SECOND EDITION

Comprehensive Textbook of AIDS Psychiatry

A Paradigm for Integrated Care

EDITED BY

Mary Ann Cohen, Jack M. Gorman, Jeffrey M. Jacobson, Paul Volberding and Scott L. Letendre

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This book is dedicated to the courageous men, women, and children with HIV and to their families and loved ones. It is dedicated to the orphans left behind by AIDS and to the HIV advocates who continue to work to diminish stigma and improve care for persons with HIV throughout the world. It is also dedicated to the devoted teams of HIV clinicians and researchers who work tirelessly to provide care and support for persons with HIV. We thank our families and friends for their support.

M.A.C., J.M.G., J.M.J., P.V., S.L.L.

TABLE OF CONTENTS

FOREWORD

There have been tremendous strides in the prevention and treatment of HIV in the decade since the last edition was published. Most people living with HIV in resource rich countries are now living longer in better health. However, there remains great need for mental health and supportive services throughout the world. While there may be an overall sense that the stigma surrounding HIV has diminished, stigma continues to be a barrier to getting tested and engaged in HIV care. The stress and stigma associated with living with HIV may create feelings of hopelessness and despair. Also, individuals who are addicted to drugs or misusing prescription drugs and alcohol as well as persons with other underlying psychiatric disorders may not achieve the same benefits from the available HIV therapies, given the risk for suboptimal adherence to care and medication, or because of potential drug interactions between medically needed therapies to control multiple conditions. Dr. Cohen and colleagues have once again mastered the subject matter and offer us guidance on how to address the most challenging of issues confronting this delicate and at risk population. The authors have included new chapters in this edition, including a chapter on orphans, written by an AIDS orphan, a chapter on advocacy, written by HIV advocates, and new chapters on global aspects of HIV, women and HIV, stigma and gender-based violence, HIV vaccines, routine testing for HIV, and pre- and post-exposure prophylaxis. The authors provide useful and practical information on how to create integrated services to best identify, diagnose and offer appropriate medical and mental health care. Furthermore, the chapters are written to appeal to those who practice HIV primary care as well as those who are experts in neurology, psychology and psychiatry. HIV affects the person as a whole and its management cannot be delivered in silos. Cohen's textbook provides us with the insight and guidance to help us all communicate and understand the challenges and conditions that often create barriers to achieving wellness. Once again, I congratulate all for providing us with a wonderful resource.

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IN MEMORIAM

The editors and authors of our second edition acknowledge with gratitude the remarkable contributions of co-author Dr. Michael Kilby, internationally known and respected for his contributions to the care of persons with HIV and for his prodigious research and academic work in the field of infectious disease and HIV care.

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PART I

RELEVANCE AND IMPLICATIONS OF HIV PSYCHIATRY AS A PARADIGM FOR INTEGRATED CARE

1.

HIV PSYCHIATRY—A PARADIGM FOR INTEGRATED CARE

Mary Ann Cohen, Michael J. Mugavero, and Elise Hall

We shall assume that everyone is much more simply human than otherwise. . . . [M]an, . . . as long as he is entitled to the term human personality, will be very much more like every other instance of human personality than he is like anything else in the world. —H.S. Sullivan (1953)

Psychiatric factors take on new relevance and meaning in the fourth decade of the human immunodeficiency virus (HIV) pandemic. Persons with HIV are living longer and healthier lives as a result of medical care as well as advances in research and antiretroviral therapy (ART). Some of the medical advances and concomitant changes in society have catalyzed research and led to vast improvements in care. Many of these changes evolved as a result of the advocacy and activism of gay men and their clinicians from the outset of the epidemic. In some areas of the world advocates' voices have been heard and have led to diminution of HIV stigma and discrimination. However, HIV stigma, discrimination, and criminalization still exist throughout the world.

Much work is still needed, with a greater emphasis on sexual health (Satcher et al., 2015), harm reduction, and competent and compassionate care for persons with HIV and for persons with psychiatric disorders that may serve as vectors for HIV transmission (Cohen, 2016; Cohen et al., 2016). Much work is still needed to diminish stigma and discrimination against persons with psychiatric disorders (Corrigan, 2016), including substance use disorders (Beyrer and Strathdee, 2015; Choopanya et al., 2013). Despite advances in medical care and advocacy for persons with HIV, in the United States and throughout the world, some men, women, and children with HIV and acquired immune deficiency syndrome (AIDS) are unable to benefit from medical progress. Inadequate access to HIV care is multifactorial and multidimensional and includes economic, social, cultural, political, societal, and psychiatric obstacles. Psychiatric disorders and distress play a significant role in the exposure to and transmission of HIV (Blank et al., 2002; Cohen and Alfonso, 1994, 1998; Cohen et al., 2002, 2016). They are relevant to prevention, clinical care, and adherence throughout every aspect of illness, from the initial risk behavior to death. They result in considerable suffering from diagnosis to end-stage illness (Cohen and Alfonso, 2004). The prevalence of HIV in persons with untreated psychiatric illness may be 10 to 20 times that of the general population (Blank et al., 2002). Furthermore, many of the changes in the prevention and treatment of HIV have significant psychological implications.

