Among patients with HIV infection, clinical depression is the most frequently observed psychiatric disorder, affecting between 4 percent and 14 percent of gay men and non-drug-using women, with higher rates among both infected and uninfected injection drug users. But while these rates demonstrate a connection between HIV disease and depression, it is not a direct one: despite the intuition that HIV disease might bring on depression, the evidence suggests that there is rarely a cause-and-effect relationship between the two. The majority of HIV-infected people with current depressive disorders have a history of depression that antedates HIV infection, and depression is not correlated with disease stage, T-helper cell count, or HIV-related medication use.

By reviewing the data on HIV disease and depression, this article seeks to dispel the belief that the two are inextricably linked. In doing so, it clarifies when and among whom HIV-related depression is likely to arise. In these cases, both psychotherapy and aggressive antidepressant treatment can be extremely effective.

Epidemiology: Scope of the Problem

Early descriptive reports of psychiatric morbidity among those with HIV infection, which relied primarily on self-report rating scales and samples seen in medical settings, described exceptionally high rates of symptomatic depression and anxiety. More recent studies of community samples and research volunteers, using either symptom checklists or structured diagnostic instruments and trained professional interviewers, have found rates among seropositive gay men to be approximately equal to their seronegative counterparts. When researchers compare rates for HIV-infected populations to general population rates, some investigators have found higher rates of depression, while others have not. Nevertheless, it has become increasingly clear that clinical depression is not the norm and therefore should not be expected among people with HIV disease.

At the same time, while transient mood states are not routinely recorded in epidemiologic studies, it is important to recognize that the majority of HIV-infected people are likely to experience periods of sadness and distress from time to time—particularly in relation to the illness or the death of friends. This is to be expected and is common. Therefore, the absence of a current depressive episode does not necessarily signify a total absence of distress.

Follow-up studies of HIV-infected men and women suggest that rates of depression do not increase over time. For example, a Chicago study of 436 subjects using self-rating scales to assess depressive symptoms found stable scores over a period of six bi-annual evaluations. A Cornell University study of 328 seropositive and seronegative, gay and heterosexual men and women found a decline in depressive symptom severity over time on both clinician and self-rated scales. There was no difference between infected and uninfected subjects on any occasion. A Columbia University study similarly failed to observe increased rates of depressive disorders among either seropositive or seronegative gay men followed over four years or among injection drug users surveyed at three semi-annual visits.

Cross-sectional studies comparing symptomatic and asymptomatic men and
There are two perceptual—and conceptually opposite—traps regarding depression and AIDS that may trick mental health and medical providers. The first is that depressive symptoms are a normal response to the harsh realities of HIV disease and therefore are not related to a clinical and treatable condition; the second is that the existence of any depressive symptoms indicates clinical depression and requires antidepressant treatment.

**Depression versus Distress**

In this issue of *FOCUS*, Judith Rabkin and Robert Remien challenge these assumptions in a review of the literature on depression and HIV disease. They report that clinical depression prevails among only a small group of people with HIV disease, and that these individuals usually have a history of depression that predates HIV disease. But it would be a mistake to interpret Rabkin and Remien’s article as saying that people with HIV disease are free of angst. As *FOCUS* Editorial Consultant Michael Helquist points out, although HIV disease may not result in clinical depression for everyone who is infected, the series of distressing events can be so continual and unrelenting as to confound the distinction between a diagnosis of depression and distress.

In the second article in this issue, Bruce Victor briefly charts the complex relationship between sexual dysfunction and depression, focusing on the negative effects of the SSRI antidepressants (Prozac, Zoloft, and Paxil). These drugs, which have seemed to be so effective in improving mood among so many people, may not be as free of side effects as they appear to be. Most notably, they may cause sexual dysfunction, and sexual dysfunction itself may exacerbate depression. Taken together, these three perspectives suggest that depression is complex, particularly for people with HIV disease. It is there and it isn’t; it may be clinical and treatable with drugs or it may be “distress,” which may respond to therapy, to social support, or simply to time; it may be acute or chronic, pre-existing or new, severe or incipient. The response to this complexity is careful assessment, and this assessment is crucial at the time of diagnosis.

