THE “TRIPLE-THREAT” PATIENT: PSYCHIATRIC PROBLEMS, SUBSTANCE ABUSE DISORDERS, AND HIV*

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ABSTRACT

Individuals with psychiatric disorders are at increased risk of HIV infection, inadequate treatment, and poor treatment outcomes. A recent study that compared patients at an HIV clinic who had received treatment for psychiatric disorders to patients for whom psychopathology had not been assessed or treated found that patients who were receiving treatment had significantly better rates of HIV treatment initiation and adherence, and they also tended to have a lower incidence of mortality. HIV infection and psychiatric disorders have the potential to reinforce and amplify one another: psychiatric disorders increase risk of HIV infection, and HIV infection contributes to depression, demoralization, and substance abuse. The current emphasis on checklist-based psychiatric diagnosis and treatment leads to the lack of recognition of important psychiatric care issues and contributes to polypharmacy. Psychiatric disorders may be viewed from at least 4 different perspectives: as brain diseases, behavioral disorders, disorders of personality, or disorders of life experience. Disorders of life experience are common in the HIV clinic but are often difficult to recognize or treat using standardized diagnostic checklists. More effective management of psychiatric disorders and substance abuse would improve long-term clinical outcomes in patients with HIV infection. (Adv Stud Med. 2006;6(3A):S138-S144)

Several studies have shown that patients with HIV infection who also have psychiatric disorders are at increased risk of undesirable treatment outcomes, compared to HIV-infected patients without psychiatric comorbidity. Individuals with psychiatric disorders are more likely to become infected with HIV, less likely to receive highly active antiretroviral therapy (HAART), less likely to remain on HAART for long-term treatment, less likely to achieve viral load reductions, and more likely to die. Even in the absence of HIV infection, patients with psychiatric conditions often do not receive good medical care.

The relationship between mental disorders and HIV treatment outcomes was recently assessed in a study conducted at the Johns Hopkins University HIV clinic. Patients were classified as having mental disorders if they had a chart record of psychiatric evaluation, a psychiatric diagnosis, and they had received at least one prescription for psychiatric medication. These patients were compared with individuals in the HIV clinic who had none of these 3 factors, who were considered to be free of mental disorders. From survey data showing that many patients seen in the HIV clinic have undiagnosed or untreated psychiatric disorders (described in the next section), it may be assumed that many of those patients without identified disorders have unidentified and untreated psychiatric disorders or substance abuse. Therefore, this study should be regarded not as a comparison of patients with and without psychiatric disorders in HIV care, but as a comparison of patients with identified and treated psychiatric disorders versus a population of patients in which many have unrecognized mental disorders. In this study, the patients with known psychiatric conditions had better outcomes on several variables. They were more likely to receive HAART than the group of patients without known psychopathology, they began HAART sooner, and they were more likely to remain...
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HIV infection should be regarded, at least in part, as an infection driven by psychiatric disorders. Mental illness and AIDS reinforce and exacerbate one another. Patients with mental illness are more likely to behave impulsively, to have depressive symptoms, to abuse substances, and to be cognitively impaired, all of which increase the risk of infection. HIV infection and AIDS, in turn, can cause cortical damage that increases the risk of depression, cognitive impairment, demoralization, and substance abuse. These psychiatric issues are significant barriers to HIV prevention, and they create a group of patients for whom preventive approaches developed to date have not been very effective. The chronically mentally ill have the highest proportion of risk behaviors of any patient group. Sexual activity is nearlyalways coercive, because these individuals tend to be the most vulnerable. Between 50% and 55% of patients in HIV clinics have Axis I psychiatric disorders. Axis I disorders are major mental disorders, developmental disorders, and learning disabilities. Common Axis I disorders include depression, anxiety disorders, bipolar disorder, attention-deficit/hyperactivity disorder, and schizophrenia; they exclude personality disorders and retardation. Common psychiatric conditions include major depression (approximately 20% of patients), substance abuse (74%), cognitive impairment (20%), and personality disorders (26%).

A significant obstacle to adequate psychiatric care is the widespread use of checklist-based psychiatric diagnosis, in which relatively little attention is paid to the characteristics of individual patients. Rigidly defined diagnostic criteria are appropriate for research purposes. However, in clinical practice, an examination should be an inclusive examination (ie, conducted with the purpose of identifying all cases of a disorder), rather than an exclusive examination, which is intended primarily to rule out individuals who do not have the disorder. In current practice, the diagnostic criteria are often applied without adequate flexibility; a patient who meets diagnostic criteria for 3 conditions receives prescriptions for medications for each condition, creating significant problems with polypharmacy.

