TREATING HIV/AIDS

A Quick Reference Guide

Based on *Practice Guideline for the Treatment of Patients With HIV/AIDS,* originally published in November 2000. A guideline watch, summarizing significant developments in the scientific literature since publication of this guideline, may be available in the Psychiatric Practice section of the APA web site at www.psych.org.

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The development of the APA Practice Guidelines and Quick Reference Guides has not been financially supported by any commercial organization. For more detail, see APA's "Practice Guideline Development Process," available as an appendix to the compendium of APA practice guidelines, published by APPI, and online at http://www.psych.org/psych_pract/treatg/pg/prac_guide.cfm.

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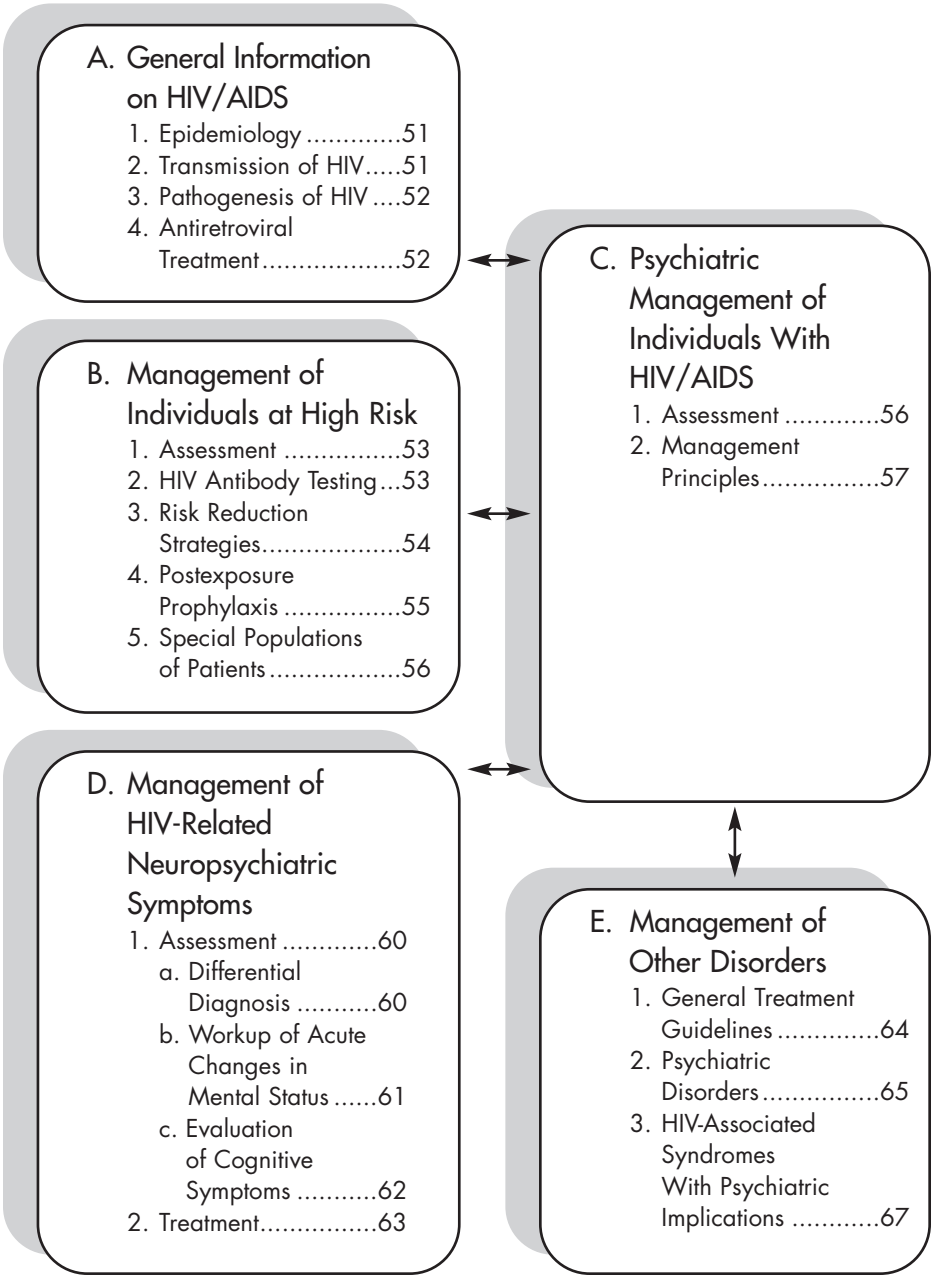
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A. General Information on HIV/AIDS

