerate unpleasant side effects (San Francisco AIDS Foundation, 1997b).

The following list of elements of a comprehensive client education program is adapted from *Human Immunodeficiency Virus (HIV-1) Guidelines for Chemical Dependency Treatment and Care Programs in Minnesota* (Pike, 1989). Clients who are HIV infected, whether they are symptomatic or not, should receive education about their disease status, prognosis, and treatment options. All clients with substance abuse disorders, whether HIV infected or not, should receive education about

- The fundamentals of HIV and AIDS
- Strategies for personal risk reduction
- Relevant treatment program policies regarding HIV/AIDS
- Confidentiality rules and expectations
- Benefits of HIV antibody testing
- Overview of local HIV/AIDS resources, including hotlines
- Available medical and social service resources and entitlements, and how to obtain them

Using support groups to connect with other clients facing similar problems can promote empowerment by helping individuals feel less isolated and overwhelmed by their problems. Specific strategies for empowering and engaging clients may include

- Holding support group meetings at the substance abuse treatment facility
- Offering educational sessions for HIV-positive substance abusers in HIV/AIDS and substance abuse treatment settings

Barriers to Care for HIV-Infected Substance Abuse Disorder Clients

Bringing substance abusers with HIV infection into the health care system is a significant challenge. Early treatment provides the maximum potential benefits for both individual and public health (Carpenter et al., 1997; Centers for Disease Control and Prevention [CDC], 1997c). Yet HIV-infected clients often delay seeking medical care. The longest delay occurs in the period of time before testing, which is why getting clients to test is so important. Many clients also delay treatment after they receive positive test results. According to one study, most enter medical care within 3 months of receiving positive test results, but 39 percent delay for more than 1 year (Samet et al., 1998). This study also showed that people with a history of IDU on average delayed entering medical care 19 months longer than those with no history of IDU. In the same study, men who abused alcohol delayed 15 months longer than men who did not. As a

result, clients who delayed seeking treatment had lower CD4+ T-lymphocyte counts (also referred to as CD4+ T cells, T-cells, or T-4 helper cells); the median CD4+ T cell count in the study was 280, below the threshold at which HIV/AIDS-related medical therapy should be considered.

Why clients wait so long to seek medical treatment is not well understood. Factors may include lack of financial resources, fear of disclosure, lack of health insurance, lack of social support, difficulty in admitting they may need treatment, an underlying psychiatric disorder, and past problems with the treatment system. Women, in particular, may delay because of responsibilities to care for others or concerns for their children and families. Many parents from low-income families, especially those without a support system, may fear that they will be deemed unworthy because of their substance abuse and subsequently lose custody of their children. Also, individuals' feelings of helplessness about addressing their substance abuse issues may compound a general sense of helplessness about taking care of their health problems. When HIV-infected substance abusers do seek medical attention, they may do so erratically, making excessive use of acute and emergency care services and underusing primary care medical services (Stein et al., 1993).

HIV among incarcerated adults in the U.S. is six times higher than in the general population (Maruschak, 1997). The behaviors that place persons, particularly women, at high risk for incarceration (e.g., substance abuse, commercial sex work) are also behaviors that place them at high risk for contracting HIV. Continuity of medical care for incarcerated persons using anti-HIV medications is critical (Dixon et al., 1993).

Models of Integrated Care

Ideally, all substance abuse treatment programs should be capable of conducting HIV risk assessments and providing basic HIV/AIDS education and counseling to clients. However, this ideal has not always been achieved. Among 2,315 clients interviewed on presentation for addiction treatment in 1992-1993, only 53 percent reported previous HIV testing (Samet et al., 1999). In addition, all programs should provide access to HIV testing and pre- and posttest counseling. If programs cannot provide testing and related counseling onsite, they must have referral relationships with other agencies that will provide these services. For guidance on structuring HIV/AIDS counseling programs, providers should consult the CDC's *Technical Guidance on HIV Counseling* (CDC, 1993).

An integrated approach to caring for HIV-infected substance abuse disorder clients requires developing collaborations and maintaining communication among alcohol and drug counselors, HIV/AIDS medical care providers, and mental health providers. Existing links, such as those established in some managed care organizations, must be developed to expand services and improve access to care (O'Connor et al., 1992a; Selwyn et al., 1989).

The 1993 Substance Abuse Prevention and Treatment Block Grants Interim Final Rule, administered by the Substance Abuse and Mental Health Services Administration, reinforces the importance of links between substance abuse treatment and primary care services, particularly when providing services to injection drug users. For example, the regulations require that

injection drug users on a waiting list for substance abuse treatment receive interim services within 48 hours of requesting them. Interim services must include referrals to HIV/AIDS health care services as well as HIV/AIDS counseling and education (see the section "Substance Abuse Prevention and Treatment Block Grant Funding" in Chapter 10).

Primary care staff providing services to HIV-infected substance abuse disorder clients should understand and be responsive to clients' needs (O'Connor and Samet, 1996). They should be aware that a client's relapse into substance abuse may result in noncompliance with medical care. In addition, staff must be sensitive to clients' prior experiences with the medical care community, cultural and language variations and issues related to race and ethnicity, sexual orientation, life experiences, and gender (see the section "Cultural Competency Issues" in Chapter 7).

At each medical visit, primary care providers should ask about the status of the client's substance abuse treatment. Documentation of ongoing substance abuse treatment is important. In certain situations, such as when a client of a program is hospitalized for medical illness, primary care physicians are required to make arrangements to ensure continuation of methadone maintenance. Also, clients need continuous reinforcement of the message that by continuing to abuse substances, they are further damaging their own health as well as placing others at risk of HIV infection (for more information about enhancing client motivation, see TIP 35, Enhancing Motivation for Change in Substance Abuse Treatment, [CSAT, 1999d]).

Medical Care Within Substance Abuse Treatment Programs

Chapter 6 provides an overview of substance abuse treatment settings and modalities. Figure 2-1 contains a description of the various models for the provision of medical care commonly found in different substance abuse treatment settings.

Models of Primary Care for a Population With Substance Abuse Disorders

Involving an HIV-infected substance abuser in a primary medical care system that provides ongoing and preventive care can be frustrating (Wartenberg, 1991). It is common for clients to lack primary medical care during periods of intense drug use. Outside of university medical centers, finding primary care physicians or clinics willing to accept HIV-infected substance abuse disorder clients can be difficult. This is partly because few primary care sites are willing to take on the financial strain of caring for uninsured or underinsured clients. Also, primary care providers generally are not educated on issues related to substance abuse or the evolving specialty of HIV/AIDS care (Samet et al., 1997). The Consensus Panel recommends connecting HIV-infected drug abusers with HIV/AIDS care providers during their substance abuse treatment. Even here, the barriers to primary medical care are apparent.

Existing primary care models should still be evaluated in order to identify how they can be modified and expanded to address the special needs of the HIV-infected, substance-abusing population (O'Connor et al., 1992b; Samet, 1995). To date, there is only one study of outcomes for clients seen in substance abuse treatment settings who are referred to available community primary care resources (Stein et al., 2000). One study that compared onsite with offsite primary care for a small group of subjects found that onsite care provided in a substance abuse treatment

setting had significant continuity-of-care advantages (Umbricht-Schneiter et al., 1994).

Onsite systems

Well-defined models exist for providing primary care to HIV-infected substance abuse disorder clients (Figure 2-2). Methadone treatment programs that provide onsite primary care medical services (whether sharing the same space or the building next door) often have been hospital- or university-affiliated programs and have benefited from a close association with affiliated medical specialists (O'Connor et al., 1992b; Selwyn et al., 1989; Sorensen et al., 1989). Onsite systems enhance client followup and adherence to therapies. ↑ TOP

Referral systems

The practice of distributing clients from substance abuse treatment programs to various clinical sites for primary medical care is called a *distributive care system*. Optimally, primary care should be multidisciplinary, with social workers, physicians, physicians-in-training, nurses, mental health professionals, and alcohol and drug counselors included in the treatment staff. A case manager may be helpful in facilitating communication among treatment personnel (see Chapter 6 for more information). For newly diagnosed clients, linkage to accessible medical care is important to prevent delay in seeking care. Counselors and nurses must continue to encourage early entry into treatment for those people who are reluctant or face barriers such as lack of transportation or child care.

Communication

When clients are sent to referral sites for primary medical care, a communication system should be in place to ensure that appointments are kept and that information about medical care is sent back to the referral point.

A memorandum of understanding between the referral site and the primary care provider is recommended to ensure that this feedback occurs systematically. Forms for transfer of confidential information should be signed by clients at their initial visits to both primary care and substance abuse treatment sites (see Chapter 9 for additional information).

The 1993 Substance Abuse Prevention and Treatment Block Grants Interim Final Rule requires States to coordinate substance abuse disorder prevention and treatment activities with other services, including HIV/AIDS services. MOUs may be used as evidence that such coordination is being sought.

Contractual arrangements

Some HIV/AIDS services may have contractual arrangements with other health care facilities. For example, clients with identified health problems, such as positive tuberculin skin test results, may be sent to a local hospital with which the referring facility has a contractual arrangement. The contractual arrangement guarantees that the client will be seen and specifies services to be rendered. Unlike referrals, a contractual arrangement contains a built-in mechanism that ensures continuity of care. Detoxification programs often have such an arrangement with medical

providers.

Recommended elements of a contractual arrangement for primary medical care services are described in Figure 2-3.

Medical StandardsOf Care

This section describes a range of practices endorsed by Consensus Panel members of this TIP. Where specific treatment recommendations exist or where data strongly indicate that a particular intervention is better than alternative treatments, this information is clearly stated. Where there are arguments for and against a particular intervention, both the advantages and disadvantages are provided.

The Consensus Panel wishes to provide clinicians treating HIV-infected substance-abusing clients with current information on which to base clinical decisions that are in the best interests of their clients. This section also provides basic information to treatment personnel who are not physicians. Many excellent online sources of information about current HIV/AIDS care are listed in Appendix F, with special reference to primary care and outpatient management.

Classification of HIV InfectionAnd AIDS

See Appendix C for a description of the clinical categories of HIV and AIDS. See Chapter 1 for a discussion of the origins and development of HIV and AIDS.

Benefits of Early Intervention

The best time to treat HIV is as early as possible. The sooner an HIV-infected individual receives treatment, the more likely his survival will be prolonged and his symptoms less dire. In the 1980s and early 1990s, researchers focused on determining the best time to begin HIV treatment. Initially, this was thought to be the stage at which a CD4+ T cell count of 500 is reached. However, due to the inadequacy of viral suppression, the virus quickly developed resistance and resumed reproduction, and the benefits were lost. Now, however, combinations of three or more different medicines are used to treat HIV, each medicine working in a different way to fight the virus. Figure 2-4 illustrates how drug therapy works at various stages in the life cycle of HIV. Most researchers agree that an HIV-infected individual with a detectable viral load who is ready to begin treatment should do so at once. The availability of new antiretroviral agents and rapid acquiring of new information have led to updates in treatment guidelines on a regular basis. Some clinicians prefer to wait until the CD4+ T cell count drops below 500 or the viral load rises above 10,000 (CDC, 1998h). Before beginning HIV treatment, however, the client must be ready to commit to taking these medicines every day for the rest of her life (i.e., must be in a stage of "treatment readiness"). Any deviation from the medication schedule can foster the development of drug resistance and hasten the appearance of AIDS.