PERSPECTIVES ON MENTAL ILLNESS

In general, there are 4 perspectives on the causes of mental illness: that disorders are caused by a disease of the brain, by temperament, by behavior, or by life story. A disease of the brain is a condition that can be modeled by a lesion. Temperament refers to persistent aspects of the personality (eg, extroversion vs introversion). Disorders of behavior may involve underlying brain biology, but represent additional learned responses. An important contrast between a brain disease and a behavioral disorder is that behavioral disorders can be modified by experience and learning, whereas brain diseases (eg, schizophrenia hallucinations) cannot be modified by learning. Conditions of life story have largely been lost in psychiatry for the past few years. Life experience can contribute to psychiatric disorders, but there is no way to demonstrate a physiological lesion in these cases. Disorders that involve life experiences are highly individualized and do not necessarily align with the checklist-based diagnoses that have come to dominate the assessment of psychiatric disorders.

Depression provides a good illustration of the brain disease model. Demoralization—a feeling of sadness in response to unpleasant life events—is part of normal experience and is not a psychiatric illness. Primary care physicians are very effective at identifying and responding to demoralization with support and encouragement. Depression is the result of abnormal functioning of the ascending mesolimbic dopaminergic reward circuitry of the brain. Individuals with depression do not experience reward from life events. Antidepressants are effective at treating people with depression; they are relatively ineffective for improving mood in people who are demoralized, who respond to support, encouragement, time, and therapeutic optimism. A large study examined depression across the life span of patients in a multicenter AIDS cohort study. Patient depression rating scores were examined for up to 48 months before the onset of opportunistic infections. As shown in Figure 1, approximately 10%
of the patient population had depression in the period between 2 and 4 years before AIDS onset, and the proportion of patients who were depressed increased before the onset of AIDS. The onset of depression in these patients may be the result of damage to the central nervous system that is caused by the HIV virus. In addition, depression also increases the risk of HIV. A recent meta-analysis showed that patients who actually have HIV are much more likely to have depression than individuals who are at risk for HIV but who are not infected. It may be that depression increases the likelihood of high-risk behaviors. Treatment studies show that patients with HIV infection or AIDS respond to treatment of depression to a degree that is similar to the general population. Approximately 66% of patients will improve with any antidepressant, and approximately 40% will experience remission. In a naturalistic, long-term study in which patients received all possible treatments, 85% of people improved, and approximately 50% exhibited remission of depression. It should also be noted that efavirenz causes depression with suicidal ideation in a subset of patients. In most cases, depression is transitory and resolves after approximately 6 weeks, and these patients also respond to antidepressant therapy. It is not always necessary to suspend efavirenz treatment.

Individuals with personality disorders are difficult to treat, difficult to get well, are extensive users of medical resources, and often demoralize healthcare providers. Two personality dimensions are of particular importance in defining disorders of temperament. The first personality axis is introversion-extroversion. Introverts are more likely to focus on the future and to choose behaviors to avoid unpleasant outcomes. Extroverts are more likely to focus on the present and to choose behaviors that provide immediate rewards. Extroverts are often difficult patients to treat; they may simply decide that they do not feel like coming to the clinic on the day of an appointment, or they may decide that they do not feel like taking their medication. The possibility of unpleasant consequences of behavior often has little impact on decision making. These individuals are reward seeking, but not consequence avoidant. Extroverts tend to be more susceptible to addictions and to engage in more high-risk behaviors. In HIV treatment, they also tend to be less adherent to HAART. Introverts are more interested in avoiding unpleasant consequences, and therefore, they are more likely to respond to messages about the negative consequences of failure to remain on treatment. It is possible to improve behaviors of extroverted patients using rewards, firm limits, and therapeutic treatment contracts, and by providing positive reinforcement and encouragement, rather than emphasizing consequences. The second personality axis is stability-instability. The unstable portion of this spectrum is defined by strong emotional responses to relatively mild stimuli, resulting in exaggerated responses to difficult situations. Unstable individuals are better able to adjust to changing situations, but they also tend to become bored more easily.

Substance use is an example of a learned behavior that is supported by a powerful positive feedback loop, as illustrated in Figure 2. The individual's environment creates the opportunity to engage in behavior. Positive responses to the behavior increase the likelihood that the behavior will be repeated in the future, whereas negative outcomes decrease the future likelihood of the behavior. Feedback loops of this type have important biological roles in shaping behaviors that are important for survival, such as eating, sleeping, and sexual behavior. The reinforcing properties of drugs, such as cocaine and heroin, usurp this circuit and drive drug-using behaviors to very high levels. This feedback loop can be influenced by factors, such as genetic vari-

