Management of Psychiatric Disorders in Patients Infected with Human Immunodeficiency Virus

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Psychiatric disorders increase the risk of acquiring human immunodeficiency virus (HIV) and increase morbidity from HIV-related illness by impeding treatment. The response to highly active antiretroviral therapies is impaired by poor patient adherence, a substantial component of which is related to mental illness and substance use disorders. The recognition of psychiatric disorders in most HIV clinics is an issue of utmost importance. We outline diagnostic and treatment issues for major depression, bipolar disorder, personality disorder, substance use disorders, and demoralization as seen in patients with HIV. Our experience at the Johns Hopkins Moore (HIV) Clinic has led us to conclude that treatment of these disorders greatly improves patient adherence to treatment and outcomes of HIV infection.

Education programs that inform the public about routes of HIV transmission and strategies for preventing infection have been widespread since the late 1980s. This has resulted in a change in the HIV epidemic; new cases of HIV infection arise principally among groups of people who are unable or unwilling to follow safer sexual or clean-needle injection practices. Patients unable to modify their behavior in the face of this level of risk can be described as vulnerable to infection. In many of these people, the vulnerability arises from 1 or more psychiatric illnesses. Further, as the epidemic progresses, knowledge of the psychiatric sequelae of HIV infection has grown tremendously. For these reasons, we present here a system of classification of mental disorders seen in patients who have contracted or have HIV infection, along with recommendations regarding treatment of these mental illnesses.

PSYCHIATRIC DISEASES

Some psychiatric disorders are best described as diseases, in which a lesion is present that provokes a reliably identifiable syndrome of observable phenomena seen across patient populations.

Major depression. Major depression and demoralization are 2 well-studied disorders in HIV-infected patients, and it is important to distinguish between them clinically. Major depression presents with a syndrome centering around low mood, in which patients complain of persistent sadness or flatness of emotional tone, and anhedonia, in which patients are unable to experience pleasure or satisfaction in things or activities that ordinarily would produce such responses. Patients describe decreased vital sense, in which there is a generalized sense of illness, decreased energy, or an overall feeling of poor health and a sense of doom, often culminating in feelings of helplessness and despair. There is a decline in self-esteem, in which patients describe feeling guilty, feeling that they have failed their loved ones, or feeling that they lack what is most important to them.

Traditionally, neurovegetative features are present, including poor sleep with early-morning awakening, fatigue, quiet voice, and a sense of being slowed down. Cognitively, patients experience poor concentration, poor memory, and difficulty producing thoughts. In extreme cases, patients have hallucinations, usually auditory hallucinations involving negative themes; delusions, such as a persistent belief that a body part is dead or rotting; and cognitive impairment with decline in functioning, the so-called pseudodementia of depression. Major depression, with its attendant change in mood, self-attitude, and vital sense, as well as anhedonia and neurovegetative features, probably represents a form of brain dysfunction in the domain of affect and thus is best classified as a psychiatric disease.

Demoralization is a psychological reaction to life stresses and
may progress to the point of disorder without the existence of a pathologic lesion of the brain. In contrast to major depression, demoralization generally presents with sadness that is specifically related to a particular event or circumstance. Demoralized patients may experience some of the same symptoms of sadness described as symptoms of depression, making it difficult to distinguish these patients from those experiencing major depression. In general, however, patients with demoralization report feeling fairly normal when distracted from thinking about the event or circumstance causing their distress, but, when reminded, they experience a welling up of sadness and overwhelming grief. Furthermore, patients can often distinguish that their sadness is a result of the event or circumstance and is separate from themselves in an essential way, even though they may have guilty thoughts or feelings about how they might have done things differently, had they known what was going to happen [1].

In a study in the Johns Hopkins Moore (HIV) Clinic that examined the distinction between depression and demoralization, approximately one-half of the patients with depressive complaints experienced major depression, whereas the other half experienced demoralization—that is, adjustment disorder, as described in the Diagnostic and Statistical Manual of Mental Disorders, Third Edition—Revised [2]. Overall, studies have shown prevalence rates of major depression among individuals infected with HIV of 15%–40% [3–5]. These data are very important from the perspective of risk of HIV spread and treatment of HIV and its complications. In the Johns Hopkins HIV clinic, we find that major depression leads patients to increased substance use and decreased care for themselves and their safety.

