Research Update

There are currently three classes of HIV antiretroviral drugs approved by the Food and Drug Administration (FDA): nucleoside reverse transcriptase inhibitors, also known as nucleoside analogs; protease inhibitors; and non-nucleoside reverse transcriptase inhibitors. All of these combat HIV by interfering with the mechanism that the virus uses to transform itself from one viral particle into many infectious units, but each class of drugs does this in a unique way. Protease inhibitors, for instance, interfere with HIV at a later stage in its development compared to reverse transcriptase inhibitors.

Historical Overview

In 1987, the FDA approved the use of AZT—a nucleoside reverse transcriptase inhibitor—making it the first drug marketed to treat HIV. For many years, people used AZT (also known as zidovudine; ZDV) by itself. Starting in 1991, one by one, other nucleoside reverse transcriptase inhibitors received FDA approval—first ddI (Videx) and ddC (Hivid), and later d4T (Zerit) and 3TC (Epivir). The approval of these drugs was important because they provided options to people who were unable to take AZT, either because of intolerable side effects or resistance to the drug. Resistance is the ability of HIV to mutate, or change itself, so that a treatment is no longer able to slow viral progression.1

Additional treatments also allowed people the option of using these drugs in combination with one another, a practice that reduces the risk of resistance1 and improves the effectiveness of a treatment regimen. Researchers attribute declining death rates from AIDS in the United States in 1996 largely to combination therapies. Last year, the FDA had approved four protease inhibitors: saquinavir (Invirase), ritonavir (Norvir), indinavir (Crixivan), and nelfinavir (Viracept), and two non-nucleoside reverse transcriptase inhibitors: nevirapine (Viramune) and delavirdine. Research and the anecdotal experience of people taking these drugs has demonstrated dramatic changes. In some cases, people whose immune systems had been severely weakened by HIV have experienced a marked turnaround in overall health and quality of life.
New medications have brought numerous clinical benefits. For example, in one study, adding a protease inhibitor such as saquinavir to an existing regimen of AZT and ddC led to a greater drop in blood level of virus and a rise in CD4+ cells, also known as T-helper cells, than just using AZT and ddC together. This effect has been seen with all the protease inhibitors. More importantly, preliminary results from several combination treatment studies that include protease inhibitors suggest such combinations reduce the rate of AIDS-defining illnesses or death in people with advanced disease, compared to regimens without protease inhibitors.

Beyond responding to HIV in the bloodstream, recent studies find that current drug combinations can reduce HIV in the lymph nodes and other body tissues. Some researchers suggest that current combinations could theoretically eliminate HIV from a patient’s body after several years of treatment. However, researchers have made clear that there are no known cases in which HIV has been eradicated from the body.

Regimen Challenges and Resistance

While they offer significant benefits, modern treatment combinations can be prohibitively expensive for people who do not have insurance coverage or do not qualify for government drug-assistance programs. Also, antiretroviral treatments can involve significant side-effects including nausea, headaches, skin rashes, liver problems, and diarrhea. Taken in combination, medications may interact and interfere with one another in unexpected ways, perhaps amplifying each other’s side effects.

Further, adhering to a drug regimen can drastically alter day-to-day life: people must take some drugs with food, or particular types of food, and others on a completely empty stomach several hours between meals. Some regimens require taking 25 or more pills daily. In addition, medications that must be taken every six hours can interrupt sleep. Given these difficulties, a person must be willing to accept the requirements of treatment regimens before starting them.

If a person does not adhere to prescribed dosing schedules for a drug, the virus can become resistant not only to that drug, but also to all the antiretroviral medications that person is currently taking. To continue treatments, this person would have to substitute three or more new drugs for the ones to which HIV has become resistant. Beyond this, there is evidence that HIV may become cross-resistant to other drugs of the same drug class if the virus mutates in response to one drug. For example, by becoming resistant to one protease inhibitor, HIV may be resistant to other protease inhibitors, even if a person has never taken the other drugs. Resistant strains of HIV create problems for anyone who may be exposed to the strain.

Researchers have made clear that there are no known cases in which HIV has been eradicated from the body.

Related Issue: Viral Load Tests

Viral load tests measure the amount of HIV in a person’s circulating blood plasma. HIV also exists in areas of the body other than circulating blood plasma, such as in lymphocytes.

High viral load indicates HIV is actively replicating, and people who have a high viral load develop AIDS-defining illnesses much more quickly than those with a low viral load. A rising viral load in somebody taking antiretroviral drugs can indicate that resistance is building, and can signal the need to change treatments.