Figure 1. Depressions as AIDS Develops

ability in the propensity to take risks, especially with alcohol addition, or in the neurochemical responses to drug exposure. For example, the propensity to become addicted to alcohol is strongly influenced in many individuals by a genetic predisposition to alcohol addiction. Cocaine addiction, in contrast, is less influenced by genetic variability in the response that it produces. Drugs also differ in their reinforcing properties and in the extent to which they motivate drug-seeking behavior. This has been demonstrated in studies in which baboons were required to repeatedly press a bar or lever to receive various drugs. A hungry baboon will activate a lever approximately 100 times to receive a food reward. A heroin-addicted baboon will press a lever approximately 5 times this number of repetitions for a dose of heroin. Baboons will bar-press an average of approximately 5000 times for a single administration of cocaine; one animal would depress a lever as many as 12,000 times for 1 dose of cocaine (Joseph Brady, Personal communication).

Problems of life story are commonly encountered in the HIV clinic. They often involve a vicious circle of experiences, meanings, assumptions, and behaviors (Figure 3). Problems with the life story usually begin with an aversive experience, such as childhood sexual abuse, unreliable parents, or some cause of disrupted childhood development. Alternatively, they can begin with the way the person interprets and assigns meaning to events. Events and their interpretations lead to assumptions about life, and assumptions drive behaviors. The behaviors then lead to more experiences, beginning the cycle again, often amplifying the effects of an initial unfavorable experience, meaning, assumption, or behavior. However, it is also possible to intervene at each of these 4 steps, and improving any of these steps can interrupt this cycle and lead to better outcomes. Patients can be encouraged to identify more positive experiences, meaning can be addressed using insight-oriented psychotherapy, assumptions can be modified with cognitive behavioral therapy, and behavior can be changed. It takes time to overcome the patient’s previous experiences.

**CONCLUSIONS**

Differences in patient personality characteristics are an important determinant of why behavioral interventions are effective for some individuals but not for others. Better tools are needed to design inter-
vention programs that are tailored to the characteristics of individual patients. Identification and management of demoralization, depression, substance abuse, and personality disorders are important in the management of patients with HIV infection. It has long been suspected that effective management of psychiatric conditions may improve survival, based on relatively indirect effects on medication adherence and patient visit adherence, for example. However, recent research has confirmed that adequate treatment of psychiatric disorders improves patient outcomes, including an increase in survival.

**DISCUSSION**

*Dr Benson:* I think you bring up an important point, that our behavior interventions have to be right for the patient that we are seeing, and if one approach doesn’t work, we need to try something else.

*Dr Cargill:* With antiviral therapy, if a regimen doesn’t work, it may be because the patient has a drug-resistant virus, and we have the tools to assess that. We don’t have the right tools to tell us that this patient will respond to a particular behavioral intervention, and we need those tools.

*Dr Treisman:* It isn’t possible to score things, such as extraversion and stability, and predict for certain what approach will work. I can tell you are more likely to win with reward than with consequences with certain people, but not much research has been done beyond that.

*Dr Rich:* It would be very useful for clinicians to have a screening tool to use when a patient enters care to help determine how we best motivate the patient to stay adherent to treatment and work effectively with the patient around secondary prevention, in his or her sexual risks and drug risks.

*Dr Benson:* The neurologists, for example, have screening tools to help identify subtle neurologic changes, which they validated in prospective clinical trials. You can do a short, 15-minute screening examination.

*Dr Treisman:* But people don’t do that in every patient.

*Dr Benson:* No. But they have actually done the work to incorporate it into a clinical trial. And now these screening tools can be administered by nurses, physicians, or other personnel and can be incorporated into screening in the office. You could incorporate these personality screening tools too, if you had them.

*Dr Treisman:* There are screening tools for all of the things I mentioned. There are screening tools for depression, personality disorders, substance use, and distress. And when we see someone who looks like he or she has a personality disorder or depression, we do a screening test. But what we really want is to go the other way. You don’t really screen people for congestive heart failure, but you don’t miss it. That is, it’s part of your examination to go through a patient fairly quickly and say, this person has a cough, swelling in his or her legs, and is having shortness of breath at night. I need to go further with that. Similarly, we want to be able to say this person is having high-risk behaviors and has intensely unstable interpersonal relationships, the patient doesn’t show up for most of his or her visits, and is injecting cocaine. I think the patient needs a personality workup.

*Dr Bartlett:* What’s the best depression test?

*Dr Treisman:* Probably a Beck Depression Inventory Fastscreen for Medical Patients (BDI-Fastscreen) and a General Health Questionnaire (GHQ) give you the best positive predictive value. You could do the whole thing in 15 to 20 minutes. But in your examination of a patient, if you are wondering whether the patient is depressed, the positive predictive value of wondering whether the patient is depressed is pretty close to a BDI-Fastscreen and a GHQ.

