The interaction between the success of HIV antiviral therapy and prevention efforts is complex, and it is becoming clear that an optimistic view of the HIV epidemic may actually lead to an increase in the number of HIV infections. Data from several sources—for example, a survey of gay men in Sydney, a study of young men who have sex with men in New York, and preliminary data on both gay men and injection drug users in New York and San Francisco—demonstrate significant increases in the rate of unsafe sexual behavior among both HIV-infected and uninfected people.

These patterns of unsafe practice are further demonstrated by the increasing prevalence of other sexually transmitted diseases around the country as illustrated by data from New York and San Francisco. Several studies suggest that the new optimistic culture arising from successful antiviral treatment has become the catalyst for behavior change that has resulted in these increases in unsafe sex. This article briefly reviews these studies and then evaluates the beliefs regarding the relationship between infectivity and treatment, which may fuel these increases in unsafe sex.

Optimism and Behavior

Recent studies have indicated that increases in unsafe sex may be related to beliefs about the lack of severity of HIV disease. For example, in a New York study of 14 serodiscordant male couples, 24 percent of respondents engaged in unprotected anal intercourse two months prior to assessment, and half of the sample agreed that a reduction in the seropositive partner's viral load decreased the risk of transmission. Similarly, a New York study of men who have sex with men—the Seropositive Urban Men's Study (SUMS)—found that men who engaged in unprotected anal intercourse with partners who were seronegative or of unknown status believed that they were less infectious because they were on antiviral therapy and had negligible viral loads. A study of 298 men attending a 1997 gay pride event in Atlanta found that those who had engaged in unprotected anal receptive intercourse indicated that they were less worried about unsafe sex because of treatment advances. Of 54 men surveyed in a 1997 San Francisco study, 26 percent were less concerned about becoming seropositive now that protease inhibitors were available: 15 percent were more willing to engage in unsafe sexual behaviors and risk HIV infection and 15 percent reported already taking such a risk.

In addition, unsafe sex between HIV-positive partners, which may lead to reinfection, has also increased in light of the new treatments. The Seropositive Urban Men's Study found that HIV-infected gay and bisexual men in primary relationships reported higher rates of unprotected insertive anal intercourse with other infected partners than with uninfected partners. Anecdotal reports indicate that some gay men in metropolitan areas attend “poz bareback parties,” where seropositive gay and bisexual men gather to have unprotected sex with multiple partners.

Complicating the effects of optimism about new antiviral treatments is a misunderstanding about the meaning of an “undetectable” viral load reading. For example, a Canadian study found that a significant proportion of participants perceived unprotected vaginal and anal intercourse to be less risky and safer sexual practices to be less important if viral load was “undetectable.”
Editorial: Transmitting Myths
Robert Marks, Editor

There is a type of scientific data that slips into human consciousness, integrated silently, like viral RNA, I guess, affecting our decisions without requiring much reflection. The success of combination therapy has injected several assumptions into the collective consciousness of those communities most affected by HIV disease.

Among these ideas are that getting infected is no big deal because drugs can treat you, that people using the new treatments are somehow less likely to infect seronegative partners, and even that having an “undetectable” viral load is tantamount to being seronegative. There has been a great deal of speculation and a rush of studies over the past 18 months seeking to determine exactly how much these attitudes, if they exist, affect behavior. For example, do people believe that low viral load diminishes infectivity, do these people increase unprotected behaviors as a result, and how many people believe this and act on this belief?

The data are inconclusive, but many studies have found that for small but significant minorities, such beliefs play an important role in precipitating unprotected sex. It remains unclear, as at least one researcher has suggested, whether this significant minority would be having unprotected sex anyway, that these individuals would have found some other justification for unsafe behavior.

In any case, it is crucial for providers to understand the science behind assumptions about infectivity and transmission in the context of the new treatment landscape. This issue of FOCUS clarifies three concepts regarding the science: the possibility of transmitting drug-resistant virus to seronegative partners, the possibility of reinfected a seropositive person with drug-resistant virus, and the possibility of transmitting HIV when the seropositive partner’s viral load is below the level of detection. Perry Halkitis and Leo Wilton seek to answer these questions by reviewing the relevant literature. Their conclusions offer no concrete answers about probability but do confirm the possibility of transmission in all three of these cases.

June Crawford, Susan Kippax, and Paul Van de Ven look at the implications of this science in the context of the explicit sexual agreements between partners in many couples. They focus on negotiated safety agreements, in which, by definition, both partners are seronegative, because this is the area where there is the most research.