**Protecting the Therapeutic Process**

As Rabkin and Remien emphasize, clinical depression is treatable, and as Victor states, there are pharmacological alternatives and responses to SSRI-induced sexual dysfunction. But the SSRIs, as omnipotent as they seem, are specific drugs that respond to specific conditions: they will not relieve all forms of distress and may bring on more serious distress themselves. They may also hide a client’s true distress from the therapist, potentially harming the therapeutic process and the client.

**References**


Risk Factors for Depression in HIV Illness

What factors related to HIV disease are likely to be associated with depression? Researchers have looked at a variety of factors including being gay, taking HIV-related medications, being immune-suppressed, and being HIV-infected. None of these studies support the conclusion that HIV disease and depression are inherently associated with one another. Studies of current and past psychopathology in community samples of gay men have revealed surprisingly high lifetime rates of depressive disorders, despite low rates of current depression. Investigators at both Cornell and Columbia reported lifetime prevalence of depression in the range of 30 percent to 35 percent for gay men compared to 5 percent for the general population. Given the recurrent nature of depression, these findings suggest increased vulnerability to future episodes of depression in this group.

There appears to be no systematic published research regarding the effects on mood of any HIV-related medication or on the interactions between these medications and antidepressant drugs. Some published case reports suggest that zidovudine (ZDV; AZT) may be mood-enhancing or mania-inducing, although occasionally clients report that ZDV causes depression. It is of course difficult to separate out the symbolism of initiating antiviral treatment from the chemical effects of the compound, or the effects of multiple HIV-related medications prescribed prophylactically or acutely as illness progresses. Overall, in view of the widespread use of these medications, especially ZDV, and the absence of documentation otherwise, the case reports may represent idiosyncratic rather than common mood effects.

It has been suggested but not demonstrated that HIV itself causes mood changes and that HIV-associated dementia induces depression. However, there is little evidence to support either of these hypotheses. A study of HIV-infected men did not find depressed mood to be associated with early subtle cognitive changes. Apathy, rather than sadness, appears to be the predominant affect in HIV-associated dementia.

Finally, published studies on the relationship between depression and HIV-related immune compromise continue to offer inconsistent results. Some investigators have reported an association between depression and the decline in T-helper cell count. In contrast, a longitudinal study of 113 seropositive gay men found no relationship between syndromal depression, psychiatric distress, or psychosocial stressors and immune status or HIV illness stage. Greater distress was not associated with greater immunosuppression or more advanced illness stage, either concurrently or over time. Other studies also support this conclusion.

Overall, the weight of the evidence does not support “a measurable or substantial effect” of psychosocial factors such as depression or stress “on enumerative measures of the immune system in relation to physical disorders such as AIDS” using the endpoints of medical outcome and death. With the advent of more direct measures of viral load such as polymerase chain reaction (PCR) and branch DNA, further study may be worthwhile.

Treatment Research

Treatment of depression in the general population is one of psychiatry’s success stories, and there is no evidence that it should be different for people with HIV disease.
Institute.

State Psychiatric Scientist at New York Columbia University, and Surgeons, College of Physicians in Psychiatry at the of Clinical Psychology is Assistant Professor Robert H. Remien, PhD HIV Treatment Patients: Partners in Doctors/Good author, with Dr. Institute. She is co-


Rabkin JG, Rabkin R, Harrison W, et al. Effect of imipramine on mood and attention during late stage illness when partners, close friends, or family members may also be at the bedside. They must also be prepared to talk about progressive physical decline, approaching death, and the circumstances of dying.

Clinicians have remarked upon the surprisingly gratifying nature of working with HIV-infected patients. As the awareness of a foreshortened life may be associated with grief and depression, it may also help patients to focus on what is important, and to motivate efforts to accomplish goals and reach clarity about concerns that really matter. Even if we cannot prolong life, we can help make life worth living.

Conclusion

It is understandable that therapists might assume that people faced with disability, pain, and a threat to life might become depressed. But the presumption that all or even most people with HIV disease suffer from clinical depression is wrong and does a disservice to clients. The data show that depression is neither more common among people with HIV infection nor likely to increase as HIV disease progresses.