The client should also be mentally and emotionally ready to undergo treatment because compliance will depend on his willingness to adhere to the medication schedule. Self-efficacy theory (Bandura, 1977) describes the necessity that an individual believe not only that an action

will achieve its desired goal but also that he will be able to perform the action effectively. If the individual receives reinforcement from many sources that the medications are effective and that it will be possible to take them correctly, he is more likely to make the attempt. Substance abuse treatment professionals can play a key role in this process. With their understanding of the day-to-day realities of their clients' lives (e.g., barriers such as homelessness), alcohol and drug counselors can aid the clinician in choosing a drug regimen that the client will be able to follow.

Drug Resistance

Although combination therapy is the most effective treatment to date, once an individual begins this form of treatment, she cannot stop taking any of the medications because the virus can then develop resistance to that medication and possibly to other related antiretroviral medications. Resistant viruses can be transmitted to others and may make treatment difficult or impossible. Although combination therapy can be complex, the counselor should strongly discourage the client from taking only some of the pills, taking "drug holidays" (which was a common practice and recommendation with AZT monotherapy), or skipping doses because these practices lead to resistance. If there is a need to discontinue any antiretroviral medication for an extended time, clients should be advised of the theoretical advantages of stopping *all* anti-HIV medications rather than continuing one or two agents.

Resistance occurs when a virus no longer responds to a drug. All viruses have the ability to learn from and possibly outwit human immune system defenses. As HIV multiplies, it makes random changes in its genetic code, which allow it to escape human immune system defenses and the suppressive effects of anti-HIV therapy. An anti-HIV drug regimen that is not followed properly can speed up this process. When a therapy does not completely suppress HIV replication, the virus produces mutations that can replicate despite the presence of anti-HIV medications. If unchecked, these mutations will significantly change the original virus, and this new, stronger version of the virus is considered to be drug resistant.

Cross-resistance occurs when a virus develops resistance to one medication, which automatically makes it resistant to other related medications. When HIV develops resistance to indinavir (Crixivan), for instance, it can also become resistant to ritonavir (Norvir). If resistance develops to one protease inhibitor (PI), then it is likely that HIV has become cross-resistant to other PIs (San Francisco AIDS Foundation, 1997b). Resistance and cross-resistance have become the most serious setbacks in the struggle against HIV/AIDS since the development of combination therapy.

Postexposure Prophylaxis

Postexposure prophylaxis (PEP) is an HIV treatment administered within 72 hours after exposure to HIV. An individual who has been exposed to the virus can prevent it from becoming established in her body if she treats it very quickly. PEP involves taking a multidrug combination that will stop the virus before it damages the immune system.

When someone is exposed to HIV, his immune system cells carry the virus to the lymph nodes, where it begins to rapidly replicate. Within 3 to 5 days, new virus particles then spill out into the

bloodstream and flood the body. This is the stage of acute HIV infection that PEP is aimed to prevent. If this can be averted, the individual may be able to clear the virus, and his immune system can safely destroy what remains (CDC, 1998f).

PEP must begin before the individual tests HIV positive and before HIV is detected on a blood viral load test. However, early treatment even after this 3- to 5-day "window of opportunity" can still slow the advance of the disease. The standard PEP treatment is a combination of three antiretroviral medications.

PEP is not a "morning-after" drug. It requires a month of daily treatments, which can produce unpleasant side effects. It is expensive, and it is not FDA-approved. Because of these factors, many insurance plans do not cover it. Also, there are concerns within the HIV treatment field that using powerful anti-HIV drugs too often may create resistance in the virus. Consequently, PEP should be administered only to health care workers who have received significant occupational exposure and in cases of accidental sexual exposure (for example, if a condom breaks or someone is raped) (San Francisco AIDS Foundation, 1997a).

Testing for HIV

Counseling and testing prior to and after HIV antibody testing has multiple goals. It is used to explain the limitations of the HIV test, to help persons assess their risks, to encourage and reinforce behavior change, and to refer infected individuals to clinical care. All counseling should be performed by a counselor trained in HIV counseling. Test results should be discussed face to face with the client (rather than by telephone or mail), and appropriate precautions must be taken regarding confidentiality of test results and potential adverse effects of testing, such as psychological stress.

Testing for HIV is a difficult decision and always an individual one. Because more effective HIV therapy is now available, an individual has more treatment choices. Treating HIV when it is discovered late is more difficult. Typically, it takes a few weeks to obtain results from standard HIV tests; unfortunately, many people who are tested do not return to learn their results. However, new rapid HIV tests are being developed (e.g., OraSure_) that can produce reliable results in hours instead of days; this may substantially increase the number of individuals who learn about their HIV status (CDC, 1998h). The sensitivity and specificity of rapid HIV tests are comparable to enzyme immunoassay tests.

Another testing option is home sample collection (HSC) tests, which allow people to test themselves for HIV. Currently, two HSC tests have been approved by the FDA. The user performs a finger stick and mails the specimen, identified by an anonymous code number, directly to the laboratory. The user later calls a toll-free number to obtain test results, counseling, and referrals (Branson, 1998). All positive home tests should be confirmed by a supplemental test.

If a person at high risk is unprepared for a positive result or unwilling to consider treatment, an HIV test may not be helpful. On the other hand, if a person has an overwhelming fear or preoccupation with HIV, it may be wise to test, even if the risk is fairly low. For those clients

who may be unprepared for a positive test result, pretest counseling may be necessary. Usually more than one pretest counseling session is held to better prepare the client before she takes the test. Another alternative is group counseling for preparing clients for HIV testing before formal pretest counseling begins.

HIV testing may be either anonymous or confidential, depending on the local laws, or both types of testing may be available. Confidential testing means that the person tested will give his name, which is reported to the State health department. Anonymous testing means that the person does not have to give his name, and no name is reported to anyone. There is much controversy surrounding HIV reporting systems.

By the beginning of 1999, 30 States had established name-based reporting systems for HIV. Of these, 11 also eliminated their anonymous testing sites. New York's law, passed in 1998, includes a partner notification provision. Three other States use unique identifier systems, where, instead of by name, clients are identified by a code combining their gender, race/ethnicity, birth date, and social security number. Three more States introduced HIV reporting bills in the 1998 legislative session that never became laws (CDC, 1999a; Fuentes, 1999). Supporters of name-based reporting, including the CDC, believe that these programs will help generate more accurate statistics concerning the spread of HIV. Opponents argue that these systems will deter people at high risk from being tested. For example, populations such as immigrants or women may not be tested because of the social risk involved in disclosure (Shelton, 1998). Alcohol and drug counselors and HIV primary care personnel should be aware of the reporting requirements in their States.

Before testing, the client's level of risk for HIV should be considered. This level can be determined by how often the client has engaged in risky behaviors. Anyone with a history of drug use should be tested because the seroprevalence in this group is much higher than in the general population. Someone who has a higher number of lifetime sexual partners is at higher risk for HIV, especially if she has engaged in high-risk behaviors. Anyone with a sexually transmitted disease (STD) should be tested. Whatever a person's risk level, it is important to remember that it only takes one exposure to HIV to become HIV-infected.

Certain symptoms might also indicate the need for an HIV test. If someone who has engaged in risky behavior has flulike symptoms, this might indicate a recent infection with HIV and the need for testing. Shingles (herpes zoster) also is a common early sign of HIV infection, causing a painful rash that occurs in a line on only one side of the body. Oral thrush in a nonpregnant adult also indicates immune dysfunction, as does chronic diarrhea, night sweats, weight loss, or fevers. Recurrent vaginal yeast infections are a common sign of HIV infection in women. TB is increasingly problematic among those with HIV infection and can occur even when the immune system is in good condition. Symptoms of TB include a chronic cough and fever.

After initial infection, there often is a long period of time (several years) during which an infected person may appear and feel healthy. Unfortunately, this means that the signs of later stage HIV disease will be the first signals that something is wrong. Many people, especially injection drug users, are hospitalized for HIV-related pneumonia or other serious diseases before

they even discover they have HIV.

CD4+ T cell counts

CD4+ T cells are the subset of white blood cells in the immune system that are specifically targeted by HIV. Although HIV also infects other types of cells, the virus's effects on CD4+ T cells cause most of the immunosuppression characteristic of HIV disease.

CD4+ T cell counts generally are the markers for the stage of a client's HIV disease. A normal CD4+ T cell count ranges from 500 to 1,400 (Laurence, 1993). Although they reflect the overall status of the immune system and are presumed to reflect the stage of illness, CD4+ T cell counts can fluctuate over time. Results can also vary among different laboratories and be affected by factors such as coexisting illnesses and time of day. (Measuring CD4+ T cell counts during acute coexisting illness is not generally recommended.) To obtain the most accurate information about trends in a client's CD4+ T cell levels over time, counts should be taken twice initially at intervals a few days apart and periodically thereafter. To increase reliability and consistency of results, tests should be done at the same laboratory each time, if possible. The CD4+ T cell *percentage,* or the percentage of lymphocytes that are CD4+ helper cells, is an additional measurement often performed as part of basic CD4+ lymphocyte subset studies. The CD4+ T cell percentage, which includes the CD4+ helper cell count, may show less variability than the CD4+ T cell count. Long-term therapy may be based on the results of these tests.

It is important to remember that CD4+ T cell counts are only an indirect measure of viral activity; they measure the effects of the virus on the target cell, not the activity or virulence (capability of causing disease by breaking down protective mechanisms of the host) of the virus itself. Viral load tests, described in the next section, quantify viral levels in blood and determine strain type and other indicators of virulence.

Despite their limitations, CD4+ T cell measurements are useful for indicating points at which treatment decisions should be made. The average yearly decline of CD4+ T cell counts in HIV-infected clients is 30 to 90 cells per year; however, the rate of decline can vary (Mellors et al., 1997). Some clients' CD4+ T cell counts decline rapidly, while others remain stable for long periods. There is no evidence that CD4+ T cell counts decline more rapidly in HIV-infected substance abusers than in other HIV-infected populations (Graham et al., 1992; Margolick et al., 1992; Saag, 1994).

Viral load testing

The plasma HIV RNA level has been shown to be the strongest predictor of the progression to AIDS (Mellors et al., 1997). The test measures the number of viral particles per milliliter of plasma. As with CD4+ T cell counts, test results can vary depending on many factors. Viral load testing should not be done during a coexisting infection or within 4 weeks of a vaccination. Currently available commercial test kits can measure down to 50 copies per milliliter, and more sensitive viral load assays are available with a sensitivity of 5 copies (U.S. Department of Health

and Human Services [DHHS] and the Henry J. Kaiser Family Foundation, 1997).

Quantification of HIV RNA is the best method of monitoring the client with HIV infection, particularly when antiretroviral therapy has begun. However, viral load tests are expensive, and some insurance plans do not cover repeated use of these tests. Higher levels of HIV RNA suggest greater viral replication and correlate with the number of acutely infected cells as well as with an accelerated rate of disease progression. Therefore, reducing the viral load as closely as possible to undetectable levels is the optimal goal. By using viral load data along with the client's CD4+ T cell count, clinicians can estimate the time to AIDS or death for clients who choose not to take or are unable to take antiretroviral medications.