1. Epidemiology

- Current U.S. information is available at www.cdc.gov/hiv/dhap.htm.
- Since 1995, there has been a large decline in death rates because of antiretroviral therapy.
- The overall prevalence of HIV/AIDS has increased because of decline in death rates plus the steady rate of new HIV infection; prevention of infection remains a high priority.

2. Transmission of HIV

Routes of transmission

- *Sexual:* Unprotected intercourse is the most common route of transmission, irrespective of gender or sexual orientation.
- *Injection drug use:* Sharing unsterilized injection equipment is a very efficient means of transmitting HIV.
- *Perinatal:* Infection from mother to infant can occur during gestation, delivery, or breast-feeding.
- *Blood transfusion:* In the U.S., screening blood for HIV has reduced the risk by transfusion to almost zero.

Cofactors that enhance transmission

- *Physical:* The presence of sexually transmitted diseases may cause genital lesions or genital/mucous membrane bleeding during sexual activity.
- *Behavioral:* Substance use lowers sexual inhibitions, impairs judgment, and increases impulsivity.

3. Pathogenesis of HIV

- During the acute phase, 50% to 90% of people experience a flulike syndrome within 3 to 6 weeks of infection.
- The clinically asymptomatic phase may last for many years. The host seroconverts. The immune system may appear to control infection, but chronic viral replication persists.
- AIDS is defined by conditions indicating significant immunosuppression (e.g., opportunistic infections) or other conditions (dementia, wasting). For criteria, see the web site of the Centers for Disease Control and Prevention (CDC) (www.cdc.gov/mmwr/preview/mmwrhtml/rr4813a1.htm).

4. Antiretroviral Treatment

- For guidelines on the use of antiretroviral agents, go to www.aidsinfo.nih.gov.
- The goal of antiretroviral treatment is to reduce viral load to undetectable levels and maintain this without interruption.
- Lack of clinical response may be due to problems with adherence, suboptimal antiretroviral treatment potency, or genetic mutation of strains.
- Adverse effects of antiretroviral treatment include lipodystrophy (fat redistribution syndromes), hyperlipidemia, nephrotoxicity, bone marrow suppression, neuropathy, nausea, diarrhea, sleep disturbances, rash, and elevation of glucose levels, possibly causing diabetes mellitus.
- Combined cost for antiretroviral agents in multidrug regimens is very expensive.
- Adherence is of utmost concern with antiretroviral treatment. Even minor deviations from the prescribed regimen can result in viral resistance and permanent loss of efficacy. Studies of antiretroviral treatment continue to indicate that near-perfect adherence is needed to adequately repress viral replication.

B. Management of Individuals at High Risk

1. Assessment

Obtain risk history.

- Risk history should be considered in every psychiatric evaluation to identify individuals at high risk.
- An ongoing appraisal of risk is sometimes needed (e.g., during acute episodes of psychiatric illness, stressful or traumatic life events, and initiation of sexual activity in adolescents).
- Sexual history should be assessed with nonjudgmental attitude (see Table 2 of APA's *Practice Guideline for the Treatment of Patients With HIV/AIDS* for risks associated with specific behaviors).
- See Table 12 of APA's *Practice Guideline for the Treatment of Patients With HIV/AIDS* for risk assessment questions.

Conform to the vocabulary and cultural beliefs of the patient.
See www.drugabuse.gov for a current list of drug terminology.

2. HIV Antibody Testing

Identify infection early.

- Early identification of HIV infection is important so that newly infected persons can be medically monitored and promptly receive antiretroviral treatment as appropriate.
- Risks of testing include worries, fears, and stigma associated with a diagnosis of HIV/AIDS.

2. HIV Antibody Testing *(continued)*

Provide pre- and posttest counseling.
- Explain the HIV test, including risks and benefits.
- Discuss the confidentiality of results.
- Review risk behaviors and present risk reduction strategies.
- Discuss plans for dealing with a positive or negative result.