While HIV-infected individuals may experience distress during the course of disease, depression is not “normal” for them. This is important for two reasons. It implies that people with HIV disease are more psychologically resilient than we may assume, and it suggests that when clinical depression does arise in a client, therapists should not dismiss it as usual and understandable but should instead treat it aggressively.
Allopathic medicine involves a series of trade-offs: the message to the patient is that one needs to endure a series of "side effects" as seeming payment for the salutary effects of a medication that relieves a more distressing problem. Before the advent of the new class of serotonin-enhancing drugs, the somatic price for alleviating major depression was a plethora of discomforts, ranging from dry mouth to constipation, that came with tricyclic antidepressants. By contrast, the advent of the selective serotonin reuptake inhibitors (SSRIs)—fluoxetine (Prozac), sertraline (Zoloft), paroxetine (Paxil), and their progeny—seemed to promise relief without sacrifice.

In recent years, however, it has become increasingly apparent that the SSRIs cause significant adverse effects to sexual functioning: studies suggest that as many as 50 percent of patients taking SSRIs suffer from some sort of sexual dysfunction. While sexual side effects certainly occurred with the tricyclic antidepressants and with monoamine oxidase inhibitors, the seeming ubiquity of the SSRIs brings the issue of sexual side effects to the forefront.

Sexual Side Effects

Both sexual function and mood depend upon the right amount of neurotransmitters as well as the balance between these neurological chemical messengers. The significant neurotransmitters for both mood and sexual function include serotonin, noradrenaline, acetylcholine, and dopamine. The SSRIs promote, in particular, the transmission of serotonin, which is especially important in mood stabilization. The enhancement of serotonergic function, however, can potentially lead to sexual side effects.

Antidepressant medication can affect sexual functioning in a number of different ways. First, any of these medications can decrease libido significantly, sometimes to the point of elimination. This effect can be seen in both men and women. Second, any class of antidepressants can lead to erectile difficulties among men. While erectile failure is gen-

Medications can reverse the sexual dysfunction caused by antidepressants such as Prozac, Zoloft, and Paxil.


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See also references cited in articles in this issue.
erally the rule, at least one antidepressant, Trazadone, has been associated with priapism—persistent, abnormal erection—in a small but significant number of men. Finally, these medications can cause profound difficulties not only in achieving orgasm, but also in orgasmic enjoyment. In men, this last effect ranges from ejaculatory delay or absence to a decrease in the sensation of orgasm.

Before the advent of the SSRIs, it was thought that sexual side effects resulted from the inhibition of other neurotransmitters such as acetylcholine and, to a certain extent, noradrenaline. However, recent research appears to support the idea that the facilitation of serotonin-based systems may also be responsible for these side effects. Part of this reasoning comes from the clinical evidence that drugs that block serotonin transmission seem to be at least partially effective in restoring previous levels of sexual functioning.

**Treatment of Sexual Dysfunction**

For some individuals, sexual dysfunction may be remedied merely by lowering antidepressant dosages. The obvious risk inherent in this approach is that the therapeutic effect of the medication may be decreased or lost, and there are many people for whom this is not an acceptable risk.

However, there are medications that can reverse sexual dysfunction. Perhaps the two most commonly used ones are cyproheptadine (Periactin) and yohimbine (Yocon). The former is actually a serotonin antagonist which was found to be effective in diminishing sexual side effects especially from the SSRIs. However, because it is a histamine blocker, it can be profoundly sedating and this effect often becomes predominant. Patients will voice their impatience with a remedy that they are instructed to take one hour before sexual activity only to be asleep within 20 minutes of ingestion. Further, in some instances, cyproheptadine, probably because of its serotonin-blocking effects, has also been reported to reverse the actual antidepressant or anti-obssesive effect of the SSRI itself.

Yohimbine enhances the transmission of epinephrine—another neurotransmitter—which, in turn, enhances sexual functioning presumably by increasing inflow of blood to erectile tissue and enhances sexual desire by increasing the activation of the cerebral cortex. While there has been no report that yohimbene reverses the salutary effects of antidepressant medication, it may increase levels of panic anxiety in those patients susceptible to it. It should also be noted that more frequent dosing is necessary if the target symptom is loss of libido rather than orgasmic or erectile difficulty.