Initial Assessment

Medical care provided to HIV-infected individuals varies depending on the stage of the infection, but all clients should receive evaluation and followup (O'Connor et al., 1994b; O'Connor and Samet, 1996). Assessment of the behaviors associated with HIV transmission, such as unsafe sex and substance abuse practices, is an important part of the initial client assessment.

At the initial assessment and periodically thereafter, substance-abusing clients should receive risk assessments and comprehensive medical examinations. These examinations can be performed onsite or at another facility through referral or a contractual arrangement.

Medical History

A thorough medical history is an important first step that helps the clinician proceed to clinical evaluation and formulate a treatment plan. Taking the history may occupy an entire client visit, particularly if it is combined with education and counseling. When taking a medical history, health professionals should consider the following:

- If the HIV test occurred elsewhere, it might be helpful to begin by asking when the client took the test and why. This question could yield information about the client's medical history and risk behaviors.
- Questions about drug use and sexual practices should be explicit, clear, open-ended, and nonjudgmental.
- Documentation of the positive HIV test result, if performed elsewhere, should also be obtained and noted in the record. If there is any suggestion that previous HIV test information is not accurate (e.g., repeatedly normal CD4+ T cell counts and undetectable virus), the HIV test should be repeated.
- Sometimes the risk history will indicate the duration of the client's infection. If so, the provider may want to discuss the usual latency period of HIV with the client and the implications of the client's history in determining the stage of the disease and the prognosis. Clients should be counseled about risk reduction and encouraged to notify past and present sexual or drug use contacts of their HIV status (see Chapter 4 for more information about risk reduction).
- Contact notification is a difficult issue for many clients, but most people cooperate once they understand that their contacts may be at serious risk. Often, State health departments

assist people in locating and notifying contacts (see Chapter 9 for more information about notification).

- Ask questions about specific symptoms of HIV infection (e.g., fevers, night sweats, diarrhea, weight loss, lymphadenopathy, thrush, vaginitis, or skin changes) or symptoms suggesting undiagnosed AIDS-defining conditions (e.g., mental state changes, visual changes, severe headaches, chronic diarrhea, shortness of breath, or difficulty swallowing).
- Questions about past medical history should be certain to cover previous diagnoses and treatment of TB, syphilis, genital herpes and herpes zoster, hepatitis B and C, purified protein derivative testing, recurring bacterial pneumonia, and (in women) abnormal Pap smears. STDs are common in substance abusers, particularly among women involved in commercial sex work or the exchange of sex for drugs.
- The client's immunization history should be recorded.
- Mental health issues should be discussed, including past psychiatric treatment and hospitalizations, chronic use of prescribed or nonprescribed psychotropic medications, and the client's current mood. Anxiety and depression are common in this population, often predating the HIV diagnosis (see Chapter 3 for more information on mental health treatment).
- Specific information should be collected about the client's social situation, including functional status, housing, employment, health insurance, and social support from family members or significant others. These questions may identify urgent social needs and prompt immediate referral to a social service agency or provider.
- A complete social history should be taken, including family genogram, financial information, assessment of coping styles and skills, current losses and grief issues, spiritual assessment, educational factors, cultural issues and beliefs about HIV status and substance abuse, and emotional assessment.
- At the conclusion of the visit, a tuberculin skin test with anergy panel should be done, a set of laboratory tests performed or ordered, and one or more needed immunizations given. At the next visit, a full physical examination can be done, and lab results reviewed.

Physical Examination

Although HIV and its complications may involve nearly every organ, the HIV-directed general physical exam should focus on (1) the skin, (2) the eyes, (3) the mouth, (4) the anogenital region, (5) the nervous system, (6) the lymphatic system, and (7) client weight and temperature. Knowledge of a client's immune status may also direct the physician toward screening other areas. For example, the eyes should be examined for retinitis in clients with very low CD4+ T cell counts. If the client has particular complaints or other chronic conditions such as diabetes or asthma, the exam should focus on those conditions.

Skin

- The skin may be affected early in the course of HIV infection and in many cases may have been the reason why HIV testing was originally done.
- Bacterial agents may cause folliculitis, impetigo, and bacillary angiomatosis. Injection

drug users may have infected tracks, skin abscesses, or cellulitis.

Topical fungal infections are common (e.g., candidiasis, angular cheilitis at corners of lips).

- *Molluscum contagiosum*, pearly papules most often found on the genitalia and face, may lead to serious cosmetic concerns. Warts are also common.
- Herpes, both simplex and zoster, may be the initial indication of HIV disease and often is more severe in clients who are HIV positive.
- Many clients suffer from xerosis (dry skin) or chronic itchiness.
- Inflammatory conditions such as seborrheic dermatitis, psoriasis, and eosinophilic folliculitis are common and often difficultto treat.
- Kaposi's sarcoma, now a relatively rare complication, presents as oval purplish nodules and plaques, most often on the trunk, legs, or hard palate. This disease is more common in men than in women.
- Biopsy is the appropriate step to evaluate any skin lesion that does not respond promptly to standard therapy.

Eyes

- Direct ophthalmoscopy of the optic fundi, preferably with dilation of the pupils, should be done for clients who have CD4+ T cell counts below 100 (on a regular basis if they are asymptomatic and immediately if any eye complaint arises).
- Cytomegalovirus retinitis is characterized by red or orange patches, or "floaters," on the retina and can progress quickly to blindness by affecting the macula or leading to retinal detachment. Any visual complaints that cannot be simply explained should be directed to an ophthalmologist (see Appendix D for a copy of the Amsler grid).

Mouth

- The oral cavity should be checked at every clinical visit. Any oral lesion can affect nutrition, and many cause extreme discomfort. Periodontal disease can be aggressive in persons with HIV disease, and it is important to stress regular dental care (every 6 months) and good oral hygiene.
- Oral candidiasis, or thrush, most often appears as white plaques on the buccal mucosa and tonsillar areas. Without treatment, thrush often spreads throughout the mouth; in persons with advanced disease, candidiasis can affect the esophagus, leading to severe pain on swallowing and the need for prolonged systemic treatment. When it involves only the mouth, thrush may be asymptomatic and should be treated with antifungal agents. Angular stomatitis commonly is associated with mucosal candidiasis.
- Hairy leukoplakia, a lesion related to Epstein-Barr virus, often presents as a white plaque on the side of the tongue and can be confused with thrush. Sandpapery to the gloved hand, leukoplakia may grow in size and cause difficulty in chewing, but sometimes it spontaneously regresses.
- Ulcerations that appear on keratinized epithelium--lips, tongue, hard palate--are most likely herpetic; ulcers on the buccal mucosa are most often aphthous.

- A baseline anal inspection is essential for all clients. HIV-infected persons with a history of receptive anal intercourse are at increased risk for*papillomavirus*-associated anal squamous cell cancer.
- The clinician also should check for anal discharge, warts, herpetic ulcers, hemorrhoids, fissures, and traumatic tears. Fissures, traumatic tears, and what the client might consider hemorrhoids may be recurrent genital herpes.
- The clinical role of the anal Pap smear remains undefined.
- Clients with HIV may be at risk for other STDs such as syphilis, chlamydia, gonorrhea, herpes simplex, and chancroid.
- In uncircumcised clients, it is important to retract the foreskin to check for *candida balanitis* and chancroid.
- The testicles should be palpated for tenderness, epididymal swelling (a sign of gonococcal or chlamydial infection), and masses.
- The intertriginous areas may have tinea.
- In women, the external genitalia should be inspected for warts, ulcers, and vesicles.
- Other sexually transmitted infections that are less common in this population but must be considered in women include gonorrhea, chlamydia, and syphilis.
- HIV-infected women are at high risk for cervical dysplasia and cervical cancer (see the women's health issues section later in this chapter about cervical abnormalities).

Nervous system

- A brief, structured cognitive exam, such as the Mini Mental State Examination (see Appendix H), should be performed at regular intervals on all clients, particularly those with advanced disease (see also Chapter 3).
- The clinician must consider affective disorders and alcohol or drug use when interpreting the common complaint of memory difficulty.
- The other essential part of the neurologic exam involves an evaluation for neuropathy, a problem that may be HIV related but often is medication related.
- Documenting ankle-jerk reflexes and vibratory sensation in the distal extremities is critical before starting antiretroviral therapy.

Lymphatic system

Most HIV-infected persons have palpable lymph nodes at some point during the course of disease. Such nodes--which may involve multiple sites--do not predict disease progression but often cause discomfort and distress. Clients should be reassured that these nodes are common and often spontaneously increase and decrease in size. If a client experiences a rapid or continuous enlargement, worsening pain, or drainage in a particular node, it should be examined to rule out an opportunistic infection or malignancy. In the case of unexplained constitutional symptoms, node biopsies can be useful to search for evidence of systemic infection. ↑ TOP

- Weight loss often suggests undiagnosed opportunistic infections, rapidly progressive HIV disease, depression, or substance abuse.
- Because weight loss is an early and meaningful sign of deteriorating clinical status, the client's weight should be measured at each visit.
- Lipid distribution and weight gain due to PIs should be checked.
- Fevers may indicate an underlying opportunistic infection and should be looked for at each visit.
- A current trend in nutritional management of HIV infection is bioelectrical impedance analysis (BIA). This quick and simple procedure can show the ratio of lean muscle mass to body fat and weight. It is no longer sufficient to look at total weight loss to indicate potential problems with nutrition.

Laboratory Tests

Before antiretroviral therapy is initiated in any client, certain laboratory studies should be done. The suggestions listed here should be adapted to the particular circumstances of a client and physician.

- **HIV RNA (viral load).** Viral load testing is the essential parameter that influences decisions to initiate or change antiretroviral therapies. Using quantitative methods, the clinician should measure plasma HIV RNA levels at the time of diagnosis and every 3 to 4 months thereafter in the untreated client. Ideally, viral load testing should be performed twice before therapy is started to ensure accuracy and consistency of measurement. Only one measurement is needed in clients with advanced disease. To gauge the effect of therapy, viral load should be checked 4 to 8 weeks after initiation of therapy. The indications for plasma HIV RNA testing are shown in Figure 2-5.
- **CD4+ T cell counts**. As noted above, CD4+ T cell counts at present are the standard test to assess the level of immune dysfunction in HIV-infected clients. It is preferable to perform two CD4+ T cell tests a few days apart to help determine a baseline and assess clients' eligibility for antiretroviral therapy. CD4+ T cell counts should be measured every 3 to 6 months after diagnosis.
- **Blood counts**. A complete blood count (CBC) can alert the clinician to blood abnormalities common in HIV-infected clients, including leukopenia and thrombocytopenia. In clients receiving particular antiretroviral agents, the frequency of CBCs is determined by the need to monitor for hematologic toxicity. For example, in symptomatic clients not on AZT, CBCs can be repeated at 3- to 6-month intervals; in asymptomatic clients not on AZT, repetition every 6 months to a year is advised.
- **Purified protein derivative**. Tuberculin skin testing should be performed in HIV-infected persons annually. In early stages of HIV infection, reactivity to the skin test is usually maintained. As HIV disease advances, response may be blunted or absent (anergy). A reaction greater than or equal to 5 mm indication is considered positive for defining TB infection. In populations with a high prevalence of TB, a skin test may be falsely negative. HIV-infected persons have a high risk of developing active TB if they

have positive skin tests, and they require treatment.