*Dr Bartlett:* So, who should treat major depression?

*Dr Treisman:* Everybody. It’s very easy to do, everybody should do it. Antidepressants all work approximately 66% of the time, but failure on one treatment does not mean the patient will not respond to other treatments; thus, often you must try several drugs to get an optimal response. The best approach to therapy for me has been to try to use medications in a way that the side effects work for you rather than against you. Selective serotonin reuptake inhibitors (SSRI), such as fluoxetine, sertraline, paroxetine, citalopram, and escitalopram, all have antianxiety properties, are relatively safe in overdose, and are usually the first drugs used clinically. Tricyclic antidepressants and mirtazapine cause weight gain, decrease neuropathy pain, and promote sleep. Mirtazapine is safer in overdose and less cardiotoxic but may not be quite as good for neuropathy pain. Although tricyclic antidepressants have cardiac toxicity, monitoring blood levels can help with adherence assessment. Bupropion is a relatively nonsedating drug and a good choice in
patients who want to be at 100%. The serotonin/nor-
epinephrine reuptake inhibitor (SNRI), venlafaxine
and duloxetine, have utility on chronic pain, as do the
tricyclic antidepressants, and are safer in overdose than
tricyclic antidepressants. SNRIs are less sedating and
cause less weight gain than tricyclic antidepressants.
Overall, the best drug is the one that works for the
patient, and so far it is difficult to predict which
patient will respond and tolerate which drug, thus a
series of trials may be needed to find the best treat-
ment for any patient.

**Dr Benson:** In substance abuse, if somebody
comes into the clinic with ascites and tremor, you're
usually going to be able to make a diagnosis of alco-
holism. But the hard part is recognizing it before the
ascites develops, especially when people hide their sub-
stance abuse from their healthcare providers and every-
body else until it reaches a point where they can't hide
it anymore. What you want is to intervene before they
get to that point.

**Dr Treisman:** A CAGE questionnaire (a series of 4
questions about substance use) is positive early in
treatment, but people tend not to do it. You can ask
whether other people bother them about alcohol use
or drug use, what drugs they use, and in what quanti-
ties. Patients do hide their substance use on a very
casual interview, but if you just push a little bit, it
often starts to come out.

**Dr Benson:** I think many HIV-infected patients
are more forthcoming about their substance abuse,
particularly if they have a healthcare provider who is
sensitized to the issue.

**Dr Mayer:** I think the presumption is that once we
have diagnosed, it is pretty easy for us to treat is not
necessarily true. Having done this for a while, I feel
pretty capable of making most of these diagnoses. But
many of our patients have multifactorial problems,
with interactions between, for example, depression,
personality disorder, and early childhood events. It is
not always easy to know what specific medication is
best for a particular patient, or whether talk therapy
will be a helpful adjunct. Very often, it's not the med-
ications alone that will provide the full relief from the
psychiatric problem.

**Dr Treisman:** In psychiatry, it has to be the same
as in general medicine: you feel comfortable up to this
point, and at that point, you get help. Part of the prob-
lem has been that there hasn't been much help, in most
medical clinics. Having recognized the problem, you

need a place to send the patient for treatment.

**Dr Bartlett:** Do you prophylactically give people
antidepressants if you are going to give them interferon?

**Dr Treisman:** This is a hotly debated topic. If the
patient has ever had depression before, and responded
to treatment, I use an antidepressant prophylactically. If
the patient has no history of depression and no sugges-
tion whatsoever of current depression, then I do not use
prophylaxis. If there is any suggestion that the patient is
depressed, I treat aggressively. Also, interferon-induced
depression sometimes manifests entirely by fatigue,
sometimes by apathy or irritability. The patients with
irritability sometimes become worse with SSRI treat-
ment and eventually require lithium or a neuroleptic.
But we have had very few people we couldn't keep on
interferon. Anecdotally, our experience has been when
people become depressed on interferon, they won't
respond to antidepressants until their hematocrit
increases to 35% or greater.

**Dr Bartlett:** What about smoking cessation?

**Dr Treisman:** I use pharmacologic and nonphar-
cologic interventions. Introverts may respond to
aversive interventions, putting your hand in an ash-
tray, and so on. Hypnotherapy can be very effective
for some patients. For extroverts, I focus on rewards.
Bupropion will decrease drive, and I use it in virtu-
ally everybody who wants to quit smoking. Nicotine
patches decrease withdrawal. But behavioral programs are necessary because cravings will be triggered, and behavior therapy helps. For about 3 months, you have to work to extinguish all of the behavioral reinforcers of smoking, such as learning not to sit in smoking sections of restaurants. They can be very subtle. It has to be individualized for that person.

REFERENCES