There’s a faint aroma of complacency in the air these days and a sense that not only have the consequences of HIV infection changed, but also the science of transmission. In order for clients to make appropriate decisions about risk, they must understand the certainty and limits of scientific knowledge. Mental health providers cannot expect themselves to interpret complex studies of basic HIV science, but they can become aware of the current scientific consensus in key areas and inform discussions of risk that arise within the counseling room.

References

Ultimately, however, the beliefs some people have about the effects of treatment success and the meaning of viral load are not supported by the scientific literature. First and foremost, the long-term efficacy of antiviral treatment remains unclear, suggesting that the success of the new treatments may lead to a false sense of security. Second, research indicates that problems in treatment, medication adherence, and the natural evolution of the virus may result in viral mutations and increased drug resistance. Finally, while antiviral treatment has been proven to reduce viral load in the blood, HIV may lie dormant, potentially in a mutated state, in the lymph and other systems. Recent data also suggest that some people have been infected with mutated and drug-resistant strains of the HIV virus, diminishing or eliminating options for treatment. While not proven, it appears that this may occur not only with seronegative people but also with seropositive individuals, who may become reinfected with a drug-resistant or more virulent strain of HIV, events that may complicate treatment. The rest of this article reviews the most recent research on viral mutation and drug resistance, the potential for reinfection, and the meaning of viral load and implications for infectivity.

Viral Mutation and Resistance

Like all bacteria and viruses that cause disease, HIV has the potential to alter its genetic composition, yielding a variety of strains and subtypes. The introduction of combination therapy, in particular, the widespread use of protease inhibitors as well as continued use of nucleoside analogues such as zidovudine (ZDV; AZT), has significantly increased the prevalence of mutated viruses that can “outsmart” antiviral treatments. According to the Stanford HIV RT and Protease Sequence Database, drug resistance arises from mutations in the HIV genome specifically in the regions that encode the molecular targets of therapy: the
Even at viral load levels of less than 500, HIV replication and mutation still occur.


protease and reverse transcriptase enzymes.

For individuals who initially succeed on combination therapy, the development of drug resistance is often associated with increases in viral load as medications fail to control infection. Evidence suggests that even when viral load is detected at levels less than 500, replication and mutation of the virus can still occur.

Treatment failures due to drug resistance can lead to disease progression and limited treatment alternatives.

Equally important, drug-resistant strains of HIV may be transmitted to others, similarly limiting their treatment options.

Concern regarding drug resistance has emerged largely as a result of the introduction of protease inhibitors, although there has been ample evidence of virus resistant to medications, including the nucleoside reverse transcriptase inhibitors zidovudine (ZDV), didanosine (ddI), and zalcitabine (ddC), and lamivudine (3TC), and the non-nucleoside reverse transcriptase inhibitors.

Research also indicates that a virus can contain several mutations and therefore be resistant to drugs in many classes. As significantly, viral mutation in response to one medication in a class of drugs, for example, the protease inhibitors, may result in resistance to all medications in that class. For example, the Stanford project cited above found that of the 18 mutations induced to evade indinavir, 17 evaded ritonavir, and 16 evaded saquinavir. Another example is that a similar mutation at one spot can cause resistance to all three licensed non-nucleoside reverse transcriptase medications.

Resistance is closely connected to proper dosage and adherence to medications. For example, in one study of 88 people, treatment failure was directly related to adherence rates. The study found that treatment failure, as measured by viral load level, increased from 20 percent to 94 percent when adherence rates fell from 95 percent to 70 percent.

Data from numerous sources, including the Seropositive Urban Men's Study and the Seropositive Urban Drug Injectors' Study, indicate adherence levels are approximately 50 percent across all classes of antiviral drugs.

The Potential for Reinfection

The transmissibility of drug-resistant HIV has implications not only for seronegative but also for seropositive individuals. While the concept of “reinfection” is controversial, recent evidence suggests the existence of more than one strain of the virus in a person. The effect of such coinfection on antiviral treatment remains unclear.

Researchers have long identified several risks to unprotected sex between seropositive partners. Among these risks have been infection with other sexually transmitted diseases that would flourish in the presence of a compromised immune system, and reinfection with HIV, an event that might activate the immune system leading, ironically, to further HIV replication in immune system cells. More recently, such practices have also been associated with hepatitis C transmission. Some researchers hypothesize that reinfection may have even more serious consequences when a seropositive person becomes exposed to a drug-resistant or more virulent strain of HIV.