There is evidence in the literature that depression is a risk factor for HIV [6]. First, epidemiologic data have shown a correlation between increased risk behaviors in HIV-negative people and higher scores on screening tools for general psychological distress [7]. Another study found a 7-fold increase, compared with the rate among the general population, in the lifetime prevalence of mood disorders among patients without substance use disorders who were presenting for HIV testing [8]. Moreover, major depression has been shown to be a risk factor for a variety of behavioral disturbances that may lead to risk for HIV infection, such as increased substance use [9].

With regard to treatment of HIV infection, major depression has a profound impact on adherence. Patients with depression show a decreased interest in self-care overall, and, specifically, they ignore symptoms and medical problems. Patients may not show up for clinic appointments. In particular, antiretroviral compliance has been shown to be markedly decreased among patients infected with HIV who have depression [10].

**Treatment issues associated with major depression.** Once major depression has been diagnosed, aggressive treatment of the illness is paramount. To date, no single antidepressant has been clearly shown to be superior in treating HIV-infected patients as a group. However, although all drugs may have equal efficacy, certain drugs may be more effective for individual patients. In large part, this may be due to patients’ individual tolerances of certain side effects, but the effects on a patient’s neurotransmitter profile that result from use of a specific agent may also play a role.

In general, the first step in antidepressant treatment is to get the patient to consistently take the medicine and to use an adequate therapeutic dose. Clinicians should begin by prescribing low doses of the chosen medicine and then increase titers to full doses or therapeutic serum levels (when available) slowly, to minimize side effects.

The selection process of antidepressant medication can be based on the side effect profiles of the agents. Tricyclic antidepressants (TCAs) have side effects of sedation, weight gain, and decreased gastrointestinal motility, as well as dry mouth, urinary retention, orthostasis, blurry vision, and cardiac conduction delays. Selective serotonin reuptake inhibitors (SSRIs) generally cause increased gastrointestinal motility and nausea, can cause restlessness (also known as akathisia), and often cause the sexual side effects of decreased arousal or erections, delayed ejaculation, and anorgasmia. Certain SSRIs, such as fluoxetine, tend to be more activating and are closely associated with initial insomnia, whereas others, such as paroxetine and fluvoxamine, tend to be more sedating. There is some evidence that long-term use of SSRIs, particularly paroxetine, can lead to modest weight gain [11]. A list of individual antidepressants, dose ranges, and side effect profiles is provided in table 1.

It is often possible to match antidepressant medicines to the patient’s syndrome in such a way that the side effects work to the patient’s advantage. For example, TCAs may improve sleep, promote weight gain, and decrease diarrhea, whereas SSRIs may promote daytime alertness and possibly improve dysmotility and delayed gastric emptying. Toxic side effects specific to a patient, such as the conductive changes caused by a TCA in a patient with a bundle-branch block, should be avoided.

Once the patient is on a dose of a medication for at least 2 weeks, the patient’s mood should be reassessed, and an inventory of any persistent annoying side effects should be obtained. If the patient experiences completely intolerable side effects even after attempts at alleviation, use of the drug should be discontinued. At such a time, the patient’s condition should be reevaluated, target symptoms should be reconfirmed, and a new antidepressant should be selected. Although drugs in the same class may produce similar side effects and therefore may not be tolerated, there is evidence to suggest that a response may be seen with use of one drug but not with use of other drugs of the same class [12].