- **Screening chemistries**. Annual routine screening chemistries are recommended. Testing at 2- to 4-month intervals is indicated in clients receiving medications with potential liver, kidney, and muscle toxicity. Liver function tests must be checked more frequently because of the high risk of exposure to hepatotoxic agents. Hepatitis viruses, alcohol, and several of the antiretroviral agents commonly elevate transaminases (ritonavir in particular; didanosine [Videx] is contraindicated with a history of pancreatitis; indinivar raises the total bilirubin).
- **Syphilis**. Annual serologic screening for syphilis is recommended in sexually active persons.
- **Toxoplasmosis**. Baseline testing is useful to identify clients with past exposure to toxoplasma who may benefit from prophylaxis against this infection. Without prophylaxis, these clients have about a 30 percent chance of developing cerebral toxoplasmosis in the course of their HIV infection (especially when the CD4+ T cell count drops below 100). Annual testing is advised in clients without prior exposure.
- **Hepatitis B virus** (HBV). The prevalence of past exposure to HBV approaches 90 percent in many HIV-infected substance abuse populations in the United States (O'Connor et al., 1994b). Because of the high cost of the HBV vaccine, it is more cost-effective to first screen clients for exposure to this virus to determine if vaccination is necessary. Vaccination is indicated for HIV-infected clients without previous exposure (i.e., all markers negative).
- **Hepatitis A and C**. Injection drug users are at risk for hepatitis A (HAV) infection (although the reason for this has not been determined) and hepatitis C (HCV) infection, which, like HBV, is parenterally transmitted. HCA usually is benign and self-limited; HCV may be treated with injected interferon-alpha and ribavirin, but this treatment is expensive, only modestly effective, and often causes unpleasant side effects. Even so, it may be helpful to determine the presence of prior viral hepatitis in clients likely to be exposed to the increasing numbers of hepatotoxic medications used to treat HIV disease. This may be particularly important for HCV, which appears to persist as a chronic, active infection and is more common than HBV. It also is recommended that injection drug users receive hepatitis A vaccine (CDC, 1999e).
- **Chest x-ray**. A chest x-ray generally is optional in the initial client evaluation, although some clinics and physicians require a TB chest x-ray before they will see a client for the first time. Routine chest x-rays can provide a baseline when clients present with respiratory symptoms, but no studies support this recommendation. Chest x-rays may also be useful in clients with a past history of pulmonary disease or heavy smoking.

Evaluating Symptomatic Illness

Clinicians providing care to HIV-infected substance abusers must be familiar with the clinical manifestations of HIV disease and also be aware that these manifestations can be difficult to distinguish from common medical complications of substance abuse. Differential diagnoses in HIV-infected substance abusers can be challenging because both HIV infection and substance abuse have clinical effects on a wide range of organ systems. It is important to consider the possibility of adverse drug reactions or interactions for those clients who are taking HIV

medications (see the section, "Pharmacologic Interactions," later in this chapter). To provide optimal care to this population, clinicians must be fully aware of the combined medical effects of substance abuse, HIV infection, and HIV medications (O'Connor et al., 1994a). Figure 2-6 lists the common symptoms that may be related to either HIV infection or substance abuse.

Anorexia, weight loss, and fatigue may be complications of chronic cocaine use, caused by HIV infection, symptoms of specific AIDS-related opportunistic infections (e.g., mycobacterium avium complex [MAC], cytomegalovirus, TB, or side effects of medications). Tachycardia, flulike illness, fatigue, abdominal pain, and diarrhea may be symptoms of drug withdrawal, particularly opioid withdrawal, or they may be symptoms of acute or chronic HIV-related conditions.

Chest pain, coughing, and shortness of breath may be symptoms of crack cocaine use, bacterial pneumonia, or HIV-related pulmonary infections such as PCP. Bacterial endocarditis with fever, night sweats, and chest pain or other pulmonary effects may result from unsterile intravenous injection or may indicate HIV-related opportunistic infection. Heavy cigarette smoking in injection drug users may also make it difficult to interpret symptoms such as shortness of breath or the results of pulmonary function tests. HIV and its related opportunistic infections commonly affect the nervous system, resulting in conditions such as HIV-related dementia, CNS cryptococcosis, toxoplasmosis, and HIV-related peripheral neuropathy. Drug intoxication or withdrawal also can affect consciousness, cognition, and behavior. Heroin and cocaine use may cause stroke syndromes and other cerebrovascular diseases. Alcoholic, nutritional, and traumatic peripheral neuropathy syndromes may also be more common in substance abusers than in the population as a whole.

Psychiatric complications

In 1998 the prevalence of depression among HIV-infected persons was estimated at 30 to 40 percent. It may be higher among persons with substance abuse disorders and those symptomatic with AIDS. Increasing symptoms, progressive disability, and decline in function may bring sadness, anxiety, fear, insomnia, and a feeling of being overwhelmed. Substance-dependent persons may have few coping resources (other than substance abuse). Grief over the loss of loved ones (who may also have had AIDS) can be severe. Clinicians should make every effort to make definitive diagnoses. Situational anxiety or depressive symptoms can be treated with supportive psychotherapy. Support groups, both HIV-related and others, and encouragement toward social and family interaction are important parts of treatment. Pharmacologic interactions may be needed in severe, persistent sleep disturbances, major depression, generalized anxiety, and posttraumatic stress disorders.

Pharmacologic Aspects

HIV disease is now seen to fit the pattern of a chronic disease (with complications and remissions) rather than an illness that appears suddenly and progresses rapidly to death. Clients periodically need acute care inpatient resources, especially in the latter stages of the disease. However, as clients experience longer asymptomatic periods between illnesses, the emphasis

increasingly is on ambulatory management and primary care for HIV infection.

Medications to control HIV infection have become more available. The most effective treatment is a combination of three or more different medications. Most often, two of the medications are nucleoside reverse transcriptase inhibitors (NRTIs), and the third can be either a nonnucleoside reverse transcriptase inhibitor (NNRTI) or a PI. Combination therapy with three or more medicines generally reduces the viral load to near or below the level of detection. There are currently six FDA-approved NRTIs, one nucleotide, five PIs, and three NNRTIs, and thus many potential combinations would seem to be possible. However, once a medication from a certain class is used (e.g., PIs, NRTIs), the likelihood increases that the virus will develop resistance to some or all other drugs in that class, so the options quickly become very limited. This is known as cross-resistance. For this reason, it is widely believed that the best chance for success in HIV treatment is with the first treatment regimen, which is why adherence and followup are so critical.

All the medications administered in combination therapy have side effects and specific requirements for use. For example, AZT may be given with lamivudine (Epivir, also known as 3TC) as the two NRTIs. These both can be taken either with or without meals. A possible side effect of AZT is anemia. The clinician may add the PI indinavir, which cannot be taken with food or with other medications and also requires the client to drink a great deal of water because it causes kidney stones. A newly described side effect of PIs is weight gain in the trunk, while the arms and legs become thinner (lipodystrophy), and for women the central distribution of weight often causes breast enlargement.

Care strategies have incorporated both antiretroviral therapy and a wide range of prophylactic regimens to effectively prevent opportunistic infections. A recent study found, however, that preventive interventions such as TB prophylaxis and pneumococcal vaccine were used by only about 30 percent of eligible clients, and use of preventive interventions was lowest among HIV-infected injection drug users (Glassroth et al., 1994).

Little is known about interactions of HIV medications with street drugs, and a specialist should be consulted about interactions, even for over-the-counter drugs. PIs have the greatest potential for interacting with other drugs. For example, PIs can prevent amphetamines from leaving the system, which then build up to toxic or deadly levels. Heroin, on the other hand, may be metabolized more quickly (Horn, 1998). See Figure 2-7 for a listing of interactions between HIV medications and street drugs.

Antiretroviral Therapy

The goal of antiretroviral therapy is to improve the length and quality of the client's life. None of the medications currently available to treat HIV-infected clients is a cure, but, used in combination, they can decrease viral replication, improve immunologic status, delay infectious complications, and prolong life. The ideal time to begin antiretroviral therapy remains debatable; immune damage occurs over time, which suggests that all HIV-infected people may eventually benefit from treatment. However, given that the virus has not been eradicated, antiretroviral

medications once started must be taken for the rest of the client's life.

Although there is theoretical benefit to treating asymptomatic clients with CD4+ T cell counts greater than 500, no long-term benefit has yet been demonstrated. Those with high CD4+ T cell counts and very low HIV RNA levels may consider delaying therapy. The major dilemma confronting clients and providers is that the antiretroviral regimens with the greatest potency in viral suppression and CD4+ T cell count preservation are the most medically complex and are associated with a wide array of side effects and drug interactions (see the section, "Pharmacologic Interactions").

The decision to begin antiretroviral therapy in the asymptomatic client is difficult and often involves multiple visits to review treatment options. The factors to consider include(1) client willingness and readiness to begin therapy and remain adherent; (2) the degree of immunodeficiency; (3) the risk of disease progression as determined by plasma HIV RNA; (4) the risk of side effects; (5) the ongoing treatment of other medical conditions, such as diabetes; (6) barriers to care, such as lack of insurance and unstable housing; and (7) stability in drug use patterns and substance abuse treatment (see Figure 2-8). It is important to remember that combination therapies do not work for everyone, even for those who do follow the directions. Many long-term survivors of HIV have experienced very little improvement on the new medications.

Once the client has decided to undergo treatment, the goal of therapy should be to suppress plasma viral load to undetectable levels. Based on current data, the preferred treatment regimen is two nucleoside analogs and one PI (Figure 2-9). Alternative regimens have been used, including two PIs together with one or two NRTIs or substituting an NNRTI for the PI in a three-drug regimen. Monotherapy, the standard of care before 1995, is now outdated. If a client is only on one medication, the provider should examine this further and educate the client on current standards of care.

Highly Active Antiretroviral Therapy

Highly active antiretroviral therapy (HAART) is a combination of antiretroviral regimens that incorporates at least three antiretroviral drugs. Treatment with HAART has resulted in longer survival and improved quality of life for many people with HIV. This therapy is now considered the standard of care by most HIV specialists.

Resting CD4+ T cells are among the "safe havens" where HIV may persist for years interwoven into the cells' genes despite aggressive three-drug antiretroviral therapy. New therapies to attack these "safe havens" are under study. In resting CD4+ T cells taken from the bloodstream of a small number of study clients receiving interleukin-2 plus HAART, researchers were unable to find HIV that was capable of replicating, even when they looked for the virus in millions of cells with sensitive laboratory procedures (Folkers, 1998).

HAART may be beneficial at all stages of HIV disease, from initial exposure through acute and chronic infection and when AIDS symptoms are present. In general, people at earlier stages of HIV disease receive the most long-lasting benefits from HAART, particularly those individuals

who have never undergone HIV treatment. Those with advanced AIDS and those who have used anti-HIV drugs for years generally benefit less from HAART. For reasons that are not yet completely understood, some HIV-infected persons cannot tolerate the side effects of therapy with PIs or do not benefit from them (San Francisco AIDS Foundation, 1997c).