CDC guidelines for counseling are available at www.cdc.gov/hiv/pubs.htm.

Discuss with the patient issues surrounding disclosure of status to family, friends, or employers.

The American College of Obstetricians and Gynecologists recommends that an HIV antibody test be offered during annual examinations to all women seeking preconception care.

3. Risk Reduction Strategies

Provide education about behaviors that place patients at risk for HIV infection.

Manage risk behaviors.
- Active discussions foster changes in behavior.
- Ongoing discussions about motivation and skills are needed to ensure consistent changes.
- Problems or disorders that may promote risky behavior include impulse control disorders, untreated depression, hypersexuality associated with mania, psychotic disorders, mental disorders due to a general medical condition, binge alcohol or drug use, and personality disorders.
- Extended counseling and case management should be provided for continuing management of risk behaviors.

Implement specific risk reduction programs (e.g., needle-exchange programs, skills training groups).

Help the patient develop skills to discuss and negotiate safer sex with partners (e.g., practice communication skills through role-play).

Evaluate the patient's access to condoms and skills to use them.
See Table 13 of APA's *Practice Guideline for the Treatment of Patients With HIV/AIDS* for guidelines on condom use.

4. Postexposure Prophylaxis

- Postexposure prophylaxis (PEP) may prevent initial cellular infection and local propagation of HIV.
- PEP is currently recommended for known occupational exposure, especially percutaneous or mucous membrane exposure to blood or other bodily fluids. Its value in other exposure situations (e.g., known sexual exposure) is being studied.
- Rapid assessment is essential. A multiple-drug regimen must begin as soon as 1 to 2 hours and no later than 24 to 36 hours after exposure. The regimen must continue for at least 4 weeks.

Additional information is available through the National Clinicians' Postexposure Prophylaxis Hotline (888-448-4911) and web site (www.ucsf.edu/hivcntr).

5. Special Populations of Patients

Patients with severe mental disorders
- HIV infection may be associated with health risks caused by poor access to health care or by decreased capacity for self-care.
- Risk reduction programs tailored to the needs of this special population have been shown to reduce the risk of HIV infection.

Patients with substance use disorders
- For patients injecting drugs, risk reduction strategies include methadone maintenance treatment, needle-use education and bleach distribution, drug rehabilitation programs, safer-sex education, legal clean-needle purchase, and needle-exchange programs.
- For noninjection drugs and alcohol, treatment may reduce risk exposure secondary to disinhibition or cognitive impairment.

Victims of sexual abuse/crimes
- Ask about specific behaviors that are associated with the risk of HIV transmission.
- Determine whether a psychiatric disorder is present and whether treatment is indicated.
- Consider PEP in cases of sexual assault.

C. Psychiatric Management of Individuals With HIV/AIDS

1. Assessment

Obtain risk history; determine HIV status.

Conduct a comprehensive diagnostic evaluation.
Because of the stress associated with HIV diagnosis, special attention should be paid to assessing suicidal ideation, self-destructive behavior, and extreme anger.

Assess possible medical causes of new-onset symptoms and initiate specific treatment interventions.

Understand psychodynamic issues.

Include HIV risk assessment and prevention in the treatment plan for every patient with severe mental illness and/or an alcohol or substance use disorder.

2. Management Principles

Establish and maintain a therapeutic alliance.

- Determine the patient's understanding of stage of illness and evaluate coping mechanisms.
- Explore cultural/ethnic beliefs regarding psychiatric and HIV illness and conform to the language of the patient.
- Review issues of confidentiality. The patient should be asked to consider the psychiatrist's role in assisting in the process of disclosure of HIV status to appropriate persons.
- Be aware of transference and countertransference feelings, including personal attitudes about HIV infection and how the patient acquired it.

2. Management Principles *(continued)*

Coordinate care with other mental health and medical providers.

- It is essential to collaborate with other physicians practicing in infectious disease, primary care, and other disciplines to keep up to date—for example, through discussions of drug interactions and close monitoring and workup of unexplained or psychiatric symptoms.
- Patients need to agree to the exchange of specific information with other care providers.

Diagnose and treat all associated psychiatric disorders.