If the patient experiences some relief from any symptoms, attempts should be made to continue the trial and, if necessary,
<table>
<thead>
<tr>
<th>Drug (trade name, manufacturer)</th>
<th>Start dose</th>
<th>Usual therapeutic dose</th>
<th>Serum level</th>
<th>Advantages</th>
<th>Effects and interactions with HIV medications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nortriptyline (Pamelor, Sandoz Pharmaceuticals)</td>
<td>10–25 mg at bedtime</td>
<td>50–150 mg at bedtime</td>
<td>70–125 ng/dL</td>
<td>Promotes sleep, weight gain, decreases diarrhea</td>
<td>Fluconazole, lopinavir-ritonavir, ritonavir increase nortriptyline levels</td>
</tr>
<tr>
<td>Desipramine (Norpramin, Aventis)</td>
<td>10–25 mg at bedtime</td>
<td>50–200 mg at bedtime</td>
<td>&gt;125 ng/dL</td>
<td>Promotes sleep, weight gain, decreases diarrhea</td>
<td>Lopinavir-ritonavir, ritonavir increase desipramine levels</td>
</tr>
<tr>
<td>Imipramine (Tofranil, Novartis)</td>
<td>10–25 mg at bedtime</td>
<td>100–300 mg at bedtime</td>
<td>&gt;225 ng/dL</td>
<td>Promotes sleep, weight gain, decreases diarrhea</td>
<td>Lopinavir-ritonavir, ritonavir increase imipramine levels</td>
</tr>
<tr>
<td>Amtriptyline (Elavil, AstraZenica)</td>
<td>10–25 mg at bedtime</td>
<td>100–300 mg at bedtime</td>
<td>200–250 ng/dL</td>
<td>Promotes sleep, weight gain, decreases diarrhea</td>
<td>Lopinavir-ritonavir, ritonavir increase amtriptyline levels</td>
</tr>
<tr>
<td>Clomipramine (Anafranil, Novartis)</td>
<td>25 mg at bedtime</td>
<td>100–200 mg at bedtime</td>
<td>150–400 ng/dL</td>
<td>Promotes sleep, weight gain, decreases diarrhea</td>
<td>Lopinavir-ritonavir, ritonavir increase clomipramine levels</td>
</tr>
<tr>
<td>Doxepin (Sinequan, Pfizer)</td>
<td>10–25 mg at bedtime</td>
<td>150–250 mg at bedtime</td>
<td>100–250 ng/dL</td>
<td>Promotes sleep, weight gain, decreases diarrhea</td>
<td>Lopinavir-ritonavir, ritonavir increase doxepin levels</td>
</tr>
<tr>
<td>Fluoxetine (Prozac, Eli Lilly)</td>
<td>10 mg in the morning</td>
<td>20 mg in the morning</td>
<td>Unclear</td>
<td>Activating</td>
<td>Fluoxetine increases amprenavir, delavirdine, efavirenz, indinavir, lopinavir-ritonavir, nelfinavir, ritonavir, saquinavir levels; nevirapine decreases fluoxetine levels</td>
</tr>
<tr>
<td>Sertraline (Zoloft, Pfizer)</td>
<td>25–50 mg in the morning</td>
<td>50–150 mg in the morning</td>
<td>Unclear</td>
<td>—</td>
<td>Lopinavir-ritonavir, ritonavir increase sertraline levels</td>
</tr>
<tr>
<td>Citalopram (Celexa, Forest Pharmaceuticals)</td>
<td>20 mg in the morning</td>
<td>20–60 mg in the morning</td>
<td>Unclear</td>
<td>—</td>
<td>Lopinavir-ritonavir, ritonavir increase citalopram levels</td>
</tr>
<tr>
<td>Paroxetine (Paxil, SmithKline Beecham)</td>
<td>10 mg at bedtime</td>
<td>20–40 mg at bedtime</td>
<td>Unclear</td>
<td>Somewhat sedating</td>
<td>Lopinavir-ritonavir, ritonavir increase paroxetine levels</td>
</tr>
<tr>
<td>Fluvoxamine (Luvox, Solvay Pharmaceuticals)</td>
<td>50 mg at bedtime</td>
<td>150–250 mg at bedtime</td>
<td>Unclear</td>
<td>Somewhat sedating</td>
<td>Fluvoxamine increases amprenavir, delavirdine, efavirenz, indinavir, lopinavir-ritonavir, nelfinavir, ritonavir, saquinavir levels; nevirapine decreases fluvoxamine levels</td>
</tr>
<tr>
<td>Venlafaxine (Effexor, Wyeth-Ayerst)</td>
<td>37.5 mg in the morning</td>
<td>75–300 mg in the morning</td>
<td>Unclear</td>
<td>—</td>
<td>Lopinavir-ritonavir, ritonavir increase venlafaxine levels</td>
</tr>
<tr>
<td>Mirtazapine (Remeron, Organon)</td>
<td>7.5–15 mg at bedtime</td>
<td>15–45 mg at bedtime</td>
<td>Unclear</td>
<td>Promotes sleep, weight gain</td>
<td>—</td>
</tr>
<tr>
<td>Nefazodone (Serzone, Bristol-Myers Squibb)</td>
<td>50 mg b.i.d.</td>
<td>300–400 mg/day in divided doses</td>
<td>Unclear</td>
<td>Somewhat sedating</td>
<td>Nefazodone increases efavirenz, indinavir levels</td>
</tr>
<tr>
<td>Trazodone (Desyrel, Geneva Pharmaceuticals)</td>
<td>50–100 mg at bedtime</td>
<td>50–150 mg at bedtime for insomnia; 200–600 mg at bedtime for depression</td>
<td>Unclear</td>
<td>Promotes sleep</td>
<td>Lopinavir-ritonavir, ritonavir increase trazodone levels</td>
</tr>
<tr>
<td>Bupropion (Wellbutrin, Glaxo Wellcome)</td>
<td>100 mg in the morning</td>
<td>150–400 mg/day in divided doses</td>
<td>Unclear</td>
<td>Activating, no sexual side effects</td>
<td>—</td>
</tr>
</tbody>
</table>
to alleviate side effects. For example, a patient who experiences good antidepressant response but persistent insomnia while taking fluoxetine may fall asleep more easily with 25–100 mg of trazodone at bedtime. Similarly, a patient who responds to the antidepressant effects of nortriptyline but complains of constipation may find relief from increased water and fiber intake. SSRI-induced sexual side effects, particularly impotence, may respond to a variety of treatments [13, 14].