A typical HAART regimen includes a PI when used with two NRTI analogs. Many three- and four-drug combinations can reduce HIV to very low levels for sustained periods. For example, the NNRTI class of medication may be added to or substituted for a PI in combination with two NRTI analogs. Some physicians recommend using didanosine plus hydroxyurea, an anticancer drug, in combination with a PI and an additional NRTI analog. When beginning anti-HIV therapy with ritonavir (six 100-mg capsules twice a day for a total of 1,200 mg daily) and nevirapine (Viramune) (one 200-mg tablet daily for 2 weeks, then twice daily), these drugs are first administered at lower doses, then slowly increased to lessen the possibility of side effects. Medications used in the treatment of HIV (including those expected to become available shortly) are summarized in Figure 2-10. Figure 2-11 presents a schedule and side effects for NRTIs, NNRTIs, and PIs.

Nucleoside analogs

AZT, the first approved antiretroviral agent, taken in combination with didanosine or lamivudine is more effective than AZT alone in slowing progression to AIDS and prolonging survival. AZT plus lamivudine with or without a PI has been recommended for prevention of HIV infection after a needlestick or sexual exposure. AZT alone given to pregnant HIV-infected women at 14 to 34 weeks of gestation reduces transmission of the virus to their babies from 26 to 8 percent, but many clinicians now favor combination treatment for pregnant women. Adverse effects include anemia, neutropenia, nausea and vomiting, headache, and muscle aches. For many substance abusers, the side effects of AZT mimic substance withdrawal, especially from opioids.

Lamivudine used with AZT decreases viral load and may decrease the emergence of AZT-resistant isolates. It also is commonly used in combination with stavudine (abbreviated as D4T) (Zerit) and didanosine. Side effects include headache, nausea, diarrhea, abdominal pain, and insomnia. Lamivudine and AZT have been combined into a single pill (Combivir) for convenience.

Stavudine is most often used as a substitute for AZT in initial combination therapy, or after failure of AZT-containing regimens. When combined with didanosine or lamivudine, stavudine has potent effects. It causes dose-related peripheral sensory neuropathy, which often disappears when the drug is stopped and may not recur when it is restarted at a lower dose. Subjective complaints are infrequent and include headache, gastrointestinal intolerance with diarrhea, or esophageal ulcers. Liver function tests may increase, and pancreatitis has occurred but is rare.

Didanosine is mainly used in combination with AZT and stavudine, plus a PI or NNRTI. Treatment-limiting toxicities of didanosine include peripheral neuropathy, pancreatitis, and diarrhea. Severe lactic acidosis and retinal depigmentation also can occur. Clients with a history of pancreatitis should avoid didanosine.

Onset of abdominal pain should prompt an evaluation for possible pancreatitis. Miscellaneous side effects include rash, marrow suppression, hyperuricemia, hypokalemia, hypocalcemia, and hypomagnesemia.

Zalcitabine (Hivid) can be used in combination with AZT but is the least potent of the nucleoside analogs. Side effects include peripheral neuropathy, rash, stomatitis, esophageal ulceration, and pancreatitis.

Abacavir (Ziagen) is used primarily in combination with AZT and lamivudine. It may be part of a regimen containing a PI. The side effect of greatest concern is a hypersensitivity reaction that appears within the first 6 weeks of therapy, most commonly in the second week. Fever, nausea and vomiting, malaise, diarrhea, and sometimes rash occur. These symptoms intensify with each dose to the point of intolerability. If abacavir is discontinued because of hypersensitivity, rechallenge can result in serious, rapid, and possibly deadly recurrence of symptoms. ♠ TOP

Nonnucleoside reversetranscriptase inhibitors

Like NRTI analogs, these drugs inhibit reverse transcriptase but by a different mechanism.

Neviripine (Viramune) acts synergistically with nucleosides but must be combined with other medications to avoid rapid development of resistance. Trials of neviripine with AZT and didanosine have been effective in lowering HIV RNA to undetectable levels for up to 1 year.

Delavirdine (Rescriptor) acts synergistically with nucleosides and PIs. It should be used in combination with at least two other medications. The main side effect is a rash.

Efavirenz (Sustiva) also acts synergistically with nucleosides and PIs. It can be given in one daily dose and is used by many physicians as a first-line treatment for HIV. Side effects include rash and central nervous system disturbances, of which the most common is "disconnected" sensations such as confusion, abnormal thinking, impaired concentration, depersonalization, abnormal dreams, and dizziness. Other side effects include somnolence, insomnia, amnesia, hallucinations, and euphoria.

Protease inhibitors

PIs prevent the cleavage of protein precursors, which is essential for HIV maturation, infection of new cells, and replication. In clients with advanced HIV infection, a PI has led to marked improvement and prolonged survival. However, all PIs can cause increased bleeding in hemophiliacs, hyperglycemia, and new onset or worsening of diabetes.

Ritonavir is a potent HIV inhibitor, and when given to clients with advanced disease who are being treated with nucleosides, decreases progression to death compared with placebo (8 percent versus 5 percent) (Cameron et al., 1998). Common side effects include nausea (sometimes severe), diarrhea, asthenia, circumoral and peripheral anesthesia, altered taste, renal failure, and elevation in cholesterol and triglycerides.

Indinavir is a potent PI when used with AZT (or stavudine) and lamivudine, lowering the rate of disease progression and mortality more than

two nucleoside analogs alone. This triple combination effect has been durable; an early fall in plasma HIV RNA to undetectable levels can last more than 2 years. Kidney stones have been reported in 4 percent of clients, and asymptomatic elevation of indirect bilirubin occurs in about 10 percent of clients.

Nelfinavir (Viracept)is active in combination with many other nucleosides and PIs. Diarrhea has been the main side effect.

Saquinavir (Fortovase) combined with Ritonavir and a NRTI analog has been clinically effective. Diarrhea, nausea, abdominal pain, and increased aminotransferase activity can occur. The hard gel capsule is Invirase, and the soft gel capsule is Fortovase. Fortovase was introduced in November 1997 as the preferred formulation due to improved bioavailability.

Hundreds of clinical trials have confirmed the durable reduction in HIV RNA levels using three-drug combinations. Although the number of medication combinations is growing and new plans for initial and second-line therapies continue to evolve, client compliance remains a major concern. In addition to developing simple regimens, it is appropriate for the clinician to choose antiretrovirals at least in part on the basis of their side effects. For example, in clients with preexisting pancreatitis, didanosine should be used with extreme caution. For those with neuropathy, didanosine, zalcitabine, and stavudine should be used with caution.

Altered body fat distribution occurs commonly in persons with HIV on long-term antiretroviral therapy. Once thought to be seen only in PI users, changes in body dimensions--including increase in abdominal girth and breast size and wasting of leg muscles--have been noted in many patients independent of PI use and may be especially common in those who are on NNRTIs. The underlying mechanism for these troubling symptoms remains unclear, and an effective therapy is elusive (Gervasoni et al., 1999).

Changing antiretroviral therapy

Criteria for changing therapy include (1) suboptimal initial reduction in HIV RNA level, (2) reappearance of viremia after suppression to undetectable levels, (3) persistent and progressive decline in CD4+ T cells, (4) development of intolerable side effects, or (5) inability to remain adherent. In all cases, the clinician must determine whether the treatment failure is caused by imperfect adherence (due to toxicity, lack of resources, or client's lack of understanding), altered absorption or metabolism of one or more drugs in a combination, multidrug pharmacokinetics, or viral resistance to one or more agents. When the decision to change therapy is based on HIV RNA, a second viral load test is needed before the decision is made.

In general, it is preferable to change all the drugs used in the failing combination, except in those instances when viral loads are undetectable and a side effect can be traced to a specific medication. In some cases where the viral load is not suppressed completely, it may be best to continue the present regimen because it has been partially effective and the client's options are

limited. If the initial combination therapy was effective but the client later developed detectable viral loads, second-line (salvage) combinations are less likely to be effective.

Clients temporarily discontinue antiretroviral therapy for many reasons (Singh et al., 1996). However, there are no studies estimating the number of doses, days, or weeks missed that would increase the likelihood of drug resistance. If clients must discontinue any antiretroviral medication for an extended time, stopping all their medications simultaneously may minimize the chance of developing resistant viral strains.

Combination therapy commonly requires the client to take large numbers of pills, up to 20 per day. Arranging schedules to take medication with or away from meals, timing doses, having access to refrigeration, and keeping adequately hydrated can be a full-time job. This may be difficult for clients who are homeless, currently using drugs, relapsing, and so on, and these issues must be assessed prior to changing regimens.

Resistance to antiretroviral agents

Drug resistance remains an obstacle to achieving the full benefits of antiretroviral agents. HIV's rapid replication rate fuels continual production of HIV variants (mutations) that thrive under the selective pressure of antiretroviral therapy. Combination therapy that suppresses HIV replication can delay the emergence of drug-resistant virus. However, a viral load below the limit of detection does not always mean that viral replication has completely halted, particularly in areas such as lymph nodes. Assays to measure whether HIV can grow despite the presence of a specific medication (resistance assays) are now available, but their application remains to be established.

Pharmacologic Interactions

HIV infection does not change the need for medications to treat substance abuse. The most common medications used to treat substance abuse are methadone, disulfiram (Antabuse), buprenorphine (Buprenex), and naltrexone (ReVia). In addition, benzodiazepines, barbiturates, clonidine hydrochloride, and other medications commonly are used in detoxification. These medications can be used by HIV-infected substance abusers in the same way they are used by uninfected clients. Neither maintenance nor detoxification treatment need be altered by the presence of HIV infection.

Interactions with methadone

The best-documented interaction between substance abuse medication and HIV infection medication is that of methadone with rifampin (Rifadin), a drug used to treat TB or, less commonly, MAC (Kreek et al., 1976). Rifampin causes a faster breakdown of methadone in the liver and a faster decrease in plasma methadone level. This results in rapid onset of classic opioid withdrawal symptoms, usually within several days of taking rifampin. Increasing clients' daily methadone doses will prevent this outcome. Typically, the dosage is increased by 10 mg every 1 to 2 days, beginning on the day rifampin is started and increasing as needed to prevent symptoms of opioid withdrawal, titrated to prevent this oversedation. It often is necessary to continue this pattern until the dosage is at least 50 percent greater than the original daily dose. It is important

for the client or the physician to inform the methadone program of changes in the client's medication.

Rifabutin (Mycobutin) is a medication structurally related to rifampin and frequently used for prophylaxis and treatment of MAC in HIV-infected clients. Rifabutin may have a pharmacologic interaction with opioids similar to that of rifampin.

Phenytoin (Dilantin) and phenobarbital (Phenob) have a similar but less dramatic effect on plasma methadone levels, causing opioid withdrawal symptoms over a period of days to weeks. It may be necessary to increase methadone dosage, but usually this increase does not have to be as great or as rapid as for rifampin. Other interactions are in Figure 2-12.

When therapy with rifampin or phenytoin is discontinued, methadone doses should, in most cases, gradually be lowered to avoid oversedation. Clients usually arrive at a final stable dose that is higher than the original dosage level before the other medications were introduced (Selwyn and O'Connor, 1992).