- Actively monitor for substance abuse, because it is often associated with risk behaviors.
- Do not assume that patients who have relatively good immune functioning have no risk for CNS HIV disorders.
- Note that psychotherapeutic management of patients with HIV infection is similar to that of other patients.

Facilitate adherence to overall treatment plan.

- See Appendix A (p. 68) in this guide for strategies to increase adherence.
- Poor adherence to antiretroviral medications results in development of viral resistance.
- Comorbid psychiatric disorders (e.g., substance abuse or depression) can adversely affect adherence; adherence to both psychotropic and HIV medications is important.
- Psychoeducational approaches can reinforce the importance of adherence, encourage the patient to seek appropriate help from others, and identify barriers to adherence.
- Intensive psychodynamic psychotherapy may be helpful if the patient is still unable to modify behavior after educational approaches.
- Outreach efforts with public health nurses and services can provide adherence assistance for hard-to-reach patients.

Provide risk reduction strategies to minimize the spread of HIV.
- Risk reduction is an ongoing treatment priority.
- Risk assessment should be repeated when there are changes in the clinical status or social situation.
- Patients on high-dose antiretroviral medications should be advised that they remain contagious.

Help the patient maximize psychological and social/adaptive functioning.
- Assess social supports.
- Use appropriate community-based services.
- Encourage the patient to resolve legal and financial concerns, providing assistance when necessary.
- Assist with significant intrapersonal, interpersonal, and social stresses.

Explore the role of religion and spirituality in the patient's care.

Prepare the patient for issues of disability, dying, and death.
- Evaluate the need for work or school accommodations in line with the Americans With Disabilities Act.
- Assist the patient in drawing up a living will to guide end-of-life decisions.

Advise significant others, including family, about sources of care and support.
- Refer to support groups.
- Encourage participation in HIV/AIDS advocacy organizations.
- Consider referral of significant others and family for psychiatric evaluation and treatment, including individual or family therapy.

D. Management of HIV-Related Neuropsychiatric Symptoms

1. Assessment
a. Differential Diagnosis

Delirium
- Delirium should be considered before other diagnoses.
- Delirium is common in HIV infection.
- Most common causes are iatrogenic and psychoactive-substance–induced toxicity, infection, neoplasms, metabolic disturbances, some antiretroviral medications (e.g., zidovudine at high doses).

Other HIV-associated cognitive dysfunction

HIV-associated dementia (HAD)
- Subcortical dementia
- Clinical triad of progressive cognitive decline, motor dysfunction, and behavioral abnormalities
- Common symptoms: psychomotor slowing, decreased speed of information processing, impaired verbal memory and learning efficiency, impairment in executive functioning

Mild neurocognitive disorder
- Less severe than HAD
- Diagnosis requires functional impairment, exclusion of other possible causes, and impairment in at least two neurocognitive domains (one of which must be primarily cognitive) that is at least one standard deviation below the demographically appropriate normative mean.
- Important to diagnose and treat because it involves dysfunction rather than cell death
- May affect spinal column (e.g., vascular myelopathy of dorsolateral columns) and/or peripheral nerves (e.g., painful sensory neuropathy)

Asymptomatic neurocognitive impairment
- Occurs without any associated decrement in functional status
- Poses a risk for progression to mild neurocognitive disorder

(continued)

HIV-associated progressive encephalopathy (PE) or HIV encephalopathy in children (terms used instead of "dementia caused by HIV")

- Condition is characterized by a triad of symptoms: impaired brain growth, progressive motor dysfunction, and loss or plateau of developmental milestones.
- Markers of immunological functioning (e.g., CD4 count) do not correlate with degree of neurocognitive impairment.
- Some cognitive and language delays (e.g., receptive and expressive language and visual-motor deficits) are present even when the patient appears asymptomatic.
- Condition should be distinguished from mental retardation secondary to other causes, such as maternal drug addiction and prematurity, which can be determined only by longitudinal assessment.

Mental disorders caused by general medical conditions affecting the CNS

Patient may present with psychiatric symptoms or syndromes such as psychosis or mood disorder (see Appendix B, p. 69, in this guide).

Medication-induced mental disorders

Medications commonly used to treat conditions associated with HIV infection may have psychiatric symptoms as side effects (see Appendix C, p. 70, in this guide).