Swiss researchers have identified 159 subtype strains of HIV-1 in humans, and similar subtypes have been identified across other studies in Argentina, Brazil, Thailand, and Ukraine. The most prevalent in North America, Western Europe, and Australia is subtype B, while subtype C predominates in Africa and most of Asia. The subtypes A, D, E, and F have been found in smaller numbers. While evidence for dual infections exists, it is unclear if those infections result from simultaneous or consecutive infection.

Researchers at the University of Alabama have accumulated evidence suggesting that the possibility of humans infected with two or more strains of HIV is probably greater than originally assumed. In their work with chimpanzees, the researchers were able to infect previously infected animals with a second strain of the virus and to detect the second strain up to six weeks later. Data from a Rio de Janeiro cohort supports the possibilities of dual infection, a recombinant strain, or a mosaic composition. Of the 791 blood donors studied over the course of a year, 3.8 percent had a dual HIV infection of two subtypes of the virus, and 7.6 percent had a recombinant infection. Neither of these studies was able to determine the biochemical effects of dual infection and its impact on antiviral treatment. Among the possibilities are that the second strain of the virus will predominate or that a recombinant and potentially more pathogenic version will develop.

The Meaning of Viral Load and Infectivity

Combination treatment has been accompanied by improved monitoring of viral activity and disease progression.
Measures of serum HIV levels, referred to as viral load assays, have been used as markers of HIV disease progression and overall health, determinants of when to initiate antiviral therapy, indicators of the success of antiviral therapy, and, indirectly, measures of treatment adherence. Such assays are currently able to detect HIV at levels as low as 20 copies per milliliter of blood; however, not all laboratories use tests with sensitivities this low. Recently, researchers have suggested that viral load may have different implications for disease progression in women versus men.

Although combination therapy can reduce the concentration of HIV to levels at which virus cannot be detected by viral load assays, this does not signify the complete eradication of virus from the body. But, as noted earlier, many people have interpreted an “undetectable” viral load to mean that a seropositive person is uninfected. These extremely low viral load levels are now referred to as “below the level of detection” to indicate that HIV may still be present and to more clearly communicate that detection is affected by technology as much as by the presence of the virus. Research suggests that while blood level assays may demonstrate no significant detectable viral activity, HIV may lie dormant in the immune system, perhaps mutating naturally or in response to antiviral treatment. This phenomenon becomes apparent when people with viral loads below the level of detection discontinue antiviral treatment or when their strain of HIV becomes resistant to a drug or drugs they are taking—changes that are often accompanied by increases in viral load.

In addition, a viral load below the level of detection does not signify that other body fluids, specifically genital fluids, are free of the virus. In one study, subjects on combination therapy who had suppressed levels of HIV in their blood did not have virus-free semen samples. In another cohort, subjects with detectable viral load levels in their blood presented with equal or higher levels of HIV in their seminal fluids.

Conclusion

Risky behaviors seem to be increasing, and this increase may be associated with an optimism regarding the manageability and reduced threat of HIV disease. This optimism may be based not only on misleading media attention, but also on confusion about the effects of treatment on HIV transmissibility. In response, clinicians and educators must raise awareness among both seronegative and seropositive individuals about the possibilities of viral mutation and resistance to antiviral therapies; they must also seek to contradict assumptions about infectivity in light of treatment advances and the concept of “undetectable” viral load. Because reinfection remains a risk, providers must raise issues of safer sex for people with HIV, even when partners themselves are seropositive. As we approach the third decade of AIDS, these messages must be stronger than ever because complacency has had an impact on behavior.

Unfortunately, many AIDS service organizations have failed to respond adequately to the challenges of education regarding new treatments and adherence, the meaning of viral activity, and the dangers of drug-resistant viral transmission. The AIDS epidemic is now in its adolescence, and our increased knowledge has transformed it into a much more complex disease. Providers must respond with more sophisticated and relevant strategies that take into account the depth and range of information that we have and the depth and range of the misunderstandings this information can induce.

References


Sexual Agreements Between Men in Relationships
June Crawford, PhD, Susan Kippax, PhD, and Paul Van de Ven, PhD

Since the beginning of the epidemic, sexual partners have negotiated agreements about sexual activity both within and outside a relationship. Some of the issues covered in these agreements have included types of activity, the use of protection, and sexual activity outside the relationship.