Evaluation of the effectiveness of antidepressant medications is an ongoing process, and we consider a full trial of a medication to be at least 6–8 weeks of a standard dose or therapeutic serum level [15–17]. If the patient is receiving only partial benefit, we begin an augmentation strategy. These strategies may be beyond the scope of many providers. Once again, the “start low, go slow” rule applies, because all augmenting agents have potential side effects.

Lithium is the best-studied augmenting agent [18–21], followed by thyroid hormone preparations [22, 23]. However, many agents have been used, including bupropion, other mood stabilizers, trazodone, pindolol [24], antipsychotic medications, methylphenidate, benzodiazepines, and SSRIs and TCAs in combination, as well as sleep deprivation and bright-light therapy. Side effects of lithium include nausea, diarrhea, increased urine output, and dose-related tremor. Further, lithium may cause renal disease, hypothyroidism, and cardiac conduction impairment, so its use in patients with these preexisting conditions may be limited. Because thyroid preparations, methylphenidate, and bupropion are all activating medications, they may benefit patients who have persistent fatigue. As mentioned above, trazodone may help alleviate insomnia. It is easily combined with SSRIs, venlafaxine, nefazodone, and bupropion and may be used carefully with TCAs.

**Bipolar disorder and AIDS mania.** Patients with bipolar disorder may experience depressive episodes like those previously described, but they may also experience periods of hypomania or mania. Hypomania presents as a syndrome centering around expansive mood, which may be euphoria or extreme irritability and anger. Patients describe an overabundance of energy, with a decreased need for rest or sleep. Cognitively, thoughts are very rapid, often manifesting as a noticeable “push” of speech: patients are very difficult to interrupt when talking, and speech is fast and loud. At times, patients describe their thoughts as “racing”: they perceive more than 1 thought at a time or feel unable to keep up with their thoughts. Often, these symptoms result in reckless behavior, such as increased spending, assumption of many large projects at once, increased religious activity, or increased sexual activity.

Mania includes all of the symptoms of hypomania but is more severe. The *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* makes the distinction between the two on the basis of degree of impairment, but we use the presence of psychotic features to distinguish between the conditions. The most common psychotic symptom is a disorganization of thoughts and activities such that patients cannot coherently express themselves because their ideas are changing very rapidly and hold no bearing on one another—the so-called flight of ideas. Further, mania often causes patients to hold grandiose delusions in which they believe, in a fixed way, that they are somehow more than they are—for example, incredibly rich, intelligent, powerful, attractive, or, at times, possessing superhuman powers or a prominent position. The presence of any psychosis leads to marked impairments in function and usually results in hospitalization.

Occasionally, patients with no personal or family history of bipolar disorder develop a manic syndrome in late-stage HIV infection. Usually referred to as “AIDS mania,” it is clinically distinct from mania in bipolar disorder in symptoms, course, and treatment, and it is usually associated with AIDS dementia and late-stage disease [25, 26].

**Treatment issues associated with mania.** For acute mania or mixed states, the mainstays of treatment are mood stabilizers and antipsychotic medicines. Treatment of mania may require consultation and may be beyond the scope of most primary medical clinicians. Mood stabilizers used for this condition include lithium salts and anticonvulsants agents. Lithium should be titrated carefully to a therapeutic serum level, and trough levels should be checked after 4 full days on any given dose. Lithium is the best-studied of all the mood-stabilizing agents [27–29], but it carries with it some significant risks due to a narrow therapeutic window. Common side effects of lithium include nausea, diarrhea, increased urine output, weight gain, and dose-related tremor. With prolonged administration of high levels of the drug, lithium is toxic to kidneys, may cause diabetes insipidus, and is toxic to the thyroid, causing hypothyroidism. Use of lithium in patients with the sick sinus syndrome is contraindicated. Finally, lithium can cause or worsen delirium, and great care should be taken when it is used to treat patients who have preexisting cognitive deficits.