Several studies have shown decreases in viral load to such an extent that HIV is undetectable in testing. An undetectable viral load level, however, does not indicate that HIV has been eradicated from blood plasma or that HIV will remain at undetectable levels. Such a result means only that the viral load is below the level at which current technology can measure HIV in blood plasma.

Viral load tests cost about $150 to $200 per test. Physicians recommend a person take two viral load tests at times in relatively close proximity to one another and average the results to establish a baseline viral load. After this, a person should generally measure viral load every three to four months and more often after starting or changing therapies.
people, someone recently infected with a resistant strain would have a decreased choice of drugs.

There are tests, called genotype tests, that physicians can use to measure HIV resistance to antiretroviral drugs. Such tests have become available only recently and their value in practical application is unproven.5

The possibility that some people—perhaps because of ongoing substance abuse, homelessness, or psychological challenges—might find it too difficult to adhere to treatment regimens has, according to anecdotal reports, led some physicians not to prescribe protease inhibitors for some patients. Providers, treatment advocates, and people with HIV are currently debating ethical and other questions raised by this practice.6

**Treatment Guidelines**

Since early in the AIDS epidemic, CD4+ cell counts have been the primary marker of HIV disease progression and a guide for initiating or changing treatments. Because HIV invades CD4+ cells and destroys them in order to replicate itself, a CD4+ test, which measures the number of CD4+ cells per cubic millimeter of blood, can determine damage already done to the immune system.7 More recent is viral load testing, which determines the amount of virus in circulating blood plasma. Viral load tests have made it possible to monitor disease progression before HIV has substantially damaged the immune system.8 Some research suggests that viral load is a more precise marker of disease progression and survival prognosis than CD4+ count. [For more on viral load testing, see “Related Issue: Viral Load Tests,” on page 2.]

Using these two laboratory tools together gives valuable information about when to begin treatments and the effectiveness of treatment regimens. But, limited information about new treatments and a lack of precision in understanding markers of progression lead to differing opinions about when a person should begin treatments and the specific treatments a person should use.

Two groups—one an international panel of physicians and the other a federally convened multidisciplinary group—have recently issued HIV treatment guidelines for adults and adolescents.6, 8 The guidelines have as their goal suppression of viral load to undetectable levels. The treatment guidelines discourage monotherapy, which means taking one drug, and they generally favor regimens combining two nucleoside analogs with a protease inhibitor. Such regimens are known as triple combination therapies.

Both guidelines are clear in recommending treatment for people with symptomatic infection. For people who are asymptomatic, the international panel is more specific in its recommendations. This panel recommends therapy for all people with viral load counts greater than 5,000 to 10,000 copies of HIV RNA per milliliter of plasma, regardless of CD4+ cell count, and for all people with CD4+ cell counts below 500, and, in particular below 350. At the very least, the panel recommends, anyone with HIV and detectable viral load should “consider” therapy. The panel states that pregnancy can make antiretroviral treatment decisions more complex, but that antiretroviral therapy should not be withheld because of pregnancy.6

To prevent perinatal transmission, the federal panel recommends monotherapy with AZT for relatively healthy pregnant women who do not require antiretroviral treatment for their own care.8

While both sets of guidelines address common treatment practices, they do not represent the practices or opinions of all physicians. Some physicians believe that a relatively low viral load may persist for long periods, and that initiating drug treatment might cause resistance while providing relatively little benefit. If a patient has a low viral load and high CD4+ cell count, he or she may safely defer therapy while monitoring viral load every three to six months.6 Conversely, others believe that any viral load can represent a need to begin therapy. They believe that “hitting hard and hitting early” is the key to fighting HIV infection and maintaining low viral load.9

**“Primary” Infection**

In some current studies, researchers are initiating long-term treatment with combination therapies for people in the initial weeks and months after infection. This includes people who are in the “primary” stage of HIV infection. A person in this stage typically has a very high viral load but has not yet developed an antibody response to HIV. This stage is commonly marked by acute retroviral syndrome,10 a condition that usually lasts two weeks and is characterized by flu-like symptoms, including fever, skin rash, cough, sore throat, mouth sores, sore muscles and joints, nausea, headache, diarrhea, and severe fatigue.