Over the past several years, the concept of “negotiated safety,” has gained some currency, referring particularly to agreements regarding unprotected anal intercourse within gay male relationships in which both partners are seronegative. Other types of agreements are less precisely conceptualized, but do commonly occur, for example, the agreement between partners in seropositive couples—both gay and heterosexual—to have unprotected sex since both partners are already HIV-infected.

This article looks at the range of agreements among gay men regarding anal intercourse. It focuses in particular on negotiated safety and the results of a recent study on this type of agreement and its relation to risk behavior.

Negotiated Safety
In the early 1990s, U.S. and Dutch researchers identified what they called “relapse” among men who had been using condoms consistently but were no longer doing so. Australian and British researchers questioned this interpretation, noting that the relapse data did not draw a distinction between unprotected anal intercourse within regular relationships and unprotected anal intercourse with casual partners.

Following a debate within the research community, Susan Kippax and co-researchers in Australia coined the term “negotiated safety” to describe a pattern of behavior they had observed: the partners within a regular relationship entered into an agreement that as long as each engaged in no unprotected anal intercourse outside of the relationship, then both could engage in unprotected anal intercourse within the relationship.1,2 It was appropriate in this context to use the term “safety” if both partners had been tested for HIV antibodies and found reliably to be seronegative, and provided of course that the agreement was kept.

Since that time, there has been some confusion surrounding the discourse of negotiated safety. Some have suggested that what the researchers put forward as a description of a pattern of practice devised by men as a possible safe sex


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See also references cited in articles in this issue.
strategy was being *recommended* as such an approach. Critics of the strategy called it "negotiated danger," pointing out that there was room for slippage in the practice: for example, the potential for agreements to be broken, the fact that reliable knowledge of one’s HIV status required two seronegative test results at an interval of approximately four months, and the need for mutual honesty between partners.3 It is clear that as a risk reduction strategy, negotiated safety is complicated. In continuing to research the kinds of agreements that men make and the behavior in which they engage, the Australian team has found that negotiated safety agreements, as well as agreements to engage in no unprotected anal intercourse at all, may in fact be helpful in the sustaining of safe sexual practice.4

While many studies have found that unprotected anal intercourse is far more common in regular relationships than in casual partnerships,2-5-7 only a small number of studies separately consider practices that may differ according to whether they are with regular or with casual partners. A recent large national telephone survey of men who have sex with men in Australia, known as Male Call 96, included questions about agreements in regular relationships. Out of 3,039 men who responded to the survey, 1,070 were in “regular” (sometimes referred to as “primary”) male-to-male relationships of more than six months duration. Researchers excluded from the analysis 30 men in relationships in which both partners were seropositive, leaving 1,040 men who contributed to the analysis discussed here.

One of the findings from this survey was that over 80 percent of the men in such relationships had agreements with their partners regarding sexual practice within the relationship. The most common form of agreement was to have no unprotected anal intercourse either within or outside the relationship. Negotiated safety agreements were almost as common. Again, a negotiated safety agreement is one in which both partners have tested HIV antibody negative; the partners have talked with each other and come to an agreement; and the agreement includes a provision that there will be no unprotected anal intercourse outside the relationship.

In general, the Male Call study found a close relationship between type of agreement and risk practice. Under the conditions of a negotiated safety agreement that is followed by both partners, unprotected anal intercourse within the relationship is not a risk practice because both partners are seronegative. Unprotected anal intercourse between men in serodiscordant relationships or in relationships where the HIV serostatus of one or both partners is unknown carries some risk, and all unprotected anal intercourse with casual partners is regarded as risky. (The Male Call study did not investigate oral sex practices at all.)

The study found that few people with negotiated safety agreements reported engaging in risky practices. Nevertheless, negotiated safety is not a simple and straightforward strategy, depending as it

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### References


### Comments and Submissions

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does on reliable and up-to-date information regarding the serostatus of both partners. It also requires open and honest communication between partners in the event that one of them breaks the agreement. Such an event would necessitate a return to consistent condom use or the avoidance of anal intercourse until seronegative status could be re-established.

Other Types of Agreement

In the Male Call study, a small but important minority of men in relationships, around 11 percent, had “unsafe” agreements. Such agreements included those in which partners of different or unknown serostatus agreed to unprotected anal intercourse within the relationship, and all arrangements, including those between seroconcordant partners, that did not include a pact to have no unprotected anal intercourse outside the relationship. As might be predicted, men with unsafe agreements were likely to report behavior that risked HIV transmission. For these men, most risk practice was with regular partners, and the risk was due to absence of information regarding serostatus. Encouraging regular partners to be tested and to disclose their test results to one another may be one way to decrease the number of men who have unsafe agreements.