Interactions with antiretroviral agents

No clinically significant interactions have been found between AZT and either methadone or disulfiram. One study suggested, however, that elimination of AZT may be slower in methadone-maintained clients compared with a control group not receiving methadone. However, this study found no evidence that clinical toxicity from AZT was worse in the methadone-maintained group (Schwartz et al., 1990).

Only a few studies have investigated the interactions of other antiretrovirals with methadone. Early laboratory studies showed that ritonavir and indinavir may increase methadone levels; nevirapine may decrease methadone levels, and saquinavir has no effect.

However, only one study has been reported using client plasma levels; here, ritonavir decreased methadone levels by 35 percent, the opposite of what was expected from laboratory studies. Two case reports of nelfinavir decreasing methadone levels have been documented. Further work on drug interactions is needed because in vitro data may not accurately predict in vivo results. If drowsiness or other symptoms associated with methadone excess are reported, clinicians might consider lowering methadone dose using trough methadone blood levels to guide treatment. Similarly, trough levels can be used to establish whether withdrawal symptoms are due to increased methadone metabolism (Gourevitch and Friedland, 1999a).

Pain Management

Managing acute and chronic pain in HIV-infected, substance-abusing clients can be a challenging clinical problem (Selwyn and O'Connor, 1992). Although providers may have well-founded concerns about potential drug-seeking behavior, these concerns may interfere with clinical judgment about the appropriateness of using narcotic analgesics. Like other clients, substance abusers often are undertreated for acute pain. Medication for pain control, including

narcotics, should never be withheld merely because a client has a history of substance abuse.

As with all clients in pain, the provider's primary goal is to maximize comfort while minimizing side effects. Local measures (rest, heat, ice, analgesic rubs) should be used as a first line of pain treatment where appropriate.If these measures fail to adequately relieve the pain, a systematic pharmacologic approach is recommended. Initially, over-the-counter medications such as aspirin, acetaminophen (Tylenol), and nonsteroidal anti-inflammatory agents should be used, with dosages increased as needed. Caution must be used in employing acetaminophen in clients with liver diseases such as hepatitis C, as it can worsen liver disease.

If these medications prove inadequate for pain relief, narcotic analgesia may be necessary. Because of their tolerance for narcotics, clients with opiate use disorders generally require higher doses of narcotic analgesia and more frequent dosing intervals for effective pain control. This is especially true for clients maintained on methadone. See also the section below, "Use of Unapproved Medications or Alternative Therapies."

Agents used for persistent neuropathic pain include anticonvulsants (phenytoin, carbamazepine [Tegretal], gabapentin [Neurontin]), tricyclic antidepressants (amitriptyline [Elavil], desipramine [Norpramin]), or topical agents (capsaicin [Capzasin]). These agents may be used alone or in combination with other analgesics. Acupuncture may be particularly helpful in some cases of neuropathic pain.

The treatment plan and the reason for using narcotics for pain control must be clear to both provider and patient. It is important not only that the patient know that her pain is taken seriously but also that narcotic use will not be extended beyond a time-limited period required for analgesia. Late-stage clients with AIDS who have chronic, severe pain syndromes may require long-term analgesia. Attempting to manage pain in methadone-maintained clients by increasing their daily dose of methadone is a common error. Instead, if narcotic analgesics are indicated, providers should continue the client's usual methadone dose and add a shorter acting narcotic for acute pain control. Pentazocine (Talwin) and other mixed opiate agonist-antagonists should not be used for analgesia in methadone-maintained clients because they may precipitate withdrawal.

Chronic pain management in substance abuse disorder clients is most effective if there is close primary care followup and coordination of a treatment plan with substance abuse treatment professionals. Pain management specialists should be consulted as needed to examine alternative management strategies (Selwyn and O'Connor, 1992).

Interventions

Currently, no validated protocol for HIV/AIDS pain therapy exists. Because clients with HIV/AIDS often have pain problems similar to clients with cancer, the World Health Organization's (WHO's) "cancer pain analgesic ladder" is a useful starting point for managing pain in HIV-infected persons.

1. The first step of the WHO treatment ladder is to use acetaminophen (Tylenol) or a nonsteroidal anti-inflammatory drug (NSAID) (e.g., ibuprofen, naprosyn). Long-term use

of NSAIDs is not recommended because of gastrointestinal and renal side effects and toxicities. Caution should be employed when using acetaminophen in clients with liver disease.

2. Step two of the ladder adds a "weak opioid" such as codeine, oxycodone, hydrocodone, or dextropropoxyphene to acetominophen or an NSAID. This regimen is useful for mild to moderate pain.

3. The third step is to add an adjuvant (drugs that may either enhance the effect of the opiate or have independent pain-relieving activity). Examples of adjuvants include corticosteroids, antidepressants, anticonvulsants, and antihistamines.

4. Step four should be used for clients with severe pain intensity. At this stage, clinicians recommend the use of a strong opioid like morphine, fentanyl/duragesic patches, hydromorphone, or methadone. Medication dosages should be individually titrated and scheduled around the clock with extra doses provided for "breakthrough" pain.

Additional points are as follows:

- In any setting, the quality of pain control is influenced by the training, expertise, and experience of clinicians.
- Always treat the underlying cause of the pain. Treating the cause of pain (infection, tumor, etc.) is the single best method of pain relief.
- Decisionmaking about pain control should include the input and preferences of the client and family.
- When initiating pain treatment, the least invasive route for medication administration should be selected first. This is usually the oral route, unless contraindicated for some reason.
- Continually evaluate the response to the regimen or plan. Change the drug, schedule, dose, and route; prevent and treat side effects of the pain medication as often as needed.
- Establish clear directions about whom the client or caregiver should notify in case of problems.
- Pain management should be reevaluated at points of transition in the provision of services (i.e., from hospital to home) to ensure that optimal pain management is achieved and maintained.
- Effective pain management requires collaboration across disciplines and among clinicians.
- Effective pain relief should be accomplished by developing a regimen or plan that *prevents* pain.
- Do not interrupt HIV treatment as a deliberate consequence of methadone maintenance disruptions (i.e., do not hold antiretroviral treatment "hostage").

Special Considerations for Substance-Abusing Clients

When opioids are required for pain control, the dual diagnosis of HIV/AIDS and a substance abuse disorder produces a challenge for even the most experienced clinician. Specific principles, listed below, must be followed to ensure fair assessment of the pain complaint (e.g., clients may fabricate pain to obtain drugs) and to provide the best chance of achieving satisfactory pain relief

(Portenoy and Payne, 1992).

- When developing a pain treatment plan, distinctions must be made among (1) clients who are actively using illicit opioids and
- receiving treatment for pain, (2) former drug abusers who no longer use drugs, and (3) clients in methadone maintenance (Fultz and Senay, 1975).
- Clients actively abusing heroin or prescription opioids and those on methadone maintenance should be assumed to have some degree of drug tolerance, which necessitates higher starting doses and more frequent dosing intervals of pain medication than in the nonaddicted client.
- Choose a medication route and formulation that are less likely to be diverted or abused (e.g., controlled-release oral or transdermal [patch] drug).
- Set firm limits on the ability of the client to negotiate for escalating doses of opioid.
- Use adjuvant medications to enhance opioid analgesia.
- Acting out and noncompliance are frequent responses to poor pain management.
- Clients who are actively abusing drugs often manifest psychological disorders that influence pain perception (depression, anxiety), requiring concomitant treatment.
- In clients who have abused drugs in the past or for those on methadone maintenance programs, the combined stress of HIV/AIDS and pain may manifest itself in the reappearance of substance abuse behaviors.
- Nonopioid analgesics should never be substituted for opioid analgesics to treat severe pain in the suspected or known substance abuser.

Reducing Risk of Medication Abuse

Setting clear limits and devising a consistent treatment plan help reduce the risk of medication abuse by substance-abusing clients. The following strategies are recommended:

- Designate one care provider to dispense prescriptions for controlled drugs.
- Dispense limited amounts of controlled drugs (e.g., 1 week's supply or less).
- Advise clients that lost or stolen prescriptions will not be replaced (see also "Abuse of Psychiatric Medications" in Chapter 3).

Informal verbal "contracting" with patients about the need to discuss symptoms openly and not seek prescriptions from multiple providers should occur once trust in the primary care relationship is established. Discussing the risks of serious drug interactions may allow patients to understand provider concerns.

Abuse of intravenous infusion lines

Clients symptomatic with AIDS are frequently prescribed narcotic analgesics and may even have an indwelling intravenous line for infusion therapy. Injection drug users are at very high risk of using this indwelling intravenous line to administer heroin, cocaine, and other drugs of abuse. It is therefore essential that clients with such lines who are at risk for misuse be cared for in residential health care settings, including hospice-based home care, where adequate monitoring

and support can be provided.

Clinical Trials Enrollment

Good physician-client relationships can foster client participation in clinical trials. Ongoing efforts are needed to educate clients and their families about the importance of clinical trials and to alleviate any suspicion of the medical profession. Clinicians should be aware that HIV-infected substance abusers in abstinence-based treatment programs may be reluctant to participate in clinical trials of unapproved medications because such participation reminds them of taking illicit drugs. Also, recovering substance abusers in abstinence-based treatment programs may not want to take drugs of any kind.

Specific efforts should be made to incorporate more clients with substance abuse disorders, women, and minorities into HIV clinical trials. All of these groups currently are underrepresented.

To avoid conflicts of interest, it is recommended that the clinician responsible for the clinical trial not be the client's primary care provider, if possible. When a client enters a trial, followup mechanisms for results must be in place so that this information is available to substance abuse treatment staff.

Use of Unapproved Medications And Alternative Therapies

In the face of life-threatening, chronic illness, when a cure is not available, many clients will seek unapproved medications or alternative therapies. Care providers must be aware that HIV-infected clients may be using alternative or complementary therapies, for example, acupuncture, meditation, and vitamin and herbal dietary supplements. According to one study of clients with HIV in Boston (Fairfield et al., 1998), these clients used alternative therapies at a high rate; they frequently visited alternative therapy providers, incurred substantial expenditures, and reported improvement with these treatments.

Unless a therapy is known to be harmful, however, clients need not be discouraged from trying it. Clinicians have a responsibility to find out, in a nonjudgmental manner, what alternative or unapproved therapies clients are using and then to obtain as much information as possible about these therapies. This information should be shared with clients, emphasizing that the risks and benefits of these therapies cannot always be predicted. Certain alternative therapies (e.g., acupuncture, meditation, herbal teas) may actually help to decrease clients' reliance on or need for controlled substances, narcotic analgesics, sleeping medication, and so forth.

Unsupervised antibiotic use can complicate the diagnosis and treatment of bacterial infections in HIV-infected substance abuse disorder clients. Clinicians should specifically ask clients about unsupervised antibiotic use because clients may not consider the information relevant to their medication or drug use histories (Selwyn and O'Connor, 1992).

Prophylaxis Against Opportunistic Infections

Current strategies for HIV/AIDS care include the use of prophylactic regimens to help prevent specific opportunistic infections. As clients survive for longer periods with lower CD4+ T cell counts, it is important to develop additional prophylactic regimens for infections that occur at more advanced stages of HIV (Figure 2-13). A recent review summarizes current practice regarding prophylaxis of opportunistic infections in HIV-infected clients (CDC, 1997c).