This chapter presents a list of facts, changes, and advances in the prevention of HIV and in the care of persons with HIV that have salience to HIV psychiatry. These are of particular significance in substantiating the need for an integrated approach to the care of persons with HIV and AIDS. Integrated care can improve retention in care, decrease the incidence of missed clinic visits, and decrease morbidity and mortality in persons with HIV (Flickinger et al., 2013; Levison and Alegria, 2016; Michael et al., 2014; Mugavero et al., 2014). Stigma, discrimination, and fear, in conjunction with denial, omnipotence, and lack of awareness, complicate and perpetuate the HIV pandemic. The creation of a supportive, nurturing, nonjudgmental healthcare environment can help to diminish the stigma of HIV and mental illness and can provide comprehensive and compassionate care for persons with HIV. In this chapter we also review the history of HIV psychiatry, explore HIV psychiatry as paradox and paradigm, delineate HIV health care disparities, and address issues of adherence to treatment. We outline a biopsychosocial approach to sexual health and mental health, which, along with diminution of stigma, is essential to HIV prevention and HIV care. In this chapter and throughout this textbook, we make an effort to eliminate words that stigmatize and dehumanize both medical illness and medical care and present an evidence-based approach to the prevention of HIV transmission and the care of persons with HIV and AIDS.

HIV/AIDS—THE GREAT MAGNIFIER OF MALADIES—IS ENTIRELY PREVENTABLE

If lupus, multiple sclerosis, malaria, Lyme disease, and syphilis are the "great masqueraders" because many of their symptoms are similar to those of other illnesses, HIV/AIDS can be thought of as the "great magnifier of maladies"—of symptoms, illnesses, and aspects of healthcare. HIV magnifies disparities, stigma,

and discrimination in healthcare, and it leads to transmission of HIV, lack of access to diagnosis and care, and nonadherence to treatment (Cohen, 2016). As long as HIV is stigmatized, persons who have risk behaviors or suspect that they have HIV will fear discrimination or ostracism and may delay or avoid getting tested, being diagnosed, disclosing HIV to potential partners, or accessing care. Hence, there are extremely negative aspects of HIV as the great magnifier of maladies.

The negative aspects of HIV as magnifier are as follows:

- Health care disparities
- Stigma and discrimination
  - Ageism
  - Misogyny
  - Racism
  - Addictophobia
  - Homophobia
  - Mental illness stigma
  - AIDSism
- Avoidance of getting tested
- Avoidance of access to care
- Treatment refusal
- Nonadherence to care
- Many medical and psychiatric illnesses occur in persons with HIV
- HIV occurs with much higher frequency in persons with psychiatric illness
- Non-disclosure of HIV infection for fear of rejection or ostracism
- Criminalization of HIV, of risk behaviors, and of persons at potential risk

Ironically, as a consequence of the concerted efforts of advocacy and activism on the part of gay men with HIV and AIDS and by some of their clinicians, there are positive aspects of HIV as the great magnifier of maladies. The HIV pandemic and its advocates forced topics of sexuality, gender identity, and death to "come out of the closet," which led to the need for integration of medical and mental health care and contributed to the development and application of bioethical principles such as patient self-determination, advance directives, and care planning.

Positive aspects of HIV as magnifier are as follows:

- Need for a biopsychosociocultural approach to care in order to
  - Prevent transmission
  - Ensure comprehensive assessment and diagnosis
  - Access treatment
  - Improve and enhance doctor patient communication and care
  - Improve doctor and patient satisfaction
- Need for integration of mental health care into HIV medical care
- Need for compassionate empathic care
- Need for routine HIV testing as part of health care and prevention of HIV
- Involvement of every system and organ in the body, including the brain
- Need for the skills of every discipline and subspecialty
- Need for awareness of bioethical issues
- Entirely preventable through risk reduction, behavior change, and integrated medical and psychiatric care and antiretroviral medication