1. Assessment
b. Workup of Acute Changes in Mental Status

Rule out treatable and reversible medical causes—especially if CD4 counts drop or viral load rises. Note that acute changes in mental status may *not* correlate with changes in CD4 counts or viral load and may be due to other causes.

1. Assessment
b. Workup of Acute Changes in Mental Status (continued)

Workup for patients with or at high risk for HIV infection who present with acute onset with no previous psychiatric history:

- Complete medical evaluation, including physical/neurological examination (see Appendix B, p. 69, in this guide for CNS manifestations of HIV infection)
  - Focal deficits may indicate a space-occupying lesion.
  - Sensory changes may indicate peripheral neuropathy.
  - Ataxia or changes in gait may indicate myelopathy.
- Oxygen saturation of blood and, in patients with pneumonia, arterial blood gas
- Laboratory analyses
  - Complete blood count (CBC) with differential
  - Serum chemistries
  - VDRL, fluorescent treponemal antibody
  - Vitamin B_{12}, folate levels
  - CD4 count and viral load
  - Toxicology screen
- Brain imaging studies to rule out space-occupying lesion
- Comprehensive assessment to rule out infectious processes; consider lumbar puncture
- Neuropsychological testing (e.g., AIDS Dementia Rating Scale, Finger Tapping Test, Trail Making Test)

1. Assessment
c. Evaluation of Cognitive Symptoms

- A comprehensive psychiatric assessment, formulation of a differential diagnosis, and possible medical workup are required.
- Differentiate subcortical from cortical involvement: early cognitive changes differ from symptoms associated with cortical dementia; more commonly presents with psychomotor slowing, short-term memory dysfunction, or attention deficits rather than deficits in language or visual recognition.

(continued)

- Mini-Mental State Exam (MMSE) is not sensitive in picking up early HIV-associated cognitive-motor symptoms (see Table 14 of APA's *Practice Guideline for the Treatment of Patients With HIV/AIDS* for a list of sensitive screening examinations).
- Patient self-assessment is not reliable.
- Baseline screening examination should be done on every patient with HIV.
- Cognitive screening examinations should be readministered on a regular basis.
- Once cognitive dysfunction is identified, formal neuropsychological testing is helpful to fully document dysfunction and identify areas of relative strength when there is evidence of impairment.
- Once the symptoms are identified, the practitioner should collaborate with other clinicians regarding further medical care.

2. Treatment

Delirium

- Treat delirium per APA's *Practice Guideline for the Treatment of Patients With Delirium* (also see "Treating Delirium: A Quick Reference Guide"). Intervention should correct underlying causes (see Appendix D, p. 72, in this guide for a list of etiologies).

Dementia

- Use potent antiretroviral therapy to target the underlying HIV infection.
- Use psychotropic medication for comorbid conditions such as depression.
- Consider antipsychotic or stimulant agents for symptomatic management of HIV-associated dementia (e.g., agitation or fatigue).
- Consider psychotherapy for mild to moderate dementia to help patients understand, mourn, and adapt to this new impairment of functioning.

E. Management of Other Disorders

1. General Treatment Guidelines

Provide psychotherapy.
Psychotherapeutic management of patients with HIV infection should follow the same general principles used with other patients.

Provide pharmacotherapy.

For all HIV-infected patients:

- Follow principles similar to those for geriatric patients or patients with comorbid medical illnesses.
- Be aware that some medications for HIV can potently inhibit or induce the cytochrome P450 (CYP450) system (see Appendix E, p. 73, in this guide).
- Judiciously use psychotropics that share metabolic pathways.

Particularly for patients with symptomatic HIV disease:

- Use lower starting doses and slower titration.
- Provide the least complicated dosing schedules possible.
- Focus on drug side effect profiles to avoid unnecessary adverse effects (e.g., anticholinergic effects from tricyclic antidepressants, leukopenia from carbamazepine).
- Maintain awareness of drug metabolism/clearance pathways and possible end-organ effects to minimize drug-drug interactions.
- Collaborate with primary HIV provider to ensure that all medications prescribed are compatible.