Valproate has been fairly well studied [30, 31] and has been approved by the US Food and Drug Administration for use in patients with bipolar disorder. Once again, care should be taken to titrate the dose to achieve a therapeutic serum level slowly, because valproate can induce delirium in some patients. Approximately 20 mg/kg/day generally achieves a therapeutic level. The side effects of valproate are sedation, weight gain, hair loss, dose-related tremor, ataxia, and nystagmus. Many patients will have a transient rise of 10%–15% in serum transaminase levels; the medicine should be stopped only if levels exceed this expected finding. Last, hemorrhagic pancreatitis has been associated with the use of valproate in some patients; clinicians should perform a careful evaluation of any abdominal com-
used aggressive regimens of highly active antiretroviral therapy [38]. Unfortunately, mania significantly complicates patients’ acceptance of HAART, and antipsychotics may be a necessary part of their care.

**PERSONALITY DISORDER AND DIMENSIONS OF ENDOWMENT**

There are measurable, enduring traits of disposition that describe the type of person a clinician is seeing. On the basis of the work of Eysenck and Rachman [39], we can broadly consider 2 categories of temperament: extroversion and introversion.

**Antipsychotics**

Antipsychotic agents are of great benefit in treating patients with acute mania and often get results before mood stabilizers can achieve therapeutic serum levels. Higher-potency agents, such as haloperidol and fluphenazine, are easily begun as a single nightly or daily divided dose, as the case may warrant. Potent antipsychotic agents cause minimal sedation but are associated with orthostasis and idiosyncratic acute dystonic reactions. If such a reaction arises, it should be immediately treated with diphenhydramine or benztpine administered orally, im, or iv. Antipsychotic agents are associated with extrapyramidal symptoms, including cogwheel rigidity, tremor, bradykinesia, and drooling. These side effects should be treated, if they occur, with orally administered anticholinergic agents. Akathisia, an uncomfortable restless feeling that occurs primarily in the legs, can be treated with anticholinergic agents or with beta-blockers.

Newer, atypical antipsychotic agents are thought to cause fewer extrapyramidal symptoms, and therefore their use may be advantageous. Risperidone dosages usually are 0.5–8 mg/day in single or divided doses. Olanzapine is often given as a single dose of 2.5–20 mg at night, because it is sedating. Its use also is associated with akathisia and weight gain. Quetiapine is very sedating, and use of this drug has been associated with development of lenticular opacities, but it may cause less weight gain than the others. The usual dose range is 25–700 mg, and the drug is given at night.

Patients with AIDS mania (which is usually associated with AIDS dementia or significant cognitive impairment [37]) are particularly difficult to treat. We have had significant problems, particularly with the side effect of delirium, using mood stabilizers to treat these patients and have relied heavily on the use of low-dose antipsychotic agents. In recent years, we have used aggressive regimens of highly active antiretroviral therapy (HAART), which usually results in significant improvement...
patients: clarifying treatment goals, creating a treatment contract, and anticipating misunderstandings driven by feelings.

Clarity of treatment goals. The first goal of treatment is health, not the many other concerns to which the provider might be sympathetic. A discussion of treatment goals should outline how treatment will improve quality of life, with comfort and removal of consequences being secondary. Thus, the patient learns to recognize that the doctor will prescribe treatments and behaviors that are good for him or her in the long run but that may cause dissatisfaction initially. An obvious example of this is an insistence on abstinence from drug use, which requires the patient to give up a pleasurable feeling to prevent longer-term sequelae, such as medical morbidity, alienation from support systems, poverty, and homelessness.