These studies, whose sites include Los Angeles, San Diego, and San Francisco, are based partly on the hope that treatments in the primary stage of infection could protect against irreversible immune system damage and possibly provide other benefits. Researchers are working with community providers to identify people seeking HIV testing or other services who have experienced symptoms of acute retroviral syndrome.11

**Post-Exposure Prophylaxis**

It has become routine to offer health care workers antiretroviral therapy for a period of four to six weeks following a significant occu-
Related Issue: Sex Risks in the Face of New Drugs

New treatments have led some service providers to express fear that people will be less concerned than in the past about protecting themselves to avoid HIV infection. This fear is based on various factors, including the possibility that with new treatments HIV disease will be less life-threatening. In addition, some providers have expressed fear that people may misinterpret viral load tests that show a person has an “undetectable viral load” to mean that he or she is “not infectious” and therefore able to engage in unprotected sex without risk of infection to another person.

In anecdotal, non-scientific reports, mainstream magazines and newspapers have described a new “sexual carelessness” resulting from treatment advances.18 HIV service providers describe the emergence of a new phenomenon among gay men of either serostatus in which unprotected sex is regarded as a sexual fetish, and referred to using terms such as “barebacking” and “raw sex.”19

Researchers acknowledge the possibility that higher rates of unprotected sex are occurring and are studying the subject. There is as yet, however, little published research on the subject. Researchers state that a person whose viral load is undetectable in viral load testing can still transmit HIV.4, 6 They also point out that viral load can increase rapidly if a person stops treatment or becomes resistant to it.

In addition, researchers have expressed concern that people with HIV who engage in unprotected sex might become reinfected with drug-resistant HIV strains. Prior to reinfection, these people may have been infected with a strain of HIV that would have responded to treatments, but because of infection with a drug-resistant strain these treatments will no longer be useful.

Partly in response to treatment advances, some mass-media prevention campaigns have recently focused less on HIV as a life-threatening illness and more as a cause of undesirable opportunistic infections. This focus underscores that HIV remains harmful and that its dangers are not eliminated by drug treatments.20 The effectiveness of these prevention approaches is not yet known.

Implications for Counseling

With the hope and potential that new treatments bring, there are also new concerns. People may incorrectly interpret treatment advances as “cures” or as a sign that HIV is no longer life-threatening and may incorrectly believe that treatment eradicates HIV from the body, making it impossible to transmit to others.

Counselors must communicate some treatment information to people who test positive. In addition, counselors must clarify the prevention implications of new treatments and viral load testing.

Clients Who Test Positive

Historically, the focus of counseling for clients who test positive has been to provide support, and refer or directly link clients to medical follow-up services. The development of new treatments has not changed this. Counselors should assess, as they always have, clients’ understanding of HIV antibody tests, additional tests, and the next steps they can take. Explore each client’s access to an HIV-knowledgeable medical provider, and past relationships with providers.

Remember that receiving a
positive result can be an overwhelming experience for a client, and this can make discussion or comprehension more difficult. Because of this, referral to other resources is especially important.

Explain that HIV is a life-threatening infection, but that treatments are more effective than ever at managing it. Learn what clients know about treatments and what they want to know. In response, provide information or referrals where clients can learn more. Counselors should always emphasize that they are not treatment experts and that, to learn more, clients must talk to medical providers and treatment experts.

Make clear that decisions of when to begin treatment are based on a person’s health and the approach a person wants to take in cooperation with a health care provider. Explain that diagnostic tests, such as viral load and CD4 counts, can indicate whether treatments are warranted. Explain also that treatment regimens are complex and that, prior to deciding to initiate treatments, a person should investigate what treatment regimens entail and consider what treatment compliance would be like.

Support the hope engendered by new treatments, while also making clear that HIV is still a life-threatening disease. Point out that treatments for HIV are not cures, that not everyone is helped by existing treatments, and that the long-term effects of new treatments are not known.

Researchers in some parts of California are conducting studies of the effectiveness of treatment regimens for people who have recently seroconverted. Determine whether these studies exist locally. Explore whether clients who believe they have been infected in recent weeks or months are interested in learning more about such studies.

Risk Assessment and HIV-Negative Disclosure Sessions

Information about treatments should not be the focus of a risk assessment or a negative test disclosure session. Counselors should directly answer questions about treatment options in these sessions, but avoid allowing a discussion of treatments to dominate. When a client expresses a strong interest in treatments, explore why this might be occurring. Ask how the topic of medical treatments relates to the client’s own risks or needs. For instance, are there others in the client’s life, perhaps sex or needle-sharing partners, who are infected?

Keep in mind that some clients may focus on treatments as a way to avoid examining their own risks. In risk assessment sessions, explain that treatment discussions are more pertinent to the disclosure session, and in a negative disclosure session explain that treatment information is more pertinent to someone with HIV. In a negative disclosure session, direct the client to a discussion of behavior changes that will assist him or her in remaining uninfected.