Because of the range of medications that an HIV/AIDS patient may take, another critical strategy for HIV/AIDS care is to designate someone (other than the physician) as a medication "case manager." This person would communicate with all the specialists a patient is seeing and monitor all the drugs prescribed so that no harm is done to the patient.

Pneumocystis Carinii Pneumonia

Pneumocystis carinii pneumonia (PCP) was the first opportunistic infection for which prophylactic regimens were developed. Since the late 1980s, widespread use of PCP prophylaxis has resulted in a dramatic decrease in incidence of this opportunistic infection. However, despite the availability of effective prophylaxis, PCP is still the most common opportunistic infection; many clients who develop PCP are unaware of their HIV status and hence are not receiving prophylaxis.

The risk of PCP increases significantly when a client's CD4+ T cell count drops to around 200. It is recommended that all clients with CD4+ T cell counts of 200 or below receive ongoing PCP prophylaxis. Because of their high risk of progressing to AIDS, HIV-infected clients with histories of oral candidiasis or other AIDS-defining infections should be offered PCP prophylaxis regardless of their CD4+ T cell levels. This includes clients who have had PCP before because there is a high rate of recurrence of PCP (more than 30 percent within 1 year).

Trimethoprim-sulfamethoxazole (TMP-SMX) (Bactrim DS, Septra) is the most effective anti-PCP medication (Bozzette et al., 1995). A single daily dose of one double-strength tablet is most commonly prescribed, although thrice-weekly dosing may be adequate. A daily single-strength tablet may also be effective and may improve adherence.

Clients who comply with this prophylactic regimen have only a 5-percent chance of developing PCP. Additionally, clients taking TMP-SMX for PCP prophylaxis may also decrease their chances of contracting cerebral toxoplasmosis and pyogenic bacterial infections. This may be especially important for HIV- infected substance abusers who are at high risk for sinusitis, bacterial pneumonia, and endocarditis.

For clients who cannot tolerate TMP-SMX, dapsone is a reasonable alternative. Dapsone, however, can cause hemolytic anemia in clients who are deficient in the enzyme glucose 6-phosphate dehydrogenase (G6PD), especially people of African descent. Therefore, clients must be screened for this deficiency before beginning therapy. The minimal effective dose of dapsone is unknown; regimens of 50 mg per day, 100 mg per day, and 100 mg three times per week are common.

Aerosolized pentamidine, in a single dose of 300 mg per month, is another option for PCP prophylaxis. The advantages of aerosolized pentamidine are that it has little, if any, systemic toxicity, and it may be the only medication a client can tolerate. However, it is clearly inferior to TMP-SMX for persons with CD4+ T cell counts below 50. Secondary breakthrough rates of PCP in clients on pentamidine may exceed 15 percent a year. In addition, extrapulmonary pneumocystosis, where clients show evidence of PCP infection outside the lung, has been seen. These manifestations occur more commonly in clients receiving only inhaled pentamidine rather than systemic prophylaxis with TMP-SMX or dapsone.

Pentamidine should be administered only in settings with adequate ventilation that are consistent with CDC standards. Not only can pentamidine administration produce bronchospasm and cough, but the coughing has been associated with transmission of TB in inadequately ventilated settings. Some substance abuse treatment programs offering onsite aerosolized pentamidine use specially designed sputum induction and pentamidine administration booths equipped with strong exhaust systems and high-efficiency particulate air filters to decrease the risk of contamination.

Side effects

TMP-SMX is well tolerated, with a low incidence of side effects. However, clients with HIV infection have a higher risk of allergy to sulfonamides than other client populations and must be monitored for adverse effects. Possible side effects, which tend to be dose related, include fever, rash, leukopenia, anemia, nausea, and vomiting. Serious reactions such as Stevens-Johnson syndrome, mucous membrane ulceration, hepatitis, and serum sickness are unlikely but potentially serious.

Clients on dapsone may experience rash, gastrointestinal upset, and anemia. Less common side effects include mental state changes and peripheral neuropathy. Sulfa allergy is generally not a contraindication to dapsone. Many clients who have developed rashes on TMP-SMX are able to tolerate dapsone without adverse effects; however, they should be monitored as part of routine followup.

Prophylaxis during pregnancy

The current standard of care is to offer a pregnant woman PCP prophylaxis if she would be so treated if not pregnant (e.g., CD4+ T cell count less than 200, or preexisting HIV-related disease). Although the possible risks or benefits to the fetus are uncertain, it has become standard to use TMP-SMX until 36 weeks of gestation and then change to aerosolized pentamidine to prevent neonatal exposure to sulfonamides (which can cause jaundice in the newborn). ↑ TOP

Toxoplasmosis

Cerebral toxoplasmosis, another common opportunistic infection in clients with AIDS, occurs most frequently in people who previously had a positive antitoxoplasma antibody test. Serologic testing for toxoplasma antibody is recommended as part of the basic primary care approach to HIV infection, in order to detect clients at high risk for this opportunistic infection.

For clients with CD4+ T cell counts below 100, a positive antitoxoplasma antibody test is reason to consider toxoplasmosis prophylaxis. TMP-SMX also offers protection against the development of toxoplasmosis, but for clients who cannot tolerate TMP-SMX it has been suggested that dapsone plus pyrimethamine may provide effective prophylaxis against toxoplasmosis as well as PCP. Practitioners may also want to remind clients who own cats that changing cat litter without gloves and a mask may put them at higher risk for toxoplasmosis. Clients with a history of toxoplasmic encephalitis and other diseases from toxoplasmosis are maintained on chronic suppressive therapy with sulfadiazine (Sulfadine) and pyrimethamine plus folinic acid.

Mycobacterium Avium Complex

Clients with AIDS also are at risk for infection with atypical mycobacteria, especially MAC. This is a late-stage complication of HIV disease that generally occurs in its disseminated form (e.g., in the blood) only in clients with CD4+ T cell counts less than 50. As clients survive longer with low CD4+ T cell counts, prevention and treatment of this common complication will be increasingly important. Started at CD4+ T cell counts of 75 to 100, there are three options for prophylaxis against MAC. The macrolide antibiotics, clarithromycin (Biaxin) (500(1,000 mg daily) and azithromycin (Zithromax) (1,200 mg once a week), are effective. The rifampin-like drug rifabutin also is approved for prophylaxis (300 mg daily). Rifabutin, like rifampin, causes accelerated metabolism of methadone; as a result, caution should be exercised in prescribing rifabutin to methadone-maintained clients. Rifabutin may also interact with other HIV medications. For a list of methadone interactions with HIV medications, see Figure 2-12.

Because of the potential for adverse drug interactions and the overload of daily pills for clients with low CD4+ T cell counts, some clinicians opt to wait until the CD4+ T cell count drops to 50 before initiating prophylaxis for MAC, and others do not use prophylaxis at all. Because MAC generally responds well to treatment (although treatment usually requires two medications), prophylaxis options should be discussed.

Cryptococcosis

Cryptococcal meningitis is a relatively infrequent complication of HIV infection, but it is one of the more common AIDS-defining opportunistic infections of the CNS. Treatment of cryptococcal meningitis has been greatly aided by the introduction of new systemic triazole antifungal medications such as fluconazole and itraconazole (Sporanox). These agents have made it possible to shorten the initial course of intravenous therapy with amphotericin B for cryptococcosis and certain other systemic fungal infections (e.g., histoplasmosis) and have allowed chronic suppressive therapy with oral agents that do not require chronic intravenous administration.

Because cryptococcosis is not a common infection (occurring in fewer than 10 percent of clients with AIDS), routine prophylaxis is not cost-effective. However, intermittent prescription of triazoles for the more common oral candidiasis may unintentionally be leading to the decrease in cryptococcal disease.

Routine prophylaxis of cryptococcosis carries a risk of promoting development of resistant organisms, including resistant *candida* and other fungal species. In addition, in parts of the country where histoplasmosis and coccidioidomycosis are more common fungal complications of AIDS, the use of fluconazole has not been associated with decreased risk of occurrence of these infections.

Herpes Simplex Virus

HIV-infected clients with herpes simplex virus (HSV) may be prone to recurrent genital HSV infection, and those symptomatic with AIDS may develop widespread cutaneous disease. There is no strict threshold for initiation of prophylaxis. Clients may receive chronic prophylaxis with acyclovir (Zovirax) (generally from 1,000 to 1,500 mg daily in two or three doses) or famciclovir (Famvir) (500 mg twice daily) as might be given to clients without HIV infection. The likelihood of recurrent HSV infection increases with a declining CD4+ T cell count. Acyclovir, taken together with antiretroviral therapy, may benefit late-stage AIDS clients (Stein et al., 1994; Youle et al., 1994), although this remains controversial.

Cytomegalovirus

There has been much interest in potential prophylactic agents against cytomegalovirus (CMV), which, like MAC, has been increasingly common in clients surviving for longer periods of time at low CD4+ T cell counts. CMV most commonly causes retinitis, which can lead to blindness if untreated, and may also cause neurologic, gastrointestinal, adrenal, pulmonary, and other systemic diseases.

An oral form of ganciclovir (Cytovene), used as a prophylactic, may reduce CMV incidence although data on its effectiveness are conflicting. This medication has low serum levels that may promote CMV resistance; it has many side effects, requires careful monitoring, and requires the client to take many pills. In addition, initial retinitis is rarely sight-threatening; therefore, primary prophylaxis is not widely recommended. Currently, the treatment options for active CMV are intravenous ganciclovir, foscarnet (Foscavir), cidofovir (Vistide), or intraocular formivirisen.

Bacterial Infections

Researchers noted the presence of bacterial pneumonia and sepsis in injection drug users before the HIV/AIDS pandemic, but they occur more frequently in HIV-infected substance abusers. Bacterial pneumonia in this population is most often caused by *Streptococcus* pneumonia and *Haemophilus influenzae*. Both bacterial pneumonia and related bacteremia tend to occur in the earlier stages of HIV and can be predictors of subsequent HIV-related illness in previously asymptomatic clients. Drug smoking and cigarette smoking may account for at least some of the increased risk. Persons with HIV develop invasive pneumococcal disease at a rate of 150 to 300 times higher than uninfected persons.

Bacterial endocarditis is a well-recognized complication of IDU. Several studies have suggested that HIV infection may aggravate the frequency and severity of endocarditis, and others have shown a similar endocarditis course in HIV-positive and HIV-negative drug abusers (Nahass et

al., 1990). Active injection drug users also are at risk for a variety of serious bacterial infections involving the skin, soft tissues, bones, joints, central and peripheral nervous systems, and other anatomical sites. Proper needle hygiene and skin disinfection before drug injection may help prevent some of these complications.

Sexually Transmitted Diseases

STDs are common in substance abusers, especially crack cocaine abusers. Women and men involved in commercial sex work or the exchange of sex for drugs have particularly high rates of STDs.