Treatments contracts for patients with extroversion. As part of the treatment contract, patients describe what changes they will make to improve their condition. This may involve a quid pro quo in which the clinician agrees to provide certain things that the patient wants in a clear contract or written treatment plan. Patients with extroverted temperaments often create chaos in clinics by splitting the staff and pitting one staff member against another in an effort to get rapid acquiescence to their wishes. A written treatment plan can allow all staff members access to information about the patient’s active problems, the goals agreed upon by the team, and the consequences of adherence and nonadherence to the prescribed treatment. A reasonable beginning is the promise of a doctor’s release note in the near future to spare a patient some consequence of his or her behavior in exchange for an immediate improvement in some behavior by the patient. For example, the patient might be required to submit to several weeks of urine toxicology screens before the physician agrees to speak to parole officers and courts on the patient’s behalf. Another example would be requiring at least 6 weeks’ participation in drug or alcohol treatment from a patient who has requested that Social Security disability paperwork be completed by the doctor. Benzodiazepines and narcotic abuse can be particularly effectively handled with this method.

Misunderstandings driven by feelings. Patients prone to extroversion often have strong feelings that lead to misunderstandings. As it is an anticipated circumstance in their care that they will love the doctor one day and hate him or her the next. Planning for this allows more successful treatment. When patients have difficulty, rather than rescuing them, doctors agree to help, provided the patient is willing to make greater changes in his or her behavior than were promised in the last encounter. For example, a patient who has failed outpatient substance use management might be required to enter a 30-day inpatient rehabilitation program before receiving the requested aid. By raising the requirements for the patient’s behavior, the doctor allows the treatment to move forward, instead of rejecting the patient, and also allows patients to decide when they are ready for treatment.

In the initial relationship between the patient and the provider, the provider makes the treatment goals and assigns the treatment tasks. In this role, the doctor assumes responsibility for the treatment plan. As the patient begins to engage in the treatment plan, the doctor can allow the patient more control. Although initially doctors make and set ultimatums requiring certain behaviors, as the patient progresses doctors attempt to persuade the patient to further improve behaviors. Ultimately, the continued relationship with the doctor results in the traditional doctor-patient relationship, in which the doctor acts as a guide and an information source for patients, so that decisions can be made in the patients’ best interests, but in which guidance and information are clearly related to the patients’ goals.

SUBSTANCE USE DISORDERS AND ADDICTION

Substance use disorders increase transmission of HIV and complicate treatment of HIV infection, increasing morbidity and mortality. We have reported that 75% of patients who present to the Johns Hopkins HIV clinic have a substance use disorder [47], which is not surprising for a clinic in which the predominating risk for infection involves sharing of needles. Even homosexual men in our clinic who are not IV drug users have a rate of substance use disorders of 75% (GJ.T., unpublished observation), although they tend to use cocaine, alcohol, and benzodiazepines rather than opiates. In our experience, 3 factors associated with substance use disorders are relevant to the HIV epidemic—intoxication with a substance, the chemical effects certain substances have on the brain, and the syndrome of addiction that develops in patients.

Intoxication with any substance can be a risk factor for HIV transmission, because intoxicated people have impaired judgment and therefore may practice risky behaviors. Several studies have shown that becoming intoxicated immediately before engaging in sexual activity is associated with lower rates of condom use [48,49], although this finding has been disputed [50]. Cocaine intoxication increases sexual desire, and several studies have reported an association between cocaine use and increased numbers of sexual partners [51–53]. Notably, people who reported engaging in sexual activity while under the influence of crack cocaine also reported a history of STD infections [54]. The increase in high-risk behavior that accompanies intoxication is not limited to cocaine users; similar results have been found for alcohol users. Heavy alcohol consumption has been associated with higher rates of risky behavior, such as receptive anal intercourse or sex with anonymous partners [54,55].

For IV drug users, the risk of HIV transmission may be in-
creased by intoxication, which leads to unsafe behavior, but high-risk behavior may occur even before intoxication. Some iv drug users shoot their drugs in “shooting galleries,” places where they may rent or borrow “works” (syringes and needles) or use water or other materials taken from common receptacles [56, 57]. Repeated drug use at a single sitting leads to increasing intoxication with each use and, therefore, greater impairment of perception and judgment, thus increasing the risk that an individual will use an infected needle. Furthermore, although needle-exchange programs are available in some areas, many patients believe that it is inconvenient to obtain clean needles and will resort to sharing [58].

Patients who use drugs take other health care–related risks as well. Use of crack cocaine by pregnant women is associated with lack of prenatal care [59] and increased incidence of congenital syphilis [60, 61]. The ongoing use of drugs may lead to an exchange of sex for drugs or money. Several studies have commented on the role of this practice as a risk factor for STD transmission [62, 63].