Other biochemical stratagems have been applied to sexual dysfunction. Because it is possible that the newer SSRIs block the activity of dopamine—another neurotransmitter—agents such as amantadine (Symmetrel), bromocriptine (Parlodel), and busiprone (Buspar), which enhance both dopamine and serotonin transmission, have been shown to have some effect in reducing sexual side effects of the SSRIs. Finally, because the newer antidepressants might exhibit a small anticholinergic effect that could have an adverse effect on sexual functioning, bethanecol (Urechline), which enhances transmission of choline, has also been reported to have some benefit.

For those patients for whom antidepressant dose reduction or administration of one of the antidotes described above does not work, switching antidepressants may be effective. One study reported significant improvement in sexual response when inpatients taking fluoxetine (Prozac) discontinued this medication in favor of the nonserotonergic, mildly dopamine-enhancing antidepressant bupropion (Wellbutrin).

**Conclusion**

The dramatic sexual side effects of medications that are seen as the great biochemical hope to depression is cruelly ironic. Given the ubiquity of depression where one of the cardinal symptoms is hopelessness, especially in the context of HIV disease, providers must handle the decline or loss of sexual functioning with both creativity and compassion.

**Comments and Submissions**

We invite readers to send letters responding to articles published in *FOCUS* or dealing with current AIDS research and counseling issues. We also encourage readers to submit article proposals, including a summary of the idea and a detailed outline of the article. Send correspondence to:

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Immunity, Bereavement, and Depression

Depressed mood may be a co-factor for HIV progression, but the relationship between bereavement and the immune system remains unclear, according to a small study of a Los Angeles subset of the Multi-Center AIDS Cohort Study (MACS). The study correlated depressed mood and immune parameters associated with HIV progression in nonbereaved seropositive men; however these correlations were inexplicably absent among seropositive men who had experienced the loss of a close friend to AIDS.

Forty-five gay men who had lost one or more close friends in the past year to AIDS were matched by age and serostatus to 45 men who had not experienced recent loss. The mean age of the sample was 38 and 39 years old, and all of the men were White. The Profile of Mood States (POMS) was used to assess “depressed mood” (not clinical depression), and most individuals did not report abnormally high levels of depressed mood.

Depression scores did relate to HIV status and bereavement, but in a surprising way. Among nonbereaved subjects, HIV-infected men had a statistically significant lower average depression score than uninfected men. Bereaved seropositive and seronegative men reported approximately the same average scores. Correlating HIV status, bereavement, and depressed mood with immune parameters produced equally puzzling results. Among nonbereaved seropositive men, high depression scores were associated with predictable immunological changes related to advanced HIV infection, including significantly lower T-helper cell counts and T-killer cell counts. But bereaved seropositive men exhibited no immune changes associated with depressed mood.

Researchers hypothesized that a high POMS score in a bereaved individual may represent a grief response instead of depressed mood, a distinction that may be crucial to understanding the physiological effects of bereavement. The difference in results of bereaved and nonbereaved HIV positive men could also be explained if biological effects of bereavement are mitigated by psychological adaptation when repeated loss occurs.

Hopelessness and Injection Drug Use
Steer RA, Iguchi MY, Platt Jj. Hopelessness in IV drug users not in treatment and seeking testing and counseling. *Drug and Alcohol Dependence.* 1994; 34(2): 99-103. (University of Medicine and Dentistry of New Jersey; and Hahnemann University, Philadelphia.)

According to a large clinical study, injection drug users seeking antibody testing had surprisingly low overall levels of hopelessness, given the probability of HIV infection via drug use.

Hopelessness, defined as “negative expectancies about the future,” is a symptom of depression and has been linked to suicidal behavior and ideation. Past studies comparing overall levels of hopelessness with HIV infection status have found no relationship between the two.

A sample of 2,379 injection drug users was evaluated using the Beck Hopelessness Scale (BHS)—which rates overall hopelessness on a scale of 0 to 20—for three dimensions of hopelessness: resignation to the futility of changing the future; rejection of the possibility of a better future; and acceptance of the inevitability of a hopeless future. Of the sample, 75 percent were men and 25 percent were women; and 78 percent were African American, 14 percent were Hispanic, and 8 percent were White. All of the participants sought HIV antibody testing and counseling, but none knew their serostatus when evaluated and none were in drug treatment.