Baseline assessment should include taking the client's history of STDs and any involvement in sex-for-sale or sex-for-drugs transactions. Inspection for genital and perianal lesions should be part of the baseline physical examination. Serologic testing for syphilis, including both treponemal and nontreponemal tests (e.g., Venereal Disease Research Laboratory and fluorescent treponemal antibody-absorption, should be included in the initial laboratory testing screen.

Female substance abusers should be offered a complete pelvic examination and testing for gonorrhea, chlamydia, and HSV as well as the more common bacterial vaginosis, trichomonas, and candidiasis. (See section on women's health issues below.) Women should also have Pap smears at least annually because of the risk of cervical cancer.

Syphilis

HIV-infected clients with primary and secondary syphilis should receive three weekly doses of benzathine penicillin or treatment with supplemental antibiotics (e.g., amoxicillin or ampicillin with or without probenecid) in some cases.

While lumbar puncture and cerebrospinal fluid (CSF) examination would be required to formally rule out neurosyphilis in persons with latent syphilis, a more practical plan for treatment of an HIV-infected substance abuse population is as follows:

- Treat all latent-syphilis HIV-infected clients.
- Reserve lumbar puncture and CSF examination for clients with neurological complications or whose followup serologic tests do not indicate a clear response to antibiotic therapy.
- Have a low threshold to refer clients for further diagnostic workup or treatment as indicated.

Hepatitis

Evidence of infection with HBV and hepatitis C virus (HCV) has been found in more than two thirds of long-term injection drug users (Esteban et al., 1989;Stimmel et al., 1975). Chronic substance abusers are also at increased risk for infection with hepatitis A virus (HAV) and hepatitis delta virus (HDV), which coexists with HBV. Concurrent alcohol use may also cause

liver-function abnormalities, thus complicating clinical diagnoses. Because many commonly used HIV medications--including TMP-SMX, pentamidine, dapsone, rifampin, and ritonavir-- may cause liver toxicity, liver function tests are required.

There is no consistent evidence that coexisting chronic HBV infection adversely affects the course of HIV disease or, conversely, that HIV disease adversely affects coexisting HBV infection. However, individuals who are coinfected with HIV and HBV may have higher blood levels of HBV than individuals who are not HIV infected. Consequently, these coinfected individuals may be at higher risk of transmitting HBV infection. HIV does seem to accelerate the course of HCV infection, leading to more rapid progression to cirrhosis (Soto et al., 1997).

Drugs used in treating HIV and its complications affect HBV (lamivudine, famciclovir, interferon-alpha) and HCV (interferon). Ribavirin, which is used in the treatment of HCV, should not be used with AZT. Flares of HCV have been reported with initiation of potent antiretroviral therapy. Rebound of HBV can occur in clients with HBV when they stop taking lamivudine.

Nervous System Disease

Clinicians caring for HIV-infected clients must frequently assess clients for altered mental state and other neurologic and neuropsychiatric syndromes. Differential diagnosis in such clients may include HIV-related dementia or encephalopathy, specific opportunistic infections affecting the CNS, metabolic or toxic encephalopathy, and the effects of substance abuse (see also Chapter 3). In HIV-infected clients, underlying neurologic conditions associated with substance abuse can obscure or complicate diagnosis of the varied causes of peripheral nervous system disease.

HTLV-I and HTLV-II

These retroviruses are "cousins" of HIV. Human T-lymphotropic retrovirus type 1 (HTLV-I) has been associated with adult T-cell leukemia/lymphoma and with certain chronic degenerative neurologic diseases. Human T-lymphotropic retrovirus type 2 (HTLV-II) is less clearly associated with specific disease outcomes.

In the United States, infection with HTLV-I and HTLV-II is concentrated among injection drug users. Seroprevalence studies in the mid-1980s found that more than one-third of substance abusers in selected groups sampled in the New York City metropolitan area and in the southeastern United States were infected with HTLV-I or HTLV-II.

In at least one study, HTLV-II coinfection was associated with rapid progression of HIV disease in substance abusers infected with both viruses (Page et al., 1990). Clinicians caring for HIV-infected substance abusers should suspect coexisting HTLV-I or HTLV-II infection and consider serologic testing in clients with degenerative neurologic disease, T-cell leukemias, or rapidly progressing HIV disease.

Malignancies

Three types of cancer--Kaposi's sarcoma, malignant lymphoma, and invasive cervical cancer--are considered AIDS-defining conditions under the classification system for HIV infection and AIDS established by the CDC in 1993 (see Appendix C). HIV-infected substance abusers are at relatively low risk for Kaposi's sarcoma; however, malignant lymphomas have been documented in this population. Persistent generalized lymphadenopathy is common in HIV-infected clients, and palpable lymphadenopathy is common in injection drug users, particularly those who continue to inject drugs. Nevertheless, the presence of large (greater than 2 cm), firm, tender, or rapidly growing lymph nodes in an HIV-infected injection drug user should always prompt further diagnostic evaluation. The women's issues section in this chapter provides discussion of cervical cancer. In addition to these AIDS-defining cancers, other malignancies have been found to occur with greater frequency in HIV-infected substance abusers. These non-AIDS-defining cancers (reported in several case studies and one population-based study) include solid tumors of the lung, head and neck, and gastrointestinal tract, of which lung tumors are the most common (O'Connor et al., 1994b).

Immunizations

The CDC recommends that HIV infection be considered an indication for pneumococcal vaccination because of the markedly increased risk of pneumococcal pneumonia among HIV-infected clients. The effectiveness of this vaccine in clients with severely weakened immune systems is questionable, but it has been found to provide moderate immunity when given in the earlier stages of HIV infection.

Vaccination against *H. influenzae* type B should also be considered because HIV-infected individuals, particularly injection drug users, are at increased risk for *H. influenzae* pneumonia.

Vaccination for viral influenza is potentially useful for two reasons:

1. HIV-infected clients are known to be at increased risk of pulmonary infection with bacteria that commonly complicate influenza.
2. Because symptoms of influenza may mimic those of opportunistic infections, minimizing the incidence of influenza may prevent unnecessary diagnostic evaluations for other HIV-related conditions.

The CDC also recommends that all HIV-infected individuals and the health care workers who provide their care should receive the hepatitis B vaccine. Clients with HIV infection, if they have not already been exposed to HBV, are at high risk of acquiring it and are more likely than non-HIV-infected individuals to become chronic HBV carriers. Furthermore, HIV-infected HBV carriers may be more infectious because they are likely to have higher blood levels of HBV (see information under "Laboratory Tests"). A complete HBV serologic profile should be part of the baseline assessment of all substance abusers with or at risk for HIV infection, and clients who are negative for HBV antibody markers should be considered eligible for HBV vaccine.

All the vaccines mentioned above are more effective when administered early in the course of HIV infection. The benefits outweigh the risks, and there is little evidence that these vaccines are

harmful to HIV-infected clients.

Few data exist on the safety or effectiveness of vaccinating HIV-infected adults for diphtheria, tetanus, mumps, rubella, polio, and measles. Inactivated polio, diphtheria, and tetanus vaccines are likely to be safe. Because these infections may cause illness in clients with suppressed immune systems, vaccination appears warranted according to standard guidelines for their use in non-HIV-infected adults.

Vaccination with the live, attenuated mumps, rubella, and measles vaccines may pose a greater risk to HIV-infected persons, and the benefit is less certain. However, these vaccines are used routinely in HIV-infected children whose immune systems are not suppressed, and in recent years the measles vaccine has been safely given to HIV-infected adults during local measles epidemics (see Figure 2-14).

Women's Health Issues

Primary care providers should be aware that, in general, the incidence of gynecological disorders is likely to be higher among female substance abusers than among non-substance-abusing women (DeHovitz et al., 1994; Millstein and Moscicki, 1995). Some disorders (such as STDs) result indirectly from substance abuse, while others may result from living conditions that influence the overall health status of women, such as the lack of regular medical care.

Vaginitis

Drug-using women, with and without HIV infection, have high rates of vaginitis. The most common causes include bacterial vaginosis followed by candidiasis and trichomonas, with no difference in incidence between HIV-positive and high-risk (e.g., drug-using) women. Among HIV-infected women, the risk of severe or refractory vaginal candidiasis increases with a declining CD4+ T cell count, but in most cases the treatment is the same as for HIV-negative women.

Cervical abnormalities

Since 1993, invasive cervical cancer has been considered an AIDS-defining condition. HIV-infected women are at high risk for cervical dysplasia and cervical cancer associated with human papillomavirus. Women who are current or former substance abusers constitute approximately 50 percent of AIDS cases in women in the United States. Clinicians treating substance-abusing women should therefore be particularly alert to the possibility of cervical cancer.

A cervical Pap test should be performed at least yearly, and abnormalities should be evaluated with colposcopy. Facilities treating HIV-infected women must either provide Pap smears and gynecologic followup onsite or have contractual arrangements for provision of these services.

Pregnancy

A large number of women become pregnant after they are diagnosed with HIV disease. There is no evidence that HIV disease progression is accelerated during pregnancy, after an abortion, or in the postpartum period (Alliegro et al., 1997). A woman's options should be discussed in a way that empowers her to make her own decision about whether to continue the pregnancy with optimal prenatal care or seek a termination. The infant initially will have a positive HIV antibody test result because of the presence of maternal antibodies in its blood. New DNA-PCR tests of infants' blood can diagnose HIV infection in infants soon after birth.

Maternal-fetal transmission of HIV can occur at any stage of gestation, although it is believed to occur primarily during labor and delivery. Use of AZT during pregnancy and in the neonate postpartum decreases the rate of vertical transmission of HIV by 65 percent. AZT does not appear to have any adverse fetal effects. Cesarean sections in HIV-infected women show a reduction in risk of transmission to the newborn as well (International Perinatal HIV Group, 1999).

Treatment providers should note that the 1993 Substance Abuse Prevention and Treatment Block Grants: Interim Final Rule requires prevention and treatment programs to link pregnant clients with prenatal services. See Chapter 4 for more information about pregnancy and HIV.

Nutrition

Substance abuse treatment personnel must be aware of the special nutritional needs of HIV-infected substance abusers. Poor oral intake and malabsorption of nutrients, caused by diarrhea and alteration of levels of endogenous anabolic hormones (especially in men), contribute to wasting. Staff should also be familiar with guidelines concerning nutritional supplements and with interventions to address the causes of inadequate food consumption. (See Figure 2-15 for a summary of factors that must be considered in relation to the client's food consumption.) Clients who are losing weight and for whom oral nutritional supplements are inadequate or ineffective should be referred to an HIV specialist. There are different nutritional concerns for clients on PIs, such as weight gain, "protease paunch," and elevated triglyceride levels. Significant weight loss is a predictor of poor survival. It is important to combine approaches to weight loss, including treating underlying illness, attention to nutrition, and correcting metabolic abnormalities that cause loss of muscle mass. This can be particularly challenging for inpatient treatment centers because the schedules for snacking and eating will have to be more flexible, and the usual rules may not work for someone who is HIV positive and in substance abuse treatment.

Cigarette Smoking

Smoking is highly prevalent among substance abusers. HIV-infected smokers are more likely to develop bacterial pneumonia, oral candidiasis, and hairy leukoplakia, and heavy smokers are more likely to develop these conditions than are light smokers. Smoking cessation strategies should be pursued in substance-abusing populations (Conley et al., 1996).

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