Depressive symptoms are frequently associated with chronic substance use. Depressive symptoms and hopelessness in this population are major risk factors for acquisition of HIV and nonadherence with treatment, an association that is supported by the literature [64, 65]. Depression can be the result of the direct action of certain substances on brain chemistry; alcohol intoxication and withdrawal from cocaine or stimulants can produce depressive syndromes. Depressive syndromes may also be the sequelae of drug addiction.

“Addiction” is the term used to describe a substance use disorder that arises out of a cycle of motivated behavior. In brief, this is a cycle in which use causes intense craving, which in turn leads to increased use (figure 1). Many patients move beyond using or abusing substances to the development of an overwhelming drive to propagate the substance use behavior. The lifestyle of substance addiction leads the addict to devote increasing resources to the pursuit of the drug, thus consuming all assets, including time, money, employment, and relationships. Thus, demoralization may arise from the losses experienced by the addict and from a sense of powerlessness over the drug craving.

An understanding of the treatment of addictions is critical to successful treatment of HIV in patients who are addicted to drugs. Addiction not only increases the risk of infection but also increases the risk of noncompliance with HIV medications [66]. The treatment for substance dependence can be laid out in simplified terms as consisting of 4 steps: detoxification, rehabilitation, treatment of comorbid conditions, and relapse prevention.

Detoxification begins with confronting patients about their intoxicated state and their inability to further assess their needs before they are sober. Once the patient is detoxified and sober, rehabilitation begins with confronting the patient about the need to stop using the substances and get into treatment. This requires the construction of a support network to aid in the maintenance of abstinence and to continue the confrontation of the stigmatized behavior outside the clinic setting. The principal treatment for substance use disorders is group psychotherapy. Twelve-step groups use a stepwise rehabilitation structure to help patients achieve a series of goals. Any treatment approach must supply structure, goals, and a method by which behavior can be confronted in a positive way. Patients want to stop being addicts, but they do not want to stop the addictive behavior.

While rehabilitation is under way, patients must be assessed for comorbid psychiatric diseases and temperamental vulnerabilities that will prevent recovery. Skilled mental health evaluation is essential, but it is not always readily available in drug treatment programs. Furthermore, some drug treatment programs actively discourage treatment of mental illness with medications, claiming that it is another form of drug use. Comorbid treatment requires explanation and support.

Pharmacotherapy for addictions is almost always adjunctive. The exception is detoxification from the sedative-hypnotic class of drugs (alcohol, benzodiazepines, barbiturates, and related drugs). Withdrawal from these drugs is life threatening when it is accomplished abruptly, without tapering of the drugs. The adjunctive use of medications falls into 4 categories: to ameliorate withdrawal, to diminish craving, as a substitute for addictions, and as aversion therapy. Table 2 shows examples of all of these.

Relapse prevention is an extended form of rehabilitation. It involves replacement of the drug use–related behaviors with behaviors that are directed at achievement of a higher quality of life. Vocational rehabilitation, social rehabilitation, and the creation of a drug-free environment are essential to preventing
Table 2. Strategies for detoxification and treatment of addiction.

<table>
<thead>
<tr>
<th>Detoxification strategies</th>
<th>Addiction treatment strategies</th>
</tr>
</thead>
<tbody>
<tr>
<td>For addiction to alcohol, benzodiazepines, barbiturates, and other sedative/hypnotic agents:</td>
<td>Substituted addiction</td>
</tr>
<tr>
<td> Benzodiazepine taper</td>
<td>For addiction to opioids:</td>
</tr>
<tr>
<td> Barbiturate taper</td>
<td> Methadone, l-α-acetylmethadol, buprenorphine</td>
</tr>
<tr>
<td>For addiction to opioids:</td>
<td>For addiction to nicotine:</td>
</tr>
<tr>
<td> Agonist taper (methadone, buprenorphine, other prescription narcotics)</td>
<td> Nicotine transdermal patch, inhaler, or gum taper</td>
</tr>
<tr>
<td> Symptomatic treatment (clonidine taper, dicyclomine, methocarbamol, nonsteroidal anti-inflammatory drugs)</td>
<td>Blockade of reinforcement</td>
</tr>
<tr>
<td>For addiction to nicotine:</td>
<td>For addiction to opioids:</td>
</tr>
<tr>
<td> Nicotine transdermal patch, inhaler, or gum taper</td>
<td> Naltrexone</td>
</tr>
<tr>
<td>Addiction treatment strategies</td>
<td>Aversive conditioning</td>
</tr>
<tr>
<td>Substituted addiction</td>
<td>For addiction to alcohol:</td>
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<tr>
<td>For addiction to opioids:</td>
<td> Disulfiram</td>
</tr>
<tr>
<td> Methadone, l-α-acetylmethadol, buprenorphine</td>
<td>For addiction to other substances:</td>
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<tr>
<td>For addiction to nicotine:</td>
<td> Behavioral aversive conditioning</td>
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<tr>
<td> Nicotine transdermal patch, inhaler, or gum</td>
<td>Drive suppression</td>
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<tr>
<td>Blockade of reinforcement</td>
<td>For addiction to alcohol:</td>
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<tr>
<td>For addiction to opioids:</td>
<td> Naltrexone</td>
</tr>
<tr>
<td> Naltrexone</td>
<td>For addiction to nicotine:</td>
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<tr>
<td>Aversive conditioning</td>
<td> Sustained-release bupropion</td>
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<tr>
<td>For addiction to alcohol:</td>
<td>For addiction to cocaine:</td>
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<tr>
<td> Disulfiram</td>
<td> Antidepressants? Buprenorphine?</td>
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<td>Behavioral aversive conditioning</td>
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relapse. This also means use of ongoing group therapy directed at recovery.

**PSYCHOLOGICAL REACTIONS TO LIFE EXPERIENCES**

Patients often require help in coping with the trauma of life experiences. They become disordered in response to these experiences, even though no brain lesion or disease is present. Such experiences as rape, premature death of a loved one, or overwhelming grief from illness such as HIV can produce psychological disorders. Counseling and psychotherapy have been the mainstays of treatment for these disorders. The disorders are understood by the treating clinician at the level of empathy and sympathy rather than pathophysiology. These disorders occur principally in the context of worsening illness or social problems for patients in the HIV clinic. Psychological problems can range from those created by the patient’s own behavior, such as the consequences of drug use, to reactions to the social stigmatization of people infected with HIV.

In a common scenario, the patient, who is committed to recovery from drug use and struggling with the burdens of HIV, discovers overwhelming barriers to treatment or employment because of the diagnosis of HIV. Patients in the early 1990s often spent down their resources as their T cell levels dropped, then were confronted with the need to start their lives over after experiencing a dramatic response to HAART. Vigilance for demoralization is paramount at 2 critical points of doctor-patient interaction: the initial diagnosis of HIV and the delivery of bad news about worsening of the patient’s condition, such as the need to change HAART treatment.

In psychiatry, “psychotherapy” is the term that describes the process of changing patient feelings or actions on the basis of interaction with the provider. Although many types of psychotherapy require some technical training to perform, demoralization arising out of a life circumstance, such as infection with HIV and all of the attendant fear and suffering, may respond well to a relatively unstructured supportive interaction with a caring provider. Therapeutic optimism, such as emphasis on the availability of improved treatment regimens, along with a supportive, caring provider-patient relationship, goes far to help patients deal appropriately with illness. Demoralization responds well to regular contact with a provider, gentle reminders to maintain hope, and knowledge that someone is listening and trying to alleviate suffering. When patients continue to experience demoralization despite best efforts, referral to a psychotherapist is indicated.

Supportive counseling is the glue that holds the treatment plan together. Demoralized patients with substance use disorders, personality problems, and major depression are common in our HIV clinic. They arrive with an apparently endless list of problems that can overwhelm many clinicians. A careful description of the way in which life gets better over time, a view of the future, a focus on the strengths of the patient and on ways in which those strengths can be exploited to improve quality of life, and experience with successful outcomes for similar patients are the foundation of successful treatment. Maintenance of therapeutic optimism can be difficult in the face of these problems, but it is essential to good outcomes.

**SUMMARY**

Psychiatric disorders are a vector for infection with HIV and a barrier to its successful treatment. They provoke risk behaviors and demoralize patients. In the current medical system, patients with highly complex conditions and the need for many...
coordinated services, particularly patients with no resources, are undesirable to the institutions that reimburse care. Additionally, these patients have poorer outcomes than patients with more straightforward and easily treated problems. Unfortunately, services are less available to drug-addicted, indigent, minority, mentally ill, homeless, nonvoting, disenfranchised patients, although these are the patients most vulnerable to infection. Recognition and effective treatment of psychiatric disorders in HIV care settings will have a large impact on the future of the epidemic and should be fundamental goals in the design of care of patients who are infected with HIV.

References