Overall, 17.8 percent of the participants reported total BHS scores above nine, indicating risk for eventual suicide, and 24.5 percent reported current suicide ideation on the evaluation. Researchers theorized that seeking testing and counseling may have contributed to a sense of hope about the future.

Risk and Depression in Black Women

Women with depressive symptoms were more likely than other women to engage in HIV-related risk behaviors.
A Baltimore study of women's health centers found that women with depressive symptoms were significantly more likely than women without depressive symptoms to engage in HIV-related risk behaviors.

The predominantly African-American sample of 173 women was comprised of clients from two Baltimore health centers in economically disadvantaged areas of the city. Participants responded to a brief questionnaire assessing risk factors and depressive symptoms using the Center for Epidemiologic Studies Depression Scale (CES-D). The CES-D scores above 16 indicate significant depressive symptoms.

Approximately half of the sample scored 16 or higher on the CES-D, with a median score of 15. Women who scored 16 or higher reported more risk exposure through their sex partners than did the women with scores of 15 or lower.

Distress in Homosexually Black Americans

Cochran SD, Mays VM. Depressive distress among homosexually active African American men and women. American Journal of Psychiatry. 1994; 151(4): 524-529. (California State University, Northridge; and University of California, Los Angeles.)

Homosexually active African Americans experience higher levels of depressive distress than have been shown in previous studies of African Americans and White gay men, according to a large Los Angeles survey of gay and bisexual men and women.

The survey used the CES-D and a scale rating the frequency of life problems, including suicidal thoughts. Researchers received responses from 603 women and 829 men, all African-American. Of this sample, 84 percent of the women and 80 percent of the men stated that they considered themselves to be gay or lesbian; 11 percent of the women and 14 percent of the men considered themselves bisexual; and 5 percent of both the women and the men identified themselves as neither homosexual or bisexual, but currently homosexually active.

Based on the results of previous surveys, subjects reported unexpectedly high levels of depressive distress. The mean CES-D score in this survey was 13.6, in contrast to earlier studies that ranged from 9.9 to 11.5. Female respondents had an estimated mean score of 14.7. Male respondents had a total mean score of 12.8 with four subgroup scores: 16.7 for symptomatic HIV-infected men, 12.8 for asymptomatic HIV-infected men, 12.7 for uninfected men, and 11.4 for men whose HIV infection status was unknown. Symptomatic HIV-infected men also reported the highest prevalence of suicidal thoughts.

Depression in Low HIV Prevalence Areas


As has been shown among people in AIDS epicenters, a North Carolina study found that major depression was common among both seronegative and asymptomatic seropositive gay men in an area of low HIV prevalence.

The Coping in Health and Illness Project investigated neuropsychiatric, psychosocial, and psychoimmunological aspects of HIV infection among 169 subjects—71 seronegative gay men and 98 asymptomatic seropositive gay men. Most subjects in both groups were White.

Among the HIV-infected participants, 8 percent suffered from major depression at the time of the study, and 3 percent of the uninfected participants had current major depression. The lifetime prevalence of major depression, a significant risk factor for current depression, was 29 percent of the HIV-infected sample and 45 percent of the uninfected sample. A community sample showed 2 percent prevalence of major depression in the general population, with a lifetime prevalence of 3 percent.

Next Month

Drug abuse and treatment often arise in some way for women with HIV disease. Yet most drug treatment approaches rely on models developed by men and for men. In the September issue of FOCUS, Gillian Walker, ACSW of the Ackerman Institute in New York identifies some of the short-comings faced by women with HIV disease who access traditional drug treatment programs. She focuses her discussion on a family-centered therapeutic approach that is more tailored to the lives of these women.

Also in the August issue, Suzanne Ostermann, a consultant on substance abuse treatment who is based in southern California, critiques programs for women from a historical perspective. She looks at factors such as the traditions of Alcoholics Anonymous, the bias in government funding, and the trend toward cost containment and relates them to inappropriate treatment for HIV-infected women.
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