2. Psychiatric Disorders

Mood disorders

- Management of mood disorders is similar to that for other mood disorders with medical comorbidity.
- Fatigue and insomnia may be symptomatic of the mood disorder, especially in medically asymptomatic patients.
- The overall medical status of the patient should be assessed to take into account possible effects of concurrent illness or side effects of medication.
- Choice (and dosage) of antidepressant or mood-stabilizing agent may be influenced by the antiretroviral regimen.

Substance use disorders

- Substance use disorders should be treated (e.g., with a drug rehabilitation program) to reduce risk behavior in order to prevent further infection of others.
- During treatment of opiate dependence with methadone or LAAM, doses may need to be increased or decreased in accordance with the use of specific antiretroviral agents.

Anxiety disorders

- Psychotherapeutic approaches to situational anxiety can help patients work through intense affects.
- Standard pharmacological treatments for anxiety disorders should be used with caution (e.g., many benzodiazepines should be used very cautiously when patients are taking protease inhibitors, particularly ritonavir, because benzodiazepine blood levels may be greatly elevated).

2. Psychiatric Disorders *(continued)*

Psychotic disorders

- Psychotic symptomatology may arise from opportunistic infections, mania, HIV-associated dementia, or delirium.
- Evaluation of new-onset psychosis requires a careful medical/neurological workup.
- Practitioners should beware of drug-drug interactions and overlapping toxicities (e.g., ritonavir may elevate levels of clozapine; clozapine and zidovudine both cause bone marrow suppression).
- Second-generation (atypical) antipsychotics are first-line treatments in late-stage HIV infection because of lower incidence of extrapyramidal side effects.
- Lower doses of second-generation antipsychotics tend to be sufficient.

Adjustment disorders

- Various forms of psychotherapy may be indicated to prevent progression to a more severe psychiatric disturbance.

Sleep disorders

- May be secondary to a psychiatric disorder such as depression.
- May be a manifestation of HIV infection in the brain.
- May be secondary to complications of HIV infection (e.g., pain); medical intervention may improve sleep.
- Efavirenz (an antiretroviral) is associated with a high incidence of vivid dreams and nightmares.

Disorders of infancy, childhood, and adolescence

- Psychiatric disorders are common among infected youth, with rates of about 30% for mood disorders and 25% for attention-deficit/hyperactivity disorder.
- Psychotherapy may be of particular help for adolescents who are struggling with emerging sexuality.
- Substance abuse in adolescents is frequent and likely to involve multiple drugs.
- Issues of risk behavior and autonomy have implications for HIV prevention, adherence to treatment, and effective coping with chronic illness.

3. HIV-Associated Syndromes With Psychiatric Implications

- Somatic symptoms at the interface of medical and psychiatric disorders include fatigue, weight loss, pain, and sexual dysfunction. Psychiatrists can integrate treatment approaches and promote interdisciplinary and interspecialty dialogue; they should avoid all-or-nothing, mind-or-body approaches.
- Wasting syndrome generally occurs in patients with more advanced HIV illness and can be related to a number of physiological disturbances such as progressive HIV disease, hypogonadism, and gastrointestinal malabsorption.
- Lipodystrophy and the metabolic syndrome (hypertriglyceridemia, hypercholesterolemia, and hyperglycemia) are common and appear to be associated with protease or nucleoside reverse transcriptase inhibitor treatment.
- Chronic fatigue is frequently associated with depressed mood and physical disability.
- Common painful symptoms include headaches, herpetic lesions, peripheral neuropathy, back pain, throat pain, arthralgias, and muscle and abdominal pain.
- Sexual dysfunction has been reported to occur in both men and women with HIV infection. In both men and women, hypogonadism can be treated with testosterone replacement with physiological dosing.

APPENDIX A. Interventions to Increase Patient Adherence to Antiretroviral Regimens

Prepare patients.

- Discuss use of medications before prescribing.
- Outline pros and cons of therapy.
- Acknowledge commitment required, consequences of nonadherence, and benefits of therapy.

Provide written instructions.

- Inform patients of expectations, including side effects.
- Provide information about whom patients should call if significant side effects occur.
- Schedule a follow-up appointment soon after initiating therapy.

Review importance of therapy.

- Inform patients that they must continue to take all medications.
- Review the effects of stopping one medication.
- Outline procedure for obtaining refills.

Recognize patient lifestyle and preferences.

- Twice-daily dosing benefits may outweigh initial side effects; ritonavir may be preferred.
- Consider whether patients prefer tolerability over convenience; nelfinavir or indinavir may be preferred.
- Discuss midday dosing.
- Recommend medication timers or calendar.
- Help patients plan for away-from-home dosing.
- Simplify regimens.
- If possible, prioritize or eliminate medications when patients are overwhelmed.

Look for and address nonadherence.

- Consider regimens that minimize cross-resistance.
- Use regimens that leave options for future effective antiretroviral therapy.
- Inquire about adherence.
- Inquire about medication-taking behavior at each visit.
- Anticipate relapses in adherence, even after long-term use of medication.

APPENDIX B. CNS Manifestations of HIV-1 Infection

Type of Manifestation	Condition
Acute HIV-1 infection	• Viral meningitis • Encephalitis • Ascending polyneuropathy
Opportunistic infections (late HIV-1 infection)	• Toxoplasma cerebritis • Cryptococcal meningitis • Progressive multifocal leukoencephalopathy • Neurosyphilis • *Mycobacterium tuberculosis* meningitis • Cytomegalovirus encephalitis • Herpes simplex encephalitis
Neoplastic disease (late HIV-1 infection)	• CNS lymphoma • Kaposi's sarcoma
Other manifestations	• HIV-associated cognitive dysfunctions (see section D.1.a, p. 60, in this guide)

APPENDIX C. Neuropsychiatric Side Effects of Selected Medications Used in HIV Disease

Drug	Target Illness	Side Effects
Acyclovir	Herpes encephalitis	• Visual hallucinations, depersonalization, tearfulness, confusion, hyperesthesia, hyperacusis, thought insertion, insomnia
Amphotericin B	Cryptococcosis	• Delirium, peripheral neuropathy, diplopia
Atazanavir	HIV	• Depression, headache
β-Lactam antibiotics	Infections	• Confusion, paranoia, hallucinations, mania, coma
Co-trimoxazole	*Pneumocystis carinii* pneumonia	• Depression, loss of appetite, insomnia, apathy
Cycloserine	Tuberculosis	• Psychosis, somnolence, depression, confusion, tremor, vertigo, paresis, seizures, dysarthria
Delavirdine	HIV	• Anxiety, depression, insomnia, headache
Didanosine	HIV	• Nervousness, anxiety, confusion, seizures, insomnia, peripheral neuropathy
Efavirenz	HIV	• Nightmares, depression, confusion
Fosamprenavir	HIV	• Headache, oral paresthesia, depression or other mood disorders
Foscarnet	Cytomegalovirus	• Paresthesias, seizures, headache, irritability, hallucinations, confusion
Interferon-α	Kaposi's sarcoma	• Depression, weakness, headache, myalgias, confusion
Isoniazid	Tuberculosis	• Depression, agitation, hallucinations, paranoia, impaired memory, anxiety
Lamivudine	HIV	• Insomnia, mania
Methotrexate	Lymphoma	• Encephalopathy (at high dose)
Pentamidine	*Pneumocystis carinii* pneumonia	• Confusion, anxiety, lability, hallucinations
Procarbazine	Lymphoma	• Mania, loss of appetite, insomnia, nightmares, confusion, malaise
Quinolones	Infection	• Psychosis, delirium, seizures, anxiety, insomnia, depression
Stavudine	HIV	• Headache, asthenia, malaise, confusion, depression, seizures, excitability, anxiety, mania, early morning awakening, insomnia
Sulfonamides	Infection	• Psychosis, delirium, confusion, depression, hallucinations

(continued)

APPENDIX C. Neuropsychiatric Side Effects of Selected Medications Used in HIV Disease *(continued)*

Drug	Target Illness	Side Effects
Thiabendazole	Strongyloidiasis	• Hallucinations, olfactory disturbance
Vinblastine	Kaposi's sarcoma	• Depression, loss of appetite, headache
Vincristine	Kaposi's sarcoma	• Hallucinations, headache, ataxia, sensory loss
Zalcitabine	HIV	• Headache, confusion, impaired concentration, somnolence, asthenia, depression, seizures, peripheral neuropathy
Zidovudine	HIV	• Headache, malaise, asthenia, insomnia, unusually vivid dreams, restlessness, severe agitation, mania, auditory hallucinations, confusion

Source. Adapted from Grant I, Atkinson JH Jr: "Neuropsychiatric Aspects of HIV Infection and AIDS," in *Kaplan and Sadock's Comprehensive Textbook of Psychiatry*. Edited by Sadock BJ, Sadock VA. Philadelphia, PA, Lippincott Williams & Wilkins, 1999, pp. 308–336.

APPENDIX D. Etiologies of Delirium in Patients With HIV/AIDS

Intracranial

- Seizures
- Infections
- Cryptococcal meningitis
- Encephalitis due to HIV, herpes, cytomegalovirus
- Progressive multifocal leukoencephalopathy
- Mass lesions
- Lymphoma
- Toxoplasmosis

Extracranial

- Medications and other drugs (not exhaustive)
  - Amphotericin B
  - Acyclovir
  - Ganciclovir
  - Ethambutol
  - Trimethoprim/sulfamethoxazole
  - Pentamidine
  - Foscarnet
  - Ketoconazole
  - Sedative-hypnotics
  - Cycloserine
  - Opiate analgesics
  - Isoniazid
  - Rifampin
  - Zidovudine or didanosine
  - Vincristine
  - Dapsone
- Drug or alcohol withdrawal
- Infection/sepsis
- Endocrine dysfunction/metabolic abnormality
  - Hypoglycemia due to pentamidine, protease inhibitors
  - Hypoxia due to pneumonia
- Nonendocrine organ dysfunction
  - Renal failure due to HIV nephropathy or medication toxicity
  - Liver failure due to comorbid hepatitis and medication toxicity
- Nutritional deficiencies
  - Wasting syndrome
  - Failure to replace trace elements or vitamins in total parenteral nutrition

Source. Adapted from Bialer PA, Wallack JJ, McDaniel JS: "Human Immunodeficiency Virus and AIDS," in *Psychiatric Care of the Medical Patient.* Edited by Stoudemire A, Fogel BS, Greenberg DB. New York, Oxford University Press, 2000, pp. 871–888.

APPENDIX E. Antiretroviral Medications and Cytochrome P450 Inhibition or Induction

	Predominant Effects on CYP450 Enzymes	
Class/Drug Name	**Inhibition**	**Induction**
Protease inhibitors[a]		
Amprenavir	3A4	[b]
Atazanavir	3A4	[b]
Fosamprenavir	3A4	[b]
Indinavir	3A4	[b]
Lopinavir[c]	3A4	[b]
Nelfinavir	3A4, 2C19, 2D6	[b]
Ritonavir[c]	3A4, 2C9, 2D6	[b]
Saquinavir	3A4	[b]
Tipranavir	3A4[d]	3A4[d]
Nonnucleoside reverse transcriptase inhibitors		
Delavirdine	3A4	[b]
Efavirenz	3A4	3A4, 2B6
Nevirapine	[b]	3A4, 2B6

(continued)

APPENDIX E. Antiretroviral Medications and Cytochrome P450 Inhibition or Induction *(continued)*

	Predominant Effects on CYP450 Enzymes	
Class/Drug Name	**Inhibition**	**Induction**
Nucleoside analogue reverse transcriptase inhibitors		
Abacavir	b	b
Didanosine (formerly dideoxyinosine [ddI])	b	b
Emtricitabine	b	b
Lamivudine (formerly 3TC)[c]	b	b
Stavudine (formerly d4T)	b	b
Tenofovir	b	b
Zalcitabine (formerly 2′3′-dideoxycytidine [ddC])	b	b
Zidovudine (formerly azidothymidine [AZT])[c]	b	b
Entry and fusion inhibitors		
Enfuvirtide	b	b

[a]Relative rank ordering of CYP3A4 inhibition for protease inhibitors is ritonavir >> indinavir, nelfinavir, amprenavir, atazanavir, fosamprenavir, tipranavir > saquinavir.
[b]No clinically significant effect.
[c]Abacavir-lamivudine-zidovudine, abacavir-lamivudine, lamivudine-zidovudine, lopinavir-ritonavir, and tenofovir-emtricitabine are available as combination preparations.
[d]In combination with ritonavir.