Prevention Issues

Many people have worked hard to avoid HIV infection. Assuming that HIV can be managed in ways it could not have been before, people may now regard infection as less harmful and make decisions about what risk behaviors to engage in based on this. This may occur even for those who continue to recognize the disease as life-threatening. Assess clients’ views toward infection. Ensure that clients understand that, even with recent advances, there is no cure for HIV infection, that HIV remains a life-threatening disease, and that staying uninformed is clearly preferable to becoming infected.

Assess how the client views HIV infection and the prospect of becoming infected. Is he or she taking greater risks now based on recent treatment advances? Assess the accuracy of a client’s information about medical advances and the role this information has in his or her decision-making process. When clients say that they engage in unprotected sex or plan to do so, consider whether they are doing this because of their beliefs about treatment advances. Clarify misinformation and make sure clients understand that unprotected sex with someone infected with HIV, regardless of viral load, is unsafe. Keep in mind that a person may view his or her unprotected sex or unsafe needle-using activities as being less dangerous now compared to before recent treatment advances.

Clients who engage in unsafe behaviors may rationalize their decisions to do so. At the same time, they may express an intention to avoid transmitting the virus to others or becoming infected or reinfected with HIV. Directly
address such contradictions.

For example, if a client says, “With treatments, HIV is no big deal. It’s just like any other treatable STD,” explain that researchers do not yet consider HIV treatable. Clarify further that even if HIV was treatable, treatable does not mean “curable” and HIV treatment is not a pleasant experience and not something to be taken lightly. When a client with HIV states that he or she does not want to transmit HIV, yet engages in unprotected sex, point out the contradiction: “You said you would never want to transmit HIV to anyone else, yet I hear you saying you don’t use condoms. I wonder what’s going on for you that you’re not taking steps to protect yourself or your partners?”

Acknowledge that clients may struggle to remain committed to protecting themselves. Many people have been waiting for news that they might take as “permission” to stop using condoms. Even when counselors explain that unprotected sex or injection drug use behaviors remain risky, clients may continue to believe that treatment advances make it okay to engage in risky behaviors. Explore reasons other than treatment advances that the client may have for engaging in unsafe behaviors.

In this exploration, consider various factors. For instance, do clients feel greater pressure to engage in unprotected sex? This pressure may come from partners, or it may be perceived by clients in the absence of actual pressure from others. Recognize that clients may feel they have never been able to justify engaging in unprotected sex and can now do so because of changing views of HIV infection. Establish a safe environment for clients to explore their feelings, for instance the loss they experience by using condoms or the desire to return to an earlier time when sharing needles without cleaning was the standard. Help clients articulate their motivations to remain uninfected and reinforce reasons to avoid infection.

Post-Exposure Prophylaxis

The possibility of eradicating HIV infection through post-exposure preventative therapy, also known as prophylaxis, may raise hopes for clients who believe they have been infected recently. But, this possibility may also lead clients to be less concerned about protecting themselves from becoming infected.

If clients seek prophylactic intervention because of recent exposure to HIV, provide referrals and make sure the client understands the challenges of taking antiviral treatments and the lack of evidence regarding the effectiveness of prophylactic therapy. Beyond this, explore the behavior that has led him or her to seek prophylaxis. If it appears the client views the possibility of prophylaxis as something that will make it safe to engage in unprotected sex in the future, explore his or her feelings related to this, and make clear the dangers of expecting prophylactic treatments to be effective.

Provide referrals for the next steps they can take. Explore each client’s access to an HIV-knowledgeable medical provider, and the client’s past relationships with medical providers.

References

Case Study

Susan, who injects heroin and cocaine, tests HIV positive. She tested because she has been sick a lot the past three years, and suspected her symptoms might indicate HIV infection. In the early 1990s, she had several friends who took HIV treatments and did poorly. As a result, Susan does not view treatments as being useful, nor does she see a need to visit a physician. She says she has had poor relationships with health care providers.

Counseling

Begin by acknowledging to Susan an understanding of the fact that she has friends who did poorly and that it is reasonable for Susan to be discouraged by the failure of treatments to help her friends. Emphasize the importance of follow-up medical care to deal with HIV and other concerns, especially given that she has been in poor health for some time. Explain that treatment options have evolved significantly in the last two years.

To ascertain motivations she may have for seeking follow-up care, ask Susan more about why she sought testing. Build on this motivation by connecting it to reasons she might seek follow-up care. Explain some of the benefits of medical care.