FACTS, CHANGES, AND ADVANCES IN HIV PREVENTION AND CARE

1. Worldwide, an estimated 36.7 million people are living with HIV, and 2.1 new infections occur each year (UNAIDS, 2016; World Health Organization [WHO], 2016a).
2. In the United States an estimated 1.2 million persons are living with HIV, including 156,300 (1 in 8 persons or 12.8%) who are unaware of their infection (Centers for Disease Control and Prevention [CDC], 2015), thus emphasizing that routine testing is critically important for HIV prevention and early intervention and treatment.
3. The estimated incidence of new HIV infections in the United States has remained stable over the last decade, at about 50,000 new HIV infections per year (CDC, 2015).
4. In the United States, fewer than 50% of persons diagnosed with HIV are engaged in care, and an estimated 30% of all persons living with HIV attain viral suppression (Bradley et al., 2014).
5. HIV continues to magnify healthcare disparities in the United States and throughout the world. The global pandemic is characterized by a compilation of distinct regional epidemics, with varying geographic impact across age groups, among men, women, men who have sex with men, and persons who inject drugs. There has been a new onset of HIV transmission throughout the United States in rural areas as well as in urban settings as a result of an increase in the epidemic of heroin use. Addressing the opioid epidemic would be a crucial aspect of preventing this new incidence of HIV. Beyrer and Strathdee (2015) have documented ways to address the recent outbreak of HIV in rural Indiana catalyzed by the heroin epidemic.
6. While there are now far fewer perinatal transmissions in areas of the world with access to perinatal care and

ART, there are many more problems for children with perinatally acquired HIV transitioning to adolescence and adulthood. These include the attendant problems of nonadherence and early demise or the issues surrounding pregnancy, labor, and delivery for newborn girls who were infected perinatally and are now emerging into womanhood and motherhood.

7. Severe multimorbid medical illnesses are prevalent in persons with access to appropriate HIV medical care; these include severe illnesses requiring complex treatments, such as hepatitis C, cancers related and unrelated to HIV, renal disease, diabetes mellitus, as well as cardiovascular illness, including coronary artery disease.
8. There is evidence that early intervention can prevent the central nervous system (CNS) from becoming an independent reservoir for HIV and ultimately prevent HIV-associated neurocognitive disorders, such as HIV-associated dementia. Starting treatment as soon as HIV is diagnosed can prevent the development of independent HIV reservoirs in the brain and thus protect against HIV-associated dementia.
9. At present, one of the leading causes of death for persons with HIV is hepatitis C virus (HCV)-related liver disease. Thus, the treatment of persons with HIV/HCV co-infection has become a major concern. This of course involves understanding how to motivate people with HIV infection to get tested for HCV and to accept treatment. Issues of depression and cognitive impairment are magnified by the affinity of both viruses for the brain. Adherence to two regimens is even harder than to one. The need for integrated medical and psychiatric care is intensified in co-infected individuals.
10. One of the most salient advances in the United States has been the recommendation for routine HIV screening of all adolescents, adults, and pregnant women. The recommendation is for routine HIV testing in medical settings available to everyone from age 13 to 64 and to all persons at substantial risk at even younger or older ages.
11. Biomedical advances in prevention include pre-exposure prophylaxis (PrEP) and post-exposure prophylaxis (PEP) in combination with other prevention measures. PrEP and PEP can prevent HIV transmission from an HIV-positive to an HIV-negative individual. In 2012, the U.S. Food and Drug Agency (FDA) approved the first drug treatment for PrEP. Occupational exposure is no longer the only indication for PEP, and PEP can be used for sexual exposures such as coerced sexual encounters, unprotected sexual encounters, or parenteral exposures such as intravenous drug injection with contaminated paraphernalia.
12. Treatment as prevention (TasP) is a proven approach to prevent new infections by suppression of viral load among persons living with HIV such that they become virtually "noninfectious." In contrast to primary prevention among persons who are HIV-uninfected, via condoms, microbicides, PrEP, and PEP, secondary prevention among persons living with HIV infection via TasP is a complementary approach. Widespread scale-up of ART allowing for population-level reductions in circulating HIV is largely responsible for the 35% reduction in annual new global HIV cases since 2000 (UNAIDS, 2015; WHO 2015).
13. Simple, rapid HIV testing is widely available around the world.
14. Aging with HIV has become more complex, and research is underway to explore aspects of successful aging with HIV.
15. The *Diagnostic and Statistical Manual for Mental Disorders*, 5th edition (DSM-5), in 2013, introduced alternative categorizations and definitions of diagnoses frequently used in HIV psychiatry. These alternative categorizations include the reclassification of neurocognitive disorders and bereavement.
16. The area of adherence research continues to advance, with new evidence regarding expanding adherence beyond ART to also include adherence to clinical care (Flickinger et al., 2013; Levison and Alegria, 2016; Michael et al., 2014; Mugavero et al., 2014).
17. AIDSism (Cohen, 1989), stigma, and discrimination (Blendon and Donelan, 1988; Crowley et al., 2015; Fullilove, 1989; Kelly et al., 1987; Mahajan et al., 2008), as well as criminalization of drugs of abuse, sex work, and behaviors that may unintentionally expose individuals to HIV all serve to complicate and perpetuate the HIV pandemic (Center for HIV Law and Policy, 2010; Lehman et al., 2014).
18. Following an unanticipated, unplanned, or forced unsafe sexual encounter, any person can be encouraged to take tenofovir and emtricitabine for PEP after unsafe sex. One of the authors (MAC) had a patient who was HIV negative and unable to access PEP after unsafe sex until 74 hours after his exposure to HIV and developed an acute antiretroviral syndrome within 10 days after exposure.
19. The syndemic of substance abuse (and other mental illness), violence, and AIDS (SAVA) (Eisenberg and Blank, 2014) complicates and perpetuates the HIV pandemic.
20. There is evidence that an integrated approach to care can improve adherence to medical treatment.