In the Male Call survey, there were very few serodiscordant couples, but from this and other studies, it has been found that agreements are very common among such couples. In the case of serodiscordant couples, most agreements are to have no unprotected anal intercourse within the relationship. As might be predicted, men with unsafe agreements were likely to report behavior that risked HIV transmission. For these men, most risk practice was with regular partners, and the risk was due to absence of information regarding serostatus. Encouraging regular partners to be tested and to disclose their test results to one another may be one way to decrease the number of men who have unsafe agreements.

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Conclusion

It is important for researchers to continue to investigate what understandings gay men have regarding the new treatments, whether they incorporate these understandings (either accurate or inaccurate) into their agreements, and what happens to their sexual practice in this new context. This research is aimed at providing answers to questions that will help counselors and educators formulate programs aimed at preventing transmission of HIV.
Recent Reports

Effects of Treatment on Risk Perception

According to a Canadian study, 22 percent of seropositive subjects believed that taking some form of antiviral therapy reduced their risk of transmitting HIV to others, and 20 percent believed that treatment diminished the importance of safer practices for sex and injection drug use.

Researchers recruited 147 participants from a university-based HIV clinic, 88 percent of whom were men. Subjects reported sources of infection as follows: 77 percent through sexual intercourse (89 percent male-to-male), 8 percent through injection drug use, and 8 percent through blood transfusions. Ninety-five percent were on antiviral therapy, and 69 percent were taking at least one protease inhibitor.

Subjects completed a questionnaire assessing their perceptions of the risk of HIV transmission from an infected man with a CD4+ cell count of about 200 to an uninfected partner under three hypothetical scenarios: in the “no therapy” case, the HIV-infected partner received no treatment; in the “RTI therapy” case, he was taking zidovudine (ZDV; AZT) with lamivudine (3TC); and in the “PI therapy” case, he was on ZDV, 3TC, and a protease inhibitor and had “undetectable” viral load.

For each scenario, respondents ranked the relative risk of transmission for unprotected anal, vaginal, and oral sex, and for needle sharing. For at least one of these risk behaviors, 10 percent believed that RTI therapy reduced risk, and 20 percent believed that PI therapy reduced risk. Respondents also rated the importance of safer sexual and needle-sharing practices: 10 percent believed that RTI therapy decreased the importance of safer practices, and 19 percent believed that PI therapy decreased the importance of safer practices.

Risk Perceptions among Gay Men

A study of seronegative or untested gay and bisexual men not in long-term relationships found that 23 percent who had engaged in unprotected anal receptive intercourse during the previous six months believed that this was safe if an HIV-infected partner had an undetectable viral load. Of subjects who did not participate in unprotected anal receptive intercourse during this period, only 5 percent shared this belief.

The sample consisted of 298 men—93 percent gay and 7 percent bisexual—recruited at an Atlanta gay pride festival. The mean age was 33; and 85 percent were White, 7 percent were African American, and 8 percent were of other ethnic backgrounds. Eighty-five percent had tested seronegative, and 15 percent had not tested. Twenty percent had engaged in unprotected anal receptive intercourse in the previous six months. These “highest risk” subjects were younger and had completed fewer years of education than “lower risk” subjects.

Highest risk subjects were more likely than lower risk subjects to state that they practiced more unsafe sex than they used to and that they were less worried about becoming infected because of new treatment efficacy. Highest risk subjects considered the risks for unprotected anal receptive intercourse to be lower with HIV-infected partners taking protease inhibitors and lower still with partners with undetectable viral loads. Among lower risk subjects, however, perceived risk remained consistent regardless of a partner’s treatment status or viral load.

Next Month

The AIDS epidemic has always posed some thorny ethical issues for mental health providers. In the May issue of FOCUS, Sally Jue, LCSW, a Los Angeles trainer and consultant, reviews a recent model for ethical decision making that she and her colleagues developed for the American Psychological Association. The model outlines a process for defining and responding to ethical dilemmas and identifies key ethical principles that are crucial to this endeavor.

Also in the May issue of FOCUS, Steve Heilig, MPH, Director of Public Health and Education at the San Francisco Medical Society, discusses HIV-related “rational” suicide and issues related to societal and personal control.
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