Learn more about Susan’s experience with health care providers and address her concerns about seeing one now. Acknowledge her feelings and experiences, and ask if she considers it possible to have a beneficial relationship with a health care provider. Ask if there is a clinic or specific provider or type of provider that she definitely does or does not want to see. Assure her that she has a right to find someone she does want to see. Having researched providers, seek to link her to a provider she is more likely to find trustworthy.

Beyond these issues, address Susan’s drug use, the risk this poses to her health, and any changes she wants to consider. As appropriate, provide referrals related to this.

Case Study

Michael has tested HIV negative. He is in a long-term relationship with an HIV-infected man whose viral load tests are showing undetectable viral levels. After several years of using condoms, Michael says he and his partner would like to stop using condoms during anal sex and, based on his partner’s viral load result, believe they can safely do this.

Counseling

Acknowledge Michael’s history of condom use, and validate his desire to stop using protection. Acknowledge the personal significance of unprotected sex, the life-affirming value of this desire, and the fact that, unfortunately, reality cannot support the idea that a person can engage in unprotected sex without risk.

Ask Michael what leads him to believe that an “undetectable” viral load means a person is not infectious. Explain that “undetectable” viral load tests indicate that the technology is limited in its ability to detect lower levels of viral particles, and not that the virus has been eliminated. Explain also that a person may, at one time, have an undetectable viral load, but that it may increase without a person’s knowledge.

Explore what being infected would mean to him, and make clear that HIV remains a life-threatening infection for which there is no cure. Make clear that even if treatments are bringing his partner improved health, there is no assurance that Michael would have a similar experience.

If Michael rationalizes a decision to have unprotected anal sex, point out the contradictions of this in the face of accurate information. Acknowledge that integrating information about HIV appears to be difficult for him and that his desire to have unprotected sex with his partner appears to be interfering with his ability to evaluate the information. Learn more about the relationship and Michael’s feelings of intimacy with his partner.

Consider other motivations Michael may have for engaging in unprotected sex. For instance, is he concerned that he is not able to have intimacy with his partner if they engage only in protected sex? Does Michael feel pressure from himself or his partner to have unprotected sex? Explore these topics, and express concern about any decision to engage in unprotected sex with someone who has HIV. Support Michael for his willingness to discuss this subject and consider the extent to which he is willing to pursue this further. As appropriate, provide counseling referrals for further support.
Test Yourself

Review Questions

1. True or False: Resistance is the ability of HIV to change itself so that it resists the effects of treatment, enabling it to resume replication.

2. The goal of antiretroviral therapy is to a) decrease the amount of virus in the body; b) increase the number of CD4+ cells; c) both of the above; d) neither of the above.

3. The challenges of taking multiple antiretroviral drugs at a time might include a) adhering to a strict drug regimen; b) side-effects such as nausea, headaches, or diarrhea c) cost of the medications; d) all of the above.

4. True or False: Researchers have made clear that there are no known cases in which HIV has been eradicated from the body.

5. If a person’s viral load exceeds 10,000 and his or her CD4+ cell count is less than 350, HIV treatment guidelines recommend a) delaying the initiation of treatment; b) beginning treatment with AZT only; c) beginning treatment with a combination of therapies.

6. True or False: An undetectable viral load means that a person has no HIV in his or her body.

7. Modern treatment regimens present challenges. These include: a) prohibitive expense of drugs; b) significant side-effects; c) dosing schedules that drastically alter daily life; d) all of the above.

8. True or False: Researchers have made clear that there are no known cases in which HIV has been eradicated from the body.

Discussion Questions

1. How can counselors respond in HIV-positive disclosure sessions to clients who see no reason to seek medical care, especially given the side effects of treatments and rigorous treatment regimens?

2. How can counselors respond to clients who say that risk of unprotected oral or vaginal sex is acceptable to them given that treatments are increasingly effective in dealing with HIV?

3. How can counselors respond in risk assessment or HIV-negative disclosure sessions when clients seek to focus a counseling session on the subject of treatments?

4. How can counselors respond to clients who feel less resolved to engage in protected sex when HIV-infected partners have received viral load test results showing “undetectable” viral load levels.

Answers

1. True
2. c
3. d
4. False. CD4+ cell counts are useful for determining when to start preventative treatment for opportunistic infections. Also, CD4+ cell counts can be used in conjunction with viral load assays to decide when to start antiretroviral treatments.
5. c
6. True.
7. d
8. False: An undetectable viral load means that the instruments in use today are not sensitive enough to detect HIV in the blood below a certain threshold. Even when viral load is undetectable, HIV still exists in the blood plasma and in other places in the body.
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