HIV AND PSYCHIATRIC ILLNESS

Understanding the interplay between HIV and psychiatric illness leads to improved insight into how integration of care allows persons with HIV and AIDS to better cope with their

illness, live their lives to the fullest extent, and minimize pain and suffering for them and their loved ones. The personal and societal costs to health, productivity, fitness, careers, partners, spouses, parents, and children take an enormous toll in suffering. Related to this is the suffering of the loved ones and orphans left behind by AIDS. The tragedy of preventable death in young and productive individuals is heightened by the multiplicity of infections, severity of illness, and the multisystem and multiorgan involvement of this devastating illness. The illness is complicated by the psychological reactions to and psychiatric manifestations of HIV infection. Psychiatric disorders can accelerate the spread of the virus by creating barriers to risk reduction, including risky sexual behaviors and sharing of needles in persons who inject drugs.

Some persons with HIV may have no psychiatric disorder, while others may have one or more of the psychiatric disorders described in the *DSM-5* (American Psychiatric Association, 2013). The diagnosis of psychiatric disorders is covered extensively in Chapters 11 and 12 and the most prevalent psychiatric disorders are explored in detail in Chapters 14 through 20 of this textbook. A brief overview here of the psychiatric disorders that have most relevance to transmission of HIV and adherence to care will serve to clarify the need for the integration of psychiatric and medical care for persons with HIV. The relevant diagnoses include addictive disorders, trauma-related disorders, depressive disorders, psychotic disorders, and neurocognitive disorders.

Substance-related and addictive disorders, including alcohol and other drug use, result in multidimensional obstacles to risk reduction and adherence to care. These include obvious barriers to prevention of transmission, such as sharing of drug paraphernalia, and more subtle barriers, such as the inability to adhere to perinatal ART because of intoxication, withdrawal, and drug-seeking behaviors. Furthermore, intoxication and disinhibition associated with alcohol and drug use and exchange of sex for drugs result in risky sexual behaviors and difficulty with adherence to complex medical regimens. Cognitive disorders associated with alcohol and other drugs can also impair judgment and ability to adhere to care. Active substance use may interfere with adherence to prevention strategies, to medical care, and to the care of children infected with or affected by the virus. Mortality trends indicate an increase in death from end-stage liver disease as a result of comorbid infection with HIV and HCV in persons who inject drugs.

A trauma-related disorder, posttraumatic stress disorder (PTSD), is highly prevalent in persons with HIV infection and increases morbidity risk (Boarts et al., 2006; Cohen et al., 2001; Samuels et al., 2011; Sikkema et al., 2007). It is often overlooked in persons with HIV/AIDS because it may be overshadowed by other psychiatric diagnoses (Samuels et al., 2011). The effect is bidirectional. For example, intimate partner violence or a history of childhood trauma or childhood sexual trauma are all risk factors for HIV infection as well as for PTSD. The severity of HIV-related PTSD symptoms is associated with a greater number of HIV-related physical symptoms, extensive history of pre-HIV trauma, decreased social support, increased perception of stigma, and negative life events. Moreover, PTSD is often multimorbid with other psychiatric and medical disorders, pain, and depressive symptoms. PTSD can lead to risky behaviors and decrease harm avoidance as a result of both dissociative phenomena and a sense of a foreshortened future. Persons with PTSD as a result of early childhood trauma may have difficulty protecting themselves from harm or may unconsciously seek to re-enact their early trauma in later life.

PTSD is associated with nonadherence to risk reduction and medical care (Boarts et al., 2006; Cohen et al., 2001). The diagnosis of PTSD is further complicated by repression or retrograde amnesia for traumatic events and difficulties in forming trusting relationships and disclosing trauma if it is recalled (Samuels et al., 2011). In persons with HIV infection, there is a high incidence of early childhood and other trauma with consequent PTSD, substance use disorders, and other psychiatric disorders (Cohen et al., 2001; Samuels et al., 2011). Violence may include perpetuation of early trauma in persons with PTSD who may unconsciously seek to master early childhood trauma in adult relationships. Synergistic epidemics, or syndemics, were first described by Singer (1994) and subsequently associated with nonadherence to HIV care and poorer outcomes (Boarts et al., 2006; Eisenberg and Blank, 2014). Syndemics of triple diagnoses include co-occurring substance use disorder, other psychiatric disorder, and HIV (Meyer et al., 2011). The association of nonadherence with the syndemic of substance abuse, violence, and AIDS (the SAVA syndemic) has been documented (Eisenberg and Blank, 2014; Sullivan et al., 2015).

Other psychiatric disorders such as psychotic disorders, depressive disorders, and neurocognitive disorders may be associated with HIV transmission and nonadherence to care. Risky behavior and nonadherence may result from poor judgment with regard to sexual partner choice, lack of attention to barrier contraception, and, at times hypersexuality, disinhibition, and having multiple sexual partners. When persons are psychotic, they may seek sexual contact or may become victims of sexual predators as a result of efforts to obtain love, affection, and attention or in attempting to relieve the anguish of psychosis. Depressive disorders can lead to apathy and a negative self-image that can lead to vulnerability, self-neglect, and unsafe sex practices. Mania, due either to bipolar disorder, HIV-related infections, or use of prescribed or illicit drugs, can result in hypersexuality, poor impulse control, and impaired judgment. A further complication is the occurrence of HIV-associated neurocognitive disorders (HAND), including HIV-associated dementia (HAD). Cognitive impairment can lead to poor judgment in sexual partner choice, unsafe sex, and disinhibition. Lastly, HIV infection and AIDS also are risk factors for suicide; the rate of suicide has been shown to be higher in persons with HIV.

The high prevalence of psychiatric conditions in persons with HIV infection has resulted in closer clinical collaboration among primary care physicians, infectious disease specialists, and psychiatrists. While there are psychiatric disorders linked directly and indirectly to risk behaviors, HIV infection, or AIDS, people with HIV may have no psychiatric disorder or they may have any disorder described in the *DSM-5*.

Alternatively, psychiatric disorders may be the first and, at times, the only manifestation of HIV infection. Early diagnosis of HIV can lead to the timely introduction of treatment with appropriate HIV medical care and ART and prevent the establishment of independent CNS reservoirs for HIV. The immediate introduction of ART within 72 hours after HIV exposure may entirely prevent HIV infection as well as the establishment of independent CNS reservoirs for HIV. Early neuropsychiatric disorders can be a reaction to awareness of a diagnosis of HIV infection. Alternatively, psychopathology can be related to intrinsic involvement of the brain with HIV or opportunistic infections such as toxoplasmosis or cryptococcosis in persons who lack access to care or are nonadherent to care. In addition, antiretroviral therapies, treatments for opportunistic infections, and treatment for multimorbid illnesses, such as with chemotherapy for cancer, can have CNS side effects, including psychiatric symptoms.

In addition to the role of psychiatric disorders in the transmission of HIV, psychiatric factors also play a major role in the suffering endured by patients, their partners, families, and caregivers. If psychiatric disorders go untreated, persons with HIV may have difficulty attending appointments and adhering to the complex medical treatments involved with care. Physicians and clinicians in every specialty may find themselves frustrated that patients are not adhering to appointments and are getting ill in the same ways they did in the beginning of the pandemic, when few or no treatments were available and mortality was high. Now that perinatal HIV transmission can be prevented by antiretroviral protocols, even obstetricians may find themselves stymied when pregnant women do not adhere to prenatal care and to antiretroviral treatment. There is an ample body of evidence that psychiatric treatment can decrease transmission, diminish suffering, improve adherence, and decrease morbidity and mortality.

Persons with HIV have a high prevalence of multimorbid complex and severe medical and psychiatric illnesses with psychosocial and public health implications and consequences. Despite remarkable advances in the care of persons with HIV that has transformed AIDS from a fatal infectious disease to a chronic manageable illness, the incidence of HIV in the United States has remained stable at about 50,000 new cases annually. Missed HIV clinic visits are independently associated with all-cause mortality in persons with HIV (Mugavero et al., 2014). Thus, communication, integration, and coordination of care are of special significance in order to improve adherence to risk reduction as well as medical care. Since HIV is associated with discrimination and stigma and also disproportionately affects vulnerable populations and magnifies health care disparities, providing compassionate, comprehensive, and coordinated care becomes even more significant.

THE HISTORY OF HIV/AIDS PSYCHIATRY

In 1981, previously healthy young men and women were being admitted with pneumonia and severe respiratory distress to the intensive care unit of our municipal academic medical center in New York City. They were dying of respiratory failure, and the reason for these deaths was not clear. At about the same time, Michael Gottlieb, an immunologist in an academic medical center in Los Angeles, California, began to investigate the reasons for the occurrence of *Pneumocystis carinii* pneumonia (PCP) in five previously healthy young men. On June 5, 1981, his report of these cases was published in the *Morbidity and Mortality Weekly Report* (CDC, 1981a). Gottlieb's first patients were also described as having cytomegalovirus and candida infections. As a result of the publication of this report, specialists in pulmonary medicine, internal medicine, and infectious disease in high-endemic area hospitals recognized that the young men and women were severely ill with this new disease and that, in addition to intensive medical treatment, some would benefit from psychiatric consultations to help them cope with this devastating illness.

In a more detailed article, published on December 10, 1981, in the *New England Journal of Medicine*, Gottlieb and colleagues (1981) linked an immune deficiency with this new cluster of infections. They presented evidence for an association of the illnesses PCP, candidiasis, and multiple viral infections and "a new acquired cellular immunodeficiency" with a decrease in CD4 T cells as a hallmark. Another article (Masur et al., 1981) described this "outbreak of community-acquired *Pneumocystis carinii* pneumonia" as a manifestation of an "immune deficiency." Over the next year, several other articles described the opportunistic infections and cancers that characterized this new syndrome of immune deficiency, including not only *Pneumocystis carinii* (subsequently designated as *Pneumocystis jeroveci*) pneumonia but also cytomegalovirus retinitis, CNS toxoplasmosis and lymphoma, progressive multifocal leukoencephalopathy, and disseminated Kaposi's sarcoma. Initially, the immune deficiency was thought to occur only in gay men (CDC, 1981b), but later in 1981 and in 1982 it became clear that this acquired immune deficiency syndrome, or AIDS, as it came to be called in 1982 (CDC, 1982a), was transmitted by exchange of blood or body fluids through sexual contact, including heterosexual contact (CDC, 1983), by sharing of needles or drug paraphernalia in intravenous drug use (CDC, 1982a), through transfusions of contaminated blood and blood products (CDC, 1982b), and through perinatal transmission (CDC, 1982c). When it became evident that this immune deficiency might itself have an infectious etiology and that it led to rapidly fatal complications, many staff members became fearful of the possibility of contagion. An "epidemic of fear" (Hunter, 1990) began to develop along with the AIDS epidemic. As a result, some persons with AIDS who were admitted to hospitals for medical care experienced difficulty getting their rooms cleaned, obtaining water or food, or even getting adequate medical attention.

At a municipal hospital in New York City in 1981, initial psychiatric consultations for persons with AIDS were requested for depression, withdrawal, confusion, and treatment refusal. One of the authors of this chapter (MAC) was the psychiatrist responding to these initial consultations. It was clear that the uncertainty about the etiology of the

immune deficiency had resulted in palpable fear of contagion in staff. This fear was leading to distress and an increase in frequency of absences and requests for transfers away from the floors with the most AIDS admissions. These reactions in staff members seemed to heighten the sense of isolation and depression in patients.

In the early years of the epidemic, Many persons with AIDS were treated as lepers. Some found that they were shunned and ostracized. In some areas of the world, persons with AIDS were quarantined because of the irrational fears, discrimination, and stigma associated with this pandemic. Persons with AIDS were subjected to the agony of being rejected by family, friends, and communities. Some persons with AIDS lost their homes, some lost their jobs, and some children and adolescents were excluded from classrooms. In the early 1980s, a diagnosis of AIDS led to rejection by shelters for the homeless and by nursing homes, long-term care facilities, and facilities for the terminally ill. The attitudes of families, houses of worship, prison guards, employers, teachers, hospital staff, and funeral directors led to catastrophic stigma and discrimination. Persons with AIDS had difficulty finding support, obtaining healthcare, keeping a job, finding a home, and finding a chronic-care facility or even a place to die.

Although the AIDS epidemic was first described in the medical literature in 1981, it was not until 1983 that the first articles were published about the psychosocial or psychiatric aspects of AIDS. The first article, written by Holtz and colleagues (1983), was essentially a plea for attention to the psychosocial aspects of AIDS. They stated that "noticeably absent in the flurry of publications about the current epidemic of acquired immune deficiency syndrome (AIDS) is reference to the psychosocial impact of this devastating new syndrome." The authors deplored ostracism of persons with AIDS by both their families and their medical systems of care, and were the first to describe the profound withdrawal from human contact as the "sheet sign" observed when persons with AIDS hid under their sheet and completely covered their faces. The first psychiatrist to address these issues was Stuart E. Nichols (1983). In his article in *Psychosomatics*, Nichols described the need for compassion, support, and understanding to address the fear, depression, and alienation experienced by patients. He also made recommendations for use of psychotherapy and group therapy as well as antidepressant medications to help persons with AIDS cope with intense feelings about this new illness that was still of undetermined etiology. Nichols stated: "Since AIDS apparently is a new disease, there is no specific psychiatric literature to which one can refer for guidance. One must be willing to attempt to provide competent and compassionate care in an area with more questions than answers." The earliest articles published in the first decade of AIDS psychiatry, from 1983 to 1993, were primarily descriptive observations, case reports, case series, and documentation of prevalence of psychiatric diagnoses associated with AIDS. They were written by sensitive and compassionate clinicians, some of whom openly expressed their outrage at ostracism and rejection of persons with HIV and AIDS by not only the community at large but also the medical community. These clinicians also emphasized the need for compassion and for competent medical and psychiatric care. These early articles are summarized in Table 1.1.

In the 33 years (1983–2016) since HIV/AIDS psychiatry references first appeared in the medical literature, there have been many thousands of articles written, in addition to four textbooks (Cohen and Gorman, 2008; Cohen et al., 2010; Fernandez and Ruiz, 2006; Joska et al., 2014), other books (Treisman and Angelino, 2004), and chapters. Most of the articles reflect a growing body of research in the area as well as an evidence base for the practice of HIV psychiatry. Some of these articles provide evidence for the need for a comprehensive integrated biopsychosocial approach to the care of persons with HIV and AIDS.

HIV PSYCHIATRY: PARADOX AND PARADIGM

PARADOX

The HIV pandemic presents us with many paradoxes. One of the most tragic paradoxes of HIV is the disparity in access to care resulting from racial, political, and economic factors throughout the world. Another tragic paradox is the disparity in access to care among persons with psychiatric illness. Age, intelligence, and level of education do not necessarily correlate with ability to adhere to risk reduction, safe sexual and drug use behaviors, and medical care (Cochran and Mays, 1990; De Buono et al., 1990; MacDonald et al., 1990; Reinisch and Beasley, 1990). At every age, from adolescents, who say "I can use a condom, I just don't" (Mustanski et al., 2006), to the elderly (Goodkin et al., 2003; Karpiak et al., 2006; Stoff, 2004), who may not feel a need for barrier contraception to prevent pregnancy and whose physicians may be uncomfortable discussing sexual health and activities, there are high rates of HIV infection.

Discrimination against persons with AIDS has been described as a new form of discrimination called "AIDSism" (Cohen, 1989). AIDSism results from a multiplicity of prejudicial and discriminatory factors. It is built on a foundation of racism, homophobia, ageism, misogyny, and discomfort with mental and medical illness, poverty, sexuality, infection, and fear of contagion and death in many communities throughout the world, as well as in the United States. Discrimination and stigma were recognized early in the HIV/AIDS psychiatry literature as contributing to psychological distress (Blendon and Donelan, 1988; Chesney and Smith, 1992; Cohen, 1989; Cohen et al., 2002; Cohen and Weisman, 1986; Deuchar, 1984; Fullilove, 1989; Holland and Tross, 1985; Holtz et al., 1983; Nichols, 1983, 1984) and have been explored subsequently following the introduction of efficacious ART (Brown et al., 2003; Crowley et al., 2015; Herek et al., 2002; Kaplan et al., 2005; Mahajan et al., 2008; Parker and Aggleton, 2003).

Early in the epidemic, many physicians surveyed had negative attitudes toward persons with HIV and AIDS (Kelly et al., 1987; Thompson, 1987; Wormser and Joline, 1989). Although the medical profession has made great strides against discrimination and stigma and most physicians are "accustomed to caring for HIV-infected patients with

Table 1.1. EARLY LITERATURE OF AIDS PSYCHIATRY*

YEAR	ISSUES ADDRESSED, COMMENTS
1983	Psychosocial impact of AIDS—ostracism, the "sheet sign," and the need for psychiatric literature about AIDS (Holtz et al.)
1983	Psychiatric aspects of AIDS—need for psychiatric consultations and for group therapy; first article by a psychiatrist about AIDS psychiatry (Nichols)
1984	Psychiatric implications of AIDS—the first book about AIDS psychiatry (Nichols and Ostrow)
1984	Psychosocial aspects of AIDS—the first description of the biopsychosocial approach applied in the general care setting by Cohen (Deuchar)
1984a	AIDS anxiety in the "worried well" (Forstein)
1984b	Psychosocial impact of AIDS (Forstein)
1984	Case reports and treatment recommendations for persons with AIDS seen in psychiatric consultation (Barbuto)
1984	Psychiatric complications of AIDS (Nurnberg et al.)
1984	Neuropsychiatric complications of AIDS (Hoffman)
1984	Cryptococcal meningitis presenting as mania in AIDS (Thienhaus and Khosla)
1984	Description of a support group for persons with AIDS (Nichols)
1984	Psychiatric problems in patients with AIDS at New York Hospital (Perry and Tross)
1985	Findings in 13 of 40 persons with AIDS seen in psychiatric consultation (Dilley et al.)
1985	Description of psychiatric and psychosocial aspects of AIDS (Holland and Tross)
1986	A biopsychosocial approach to AIDS (Cohen and Weisman)
1986	Neuropsychiatric aspects of AIDS (Price and Forejt)
1987	Psychiatric aspects of AIDS (Faulstich)
1987	Dementia as the presenting or sole manifestation of HIV infection (Navia and Price)
1987	Psychiatric aspects of AIDS: a biopsychosocial approach—comprehensive chapter (Cohen)
1987	Stigmatization of AIDS patients by physicians (Kelly et al.)
1988	Discrimination against people with AIDS (Blendon and Donelan)
1988	First article on high prevalence of suicide among persons with AIDS (Marzuk et al.)
1989	AIDSism, a new form of discrimination (Cohen)
1989	Anxiety and stigmatizing aspects of HIV infection (Fullilove)
1990	Firesetting and HIV-associated dementia (Cohen et al.)
1990	Suicidality and HIV testing (Perry et al.)
1992	A biopsychosocial approach to the HIV epidemic (Cohen)
1992	Suicidality and HIV status (McKegney and O'Dowd)
1993	Manic syndrome early and late in the course of HIV (Lyketsos et al.)

*Listed here are descriptions of psychosocial and psychiatric aspects of AIDS with emphasis on discrimination. This table contains a sample of articles, chapters, and books published in the first decade of AIDS psychiatry (1983–1993).

concern and compassion" (Gottlieb, 2001), society as a whole has not kept up. In June 2006, a full quarter-century since the epidemic was first described, a child with AIDS was excluded from attending a New York sleep-away camp until his parents threatened legal action. In April 2012, a plastic surgeon refused to remove a facial lesion from a woman with HIV, citing his fear of infection. In May 2014, an allergist refused to test or treat a man with HIV. AIDS stigma and AIDSism have implications not only for the health and well-being of individuals who experience them but also for public health.

Stigma and AIDSism present a barrier to getting tested for HIV, obtaining test results, disclosing serostatus to intimate partners, obtaining optimal medical care in a timely manner, and engaging in safer sex practices and safer injection drug use. Despite availability of HIV prevention by means of barrier contraception as well as PrEP and PEP, many persons continue to engage in risky sexual behaviors.

Despite availability of competent medical care and ART, the majority of persons in treatment for HIV do not attain viral suppression; in the United States, only 30% of persons living with HIV have attained viral suppression, given those not diagnosed and those not engaged in care. While throughout the world the incidence of HIV has dropped dramatically, attributable to the scale-up of ART since 2000, in the United States the rate of new infections has remained relatively stable, at about 50,000 per year.

The process of care for persons with AIDS at the end of life is also paradoxical, in that there is a clear need for provision of care along a continuum that includes both palliative and curative care. This concept has been proposed but appears hard to implement. The need to overcome the "false dichotomy of curative vs. palliative care for late-stage AIDS" has been suggested (Selwyn and Forstein, 2003). From risk behavior to exposure, from infection to course of illness, and from progression of illness to end of life, we need to recognize, clarify, and make the changes necessary to close the gaps in care and address the treatment cascade, to maintain viral suppression and improve the lives of persons living with HIV and AIDS.

PARADIGM

Psychosomatic medicine psychiatrists who specialize in HIV psychiatry, as well as general psychiatrists and other mental health clinicians, are in a unique position to work with primary HIV clinicians, infectious disease specialists, cardiologists, neurologists, surgeons, and other physicians and health professionals to combat HIV stigma and AIDSism. For psychiatrists who subspecialize in psychosomatic medicine, AIDS and other manifestations of HIV infection may be thought of as a paradigm of a medical illness. AIDS is an illness similar to the other complex and severe medical illnesses that define the subspecialty. Psychosomatic medicine (formerly consultation-liaison psychiatry), the psychiatric care of persons with complex and severe medical illness, was designated a subspecialty of psychiatry in 2003. AIDS is a paradigm of psychosomatic medicine because it has elements of nearly every illness described in the *American Psychiatric Publishing Textbook of Psychosomatic Medicine* (Levenson, 2011). Persons with HIV and AIDS are also vulnerable to other multimorbid complex and severe medical illnesses, including those related and unrelated to HIV infection. The concept of AIDS as a paradigm of the psychiatric care of persons with medical illness (psychosomatic medicine) is illustrated in Figure 1.1.

Lipowski (1967) provided a classification of commonly encountered problems in psychosomatic medicine. Querques and Stern (2004) suggested a modification of Lipowski's original classification. With minor modifications, Lipowski's

Figure 1.1 HIV/AIDS psychiatry: a paradigm of psychosomatic medicine. CMV, cytomegalovirus; GI, gastrointestinal; PCP, phencyclidine; PEP, post-exposure prophylaxis; PML, progressive multifocal leukoencephalopathy; PrEP, pre-exposure prophylaxis; PTSD, posttraumatic stress disorder; STDs, sexually transmitted diseases; TB, tuberculosis.

classification remains relevant to HIV/AIDS psychiatric care. The five commonly encountered problems in HIV psychiatry include psychiatric presentation of medical illness, psychiatric complications of medical illnesses or treatments, psychological response to medical illness or treatments, medical presentation of psychiatric illness or treatments, and comorbid medical and psychiatric illness. These are illustrated in the following vignettes.

ILLUSTRATIVE CASE VIGNETTES

Case Vignette 1.1: Inpatient Medical Unit Psychiatric Consultation: Psychiatric Presentation of Medical Illness

Ms. A is a 62-year-old retired librarian, single and living alone, admitted with fever, abnormal chest x-ray, and late-stage AIDS (diagnosed only 1 month earlier), who was referred for psