HIV TREATMENT UPDATE

A number of promising new drugs and treatment strategies have emerged over the past four years. However, they come with uncertainties about long-term efficacy and concerns about side effects. This issue of PERSPECTIVES provides an update on HIV antiviral drugs, new treatment strategies, and related psychosocial challenges.

Research Update

An estimated 82 percent of all HIV-infected individuals in the United States use antiviral medications to treat HIV. Antiviral drugs aim to suppress levels of HIV by stopping the virus from replicating, that is, reproducing itself.

To measure suppression of HIV levels, clinicians use viral load tests to quantify the concentration of HIV circulating in a person’s bloodstream. Suppressing HIV levels causes an increase in the number of CD4+ cells, thus improving immune functioning, slowing clinical progression of HIV disease, and, in turn, prolonging life.

Designed to interrupt HIV replication, antiviral drugs approved by the Food and Drug Administration (FDA) fall into one of the following three drug classes: nucleoside reverse transcriptase inhibitors, non-nucleoside reverse transcriptase inhibitors, and protease inhibitors. The two kinds of reverse transcriptase inhibitors interfere with an early stage of the HIV replication cycle, and protease inhibitors disrupt a later stage. Other antiviral drugs as well as other types of HIV medications are in development.

To suppress HIV levels more potently, clinicians prescribe two or more antiviral drugs, a strategy known as combination therapy. Most current antiviral treatment regimens consist of a combination of at least three medications. After triple combination therapy became commonly used in 1996, it quickly became the standard of care for people with HIV disease, and the number of AIDS-related deaths in the United States began to decline: there were 37,000 AIDS-related deaths in 1996; in 1999, the number of deaths dropped to 10,000.

Combination therapy uses drugs that interfere with the HIV reproduction cycle at different stages and minimizes the possibility of drug resistance. Drug resistance is the process by which the virus mutates and becomes less sensitive to specific medications. Mutated virus then multiplies and forms new strains that predominate and may render drugs less effective or completely ineffective. HIV can also become resistant to other drugs in the same class—a phenomenon known as cross-resistance—or to a number of different drugs, causing further treatment complications. Drug resistance can occur when people do not adhere to their dosing regimens, causing lower blood levels of the drug and less complete suppression of viral growth. Other reasons for drug resistance include drug interactions with non-HIV medications and the possibility that, for some people, certain drug combinations may not be as potent as others.

Epidemiological studies have found cases of transmission of drug-resistant HIV. This means that
transmission will lead not only to HIV infection, but also to pre-existing resistance to particular HIV antiviral medications. In one four-year study of 80 newly infected people, most of whom were tested in New York or Los Angeles, 16 percent were infected with a drug-resistant strain of HIV. In a larger, five-city study, however, only 2 percent of the 141 newly infected participants carried a drug-resistant strain. In addition, anecdotal reports suggest that HIV-infected individuals may become re-infected with a drug-resistant strain of HIV.

**Treatment Success and Failure**

The long-term success of combination therapy depends on the continual suppression of HIV growth. Treatment regimens are often defined as successful if they reduce the levels of a person’s viral load below the level of detection. Some people misinterpret “undetectable viral load” to mean that HIV has been eradicated from the body and can no longer be transmitted, but it actually means that the levels of viral concentration are too low to be detected by a given test. Depending on the type of test, viral loads below the level of detection may range from less than 40 copies of viral RNA per milliliter of blood to 500 copies per milliliter. Increased viral load or symptoms of HIV disease progression often signify an unsuccessful treatment regimen. In clinical practice, about half of HIV-infected people achieve a viral load count below the level of detection.

Lack of treatment success in clinical practice can result from inadequate drug potency, drug resistance, or interactions between different drugs that can lead to severe adverse side effects or lowered therapeutic efficacy. Unsuccessful treatment can also result from poor adherence to medication.

Adherence to medication regimens is essential to treatment success because suppressing HIV and inhibiting drug resistance requires a stable level of medication in the bloodstream. To achieve a desirable viral load, people need to maintain greater than 95 percent medication adherence, which means that no more than 5 percent of scheduled doses can be missed. Maintaining adherence can be difficult because combination treatment regimens can involve up to 40 pills and six specific dosing times per day. Some pills must be taken with food, while others require an empty stomach.

A California study of 170 clients of university-based clinics found that 70 percent of participants maintained greater than 95 percent medication adherence.

Combination therapy can lead to short- and long-term adverse side effects, including vomiting, nausea, diarrhea, liver disease, bone density loss, diabetes mellitus, and peripheral sensory neuropathy, a nerve disorder that causes pain in the extremities.

Some people with HIV experience lipodystrophy, a disturbance in the way the body produces, uses, and distributes fat. Although many researchers believe lipodystrophy is a result of antiviral drugs, its cause remains unknown. Lipodystrophy can cause fat wasting of the face, arms, legs, or buttocks, and fat accumulation in the abdomen or back of the neck. The effects of lipodystrophy on physical appearance can affect self-esteem and act as a visible indication that a person is HIV-infected.

To correct the effects of lipodystrophy, some people undergo surgery to remove fat, switch antiviral drugs, or stop combination therapy altogether. A small study of lipodystrophy found that short-term treatment with recombinant human growth hormones led to improved body shape. However, this treatment is expensive, has its own side effects, and appears to correct body shape only during the timespan of treatment.

Some people misinterpret “undetectable viral load” to mean that HIV has been eradicated from the body.

### New and Experimental Treatments

Recent research has identified new HIV medications that do not belong to any of the three FDA-approved classes of HIV treatments. Currently in clinical trials, antiviral drugs called “fusion inhibitors” interfere with HIV replication by preventing the virus from entering CD4+ cells. A small study found that injections of the fusion inhibitor T-20 given over a 14-day period resulted in significant viral load declines in all 16 participants. Based on these results, T-20 appears to be as potent as currently available antiviral drugs in lowering viral load levels. Fusion inhibitors reportedly have no significant side effects and work against common drug-resistant HIV strains.

Researchers have also identified hundreds of potentially effective “integrase inhibitors,” including two highly potent compounds called luffin and saporin. Their effectiveness, however, has not been proven in clinical settings.

Some clinicians now prescribe hydroxyurea, a ribonucleotide reductase inhibitor, because of its reported ability to help nucleoside analog reverse transcriptase inhibitors to impede HIV replication. In a study of 77 HIV-infected participants taking the same two reverse transcriptase inhibitors, 54 percent of those given hydroxyurea achieved viral loads below the level of detection, compared to only 28 percent of those given placebo. Advantages of hydroxyurea include its relatively simple regimen of two capsules per day, its low cost, and its low risk of leading to drug resistance.
**Related Issue: Complementary and Alternative Treatment**

Complementary and alternative medicine encompasses a broad range of healing philosophies, approaches, and therapies that mainstream Western medicine does not commonly use or study. Most of these therapies focus on self-healing, and some integrate physical, psychosocial, and spiritual aspects of disease and wellness. A large nationwide study identified more than 230 complementary and alternative therapies being used by HIV-infected individuals. Alternative therapies popular among HIV-infected people include aerobic and non-aerobic exercise, prayer, massage, acupuncture, meditation, visual imagery, breathing exercises, vitamins, minerals, dietary therapy, and Chinese herbs.

About one-third of HIV-infected people use complementary or alternative medicine, and although many of them gain a sense of control over their health, the therapies have shown limited success in clinical research. Alternative treatments are difficult to quantify, define, or study in a controlled environment, partly because many alternative treatment providers tailor therapies to individual clients.

Research suggests that zinc and dehydroepiandrosterone (DHEA) have beneficial effects for people with HIV, while studies of certain Chinese herbs and acupuncture found no such correlation. In addition, it is uncertain if the use of some alternative medicines in combination with HIV antiviral treatments is safe. For instance, one study found that the use of St. John’s wort, an herbal anti-depressant, decreased levels of the protease inhibitor indinavir by 57 percent, potentially leading to drug resistance and treatment failure. Furthermore, adverse effects of alternative medicine may be mistaken for antiviral side effects.

There is a general lack of information regarding the pharmacology, drug interactions, and safety of these treatments. Moreover, there is a lack of industry-wide quality control for herbal products. For instance, depending on the manufacturer, the same kind of product can contain varying quantities of an active ingredient. Finally, success in combining complementary or alternative therapies has also not been well-documented.

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advantages include the risk of increased toxicity of other HIV drugs and lowered CD4+ cell counts. Another promising experimental drug is the non-nucleoside reverse transcriptase inhibitor calanolide A, a synthetic version of a compound found in nature. Research suggests that calanolide A reduces viral load and works against common drug-resistant strains of HIV.

“Immune modulators,” drugs that stimulate the immune system itself, also show signs of being effective. Two of the most promising immune modulators are interleukin-2 (IL-2) and WF10. Recent research suggests that adding IL-2 to triple combination treatment regimens improves immune function by increasing CD4+ cell counts, especially in people recently infected with HIV.

Results of a small study suggest that WF10 is clinically safe, enhances immunologic function, and does not cause seriously harmful side effects.

To simplify adherence, once-daily dosing drugs from the three FDA-approved drug classes have recently become available, and researchers continue to study others. However, this makes taking each daily dose more important and requires precise timing.

**New Treatment Strategies**

Researchers and clinicians have varied opinions about when to start antiviral therapy. The approach that became the most prevalent after the introduction of triple combination treatment is often called “hit early, hit hard.” This strategy dictates initiating an antiviral regimen that offers the most potent suppression of HIV replication as soon as possible after HIV diagnosis. The theory behind treating early and aggressively is to minimize the loss of immune function by quickly and sharply reducing viral replication.

An increasingly common strategy, however, is to delay treatment to reduce the risks of drug resistance and side effects, which increase over the duration of treatment. This strategy recognizes that treatment cannot make asymptomatic people feel better, and that side effects may make them feel worse and eventually reduce adherence.

Most experts agree that symptomatic HIV infection requires antiviral therapy. People who fail to respond to initial antiviral treatment may attempt
salvage therapy” using a new set of drugs to which the virus might be sensitive. To help determine an appropriate salvage therapy regimen, clinicians may use genotype and phenotype tests to assess which drugs are ineffective for an individual by detecting the presence of drug-resistant mutations of HIV in a blood sample.

Structured treatment interruption (STI), sometimes called structured intermittent therapy (SIT), is a controlled break from antiviral treatment under a physician’s supervision. The theory behind this recent and controversial strategy is that interrupting treatment can offer a break from rigorous schedules and adverse side effects and, at the same time, possibly strengthen the immune response to HIV during brief rises in viral levels and while the immune system is in the process of recovery. A study of 12 long-term HIV-infected participants found no harmful events during the STI, which ranged from about 14 days to 30 days, depending on viral load. After beginning antiviral treatment again, four study participants experienced boosted immune systems.

As people with HIV live longer and in better health because of antiviral treatments, they are more likely to be sexual. With a growing pool of increasingly healthy HIV-infected people, it is important to address the prevention of HIV transmission from infected people to the uninfected people with whom they may have risky contact.

Dramatic improvements in health lead many HIV-infected people to reconstruct their life plans. Some people face “hope-fear dilemmas,” in which they experience a combination of optimism and uneasiness that arises from uncertainties about antiviral medications. People who initiate an antiviral treatment regimen must balance their hopes for improved health and investments in future plans with fears about potential side effects and the possibility that the treatment will fail.

Psychosocial Impacts of Treatments

Because of the widespread efficacy of antiviral treatments, some people no longer perceive HIV to be a major threat, a belief that may affect their risk behavior. While some studies have found no such effect, most large-scale studies on this topic have found that beliefs about the efficacy of new treatments and about resulting “undetectable” viral loads affect risk behavior. For example, a seven-state study conducted between 1998 and 1999 found that 31 percent of the uninfected or untested participants were “less concerned” about becoming infected and 17 percent were “less safe” about sex or drug use because of new HIV treatments.

Commercially Available HIV Antiviral Drugs

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<tr>
<th>Generic Name</th>
<th>Abbreviation</th>
<th>Brand Name</th>
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<tr>
<td><strong>Nucleoside Reverse Transcriptase Inhibitors</strong></td>
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<tr>
<td>zidovudine</td>
<td>ZDV or AZT</td>
<td>Retrovir</td>
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<td>Videx</td>
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Implications for Counseling

One of the greatest challenges for HIV test counselors is a result of one of the greatest gains achieved by AIDS researchers. In response to the widespread efficacy of antiviral treatment, some people consider HIV risk to be less significant than it once was, and it is increasingly common for counselors to report clients having a more casual attitude about the possibility of HIV infection. Many young people have not experienced the ravages of HIV disease, while many older at-risk men and women—either out of joy or exhaustion—no longer consider AIDS to be a devastating disease.

For many people, the risk of HIV infection is no longer a sufficient reason to change their behaviors, and the prospect of taking a drug and continuing life plans uninterrupted often appears to be a more appealing option than facing the ongoing challenges of reducing risk. However, while HIV infection is now manageable for some people with proper treatment, the regimens are complex and often have adverse side effects. It also remains unclear how long antiviral treatments will be effective, and there is a growing number of HIV-infected people for whom treatments have failed or are beginning to lose their efficacy.

Making behavior changes is often overwhelming and may be more manageable in increments. By emphasizing this, counselors can help clients begin to take their next steps. If clients perceive risk reduction to be unnecessary because of the availability of new treatments, it is essential for counselors to clarify misconceptions about treatments.

HIV is Still a Threat

In light of the benefits of new treatments, it is important for counselors to help clients recognize that becoming infected with HIV can still lead to illness, and that treatments may be ineffective, may cause severe side effects, and may necessitate major life-changing activities. There is still no cure for HIV and no way to eliminate the virus from the body once a person has become infected. The best alternative to a cure remains avoiding infection. Counselors must be able to present information about HIV infection and the related disease process as objectively as possible.

When clients deny the possibility of becoming infected despite their risk behaviors, it is important to address this contradiction. It may be appropriate to help clients visualize what an HIV-infected life may be like, especially with clients who seem to have unrealistically positive ideas of what life would be like under treatment.

When discussing HIV antiviral treatment, elements of misinformation and denial come into play. Counselors must be able to provide clear and accessible factual information as needed, then guide the conversation back to the same kinds of issues counselors and clients traditionally discuss. Some clients contradict the best information available and insist either that they are exceptions to the rule or that things are “not that bad anymore.” Respond to such statements by asking clients to clarify how they see themselves as exceptional and what they mean by “not that bad.”

Contradictions between clients’ desires and actions may become apparent as clients explain their reasons for testing, discuss their risk behaviors, and describe their understanding of risk information. Counselors may find it difficult to address contradictions, partly because they may consider doing so to be too confrontational. However, it is important for counselors to distinguish between being inappropriately confrontational—in content, tone, and presentation—and reflecting a client’s contradictory statements or beliefs in a neutral and balanced way. Remaining client-centered and establishing trust and rapport helps counselors build relationships that can more effectively address and anticipate some of the dilemmas and challenges clients may have to face.

When educating clients about HIV treatments, counselors must keep in mind their limited role. Even if a counselor has a great deal of knowledge about various new medications and treatment regimens, it is not within the scope of the HIV test counseling session to discuss these topics in detail. What matters most is that counselors understand the basic facts about treatment possibilities, for example, that various drugs attack the virus at different stages of replication. It is best for HIV-positive

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A Counselor’s Perspective

“Ten years ago, I thought there would be a cure by now, but there isn’t. Now I have clients who think that a cure is around the corner. But there is no reason to expect it to happen soon.”
clients to discuss information about specific treatments with HIV-knowledgeable health care providers. With clients who test negative, concentrate as much as possible on the fallacy that HIV is easy to treat, but also refer them to other resources for further information about treatment.

Counselor Frustration

As is true for other topics that arise with clients, it is important for counselors to understand their own feelings and beliefs about HIV treatments. In particular, counselors need to explore their attitudes about the choices HIV-positive people make about treatment and the choices of people who put themselves at risk for HIV because of hopes raised by new treatments.

Because HIV is a preventable disease, it is understandable that counselors may sometimes feel frustrated. Human behavior, however, is more complex than simple educational messages sometimes suggest.

References

32. Mocchegiani E, Muzzioli M. Therapeutic application of zinc in human immunodefiency virus-negative, HIV-knowledgeable health care providers. With clients who test negative, concentrate as much as possible on the fallacy that HIV is easy to treat, but also refer them to other resources for further information about treatment.

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In the face of HIV treatment “miracles” and the profound desire to engage in behaviors that are either pleasurable, addictive, or both, some clients resist acknowledging the risk HIV poses to them and their sex or needle-using partners.

Frustration may be difficult to avoid for counselors who are aware of the consequences of HIV infection, especially when clients appear unable or unwilling to change their risk behaviors. It is important to remember, however, that each appropriate intervention can contribute to a client’s progress in the continuum of behavior change. Emotions may cause some counselors to lose sight of the fact that it is ultimately the client’s responsibility to make change. An HIV test counselor’s effort is part of a much larger decision-making process in a client’s life. It can be helpful for counselors to explore their feelings, beliefs, and values about these matters with peers and clinical supervisors.

Counselors may find it especially disturbing that HIV treatments are sometimes not effective or that there is still no cure, and it is important for them to explore and express these feelings. This can be especially significant for seasoned counselors who have witnessed many promising and often disappointing treatments become available over the years.
Test Yourself

Review Questions

1. True or False: Combination therapy is an effective HIV treatment because it eradicates the virus from the body.

2. True or False: Drug resistance refers to the phenomenon by which a drug loses its effectiveness because of a mutation, that is, a change in the structure of HIV.

3. Combination therapy has resulted in which of the following effects? a) a decrease in AIDS-related deaths; b) short- and long-term adverse effects; c) decreased incidence of opportunistic illnesses; d) all of the above.

4. True or False: An HIV-positive person who has achieved “undetectable viral load” no longer has the virus in his or her body.

5. Which of the following classes of antiviral drugs have received approval from the Food and Drug Administration (FDA)? a) nucleoside reverse transcriptase inhibitors; b) non-nucleoside reverse transcriptase inhibitors; c) protease inhibitors; d) all of the above.

6. “Salvage therapy” refers to which of the following? a) using a new set of antiviral drugs to treat HIV-infected individuals for whom initial treatment was not effective; b) prescribing a random combination of drugs; c) resorting to a treatment regimen because of its low cost; d) none of the above.

7. True or False: There have been reports of transmission of drug-resistant HIV among newly infected individuals.

8. Structured treatment interruption can have which of the following effects? a) boosting of the immune system; b) rapid increase of viral load; c) development of drug resistance; d) all of the above.

Discussion Questions

1. How can counselors correct misconceptions clients may have about HIV treatments while remaining neutral, objective, and client centered?

2. How can test counselors stay abreast of the latest developments and trends related to HIV treatments and care?

3. How can counselors maintain a current file of appropriate referrals related to HIV treatments while keeping in mind the different needs of clients depending on their test results?

4. How can counselors respond to clients who state that they no longer feel threatened by HIV because of new treatments?

5. How can counselors cope with their own frustrations about antiviral treatments and the related psychosocial impacts on clients?

Answers

1. False. Combination therapy combats HIV by suppression of viral replication and, consequently, slows disease progression. It cannot eradicate HIV from the body.

2. True.

3. d.

4. False. “Undetectable viral load” means that HIV is still present in the blood but that its concentration is too low to be detected by a given viral load test.

5. d.

6. a.

7. True.

8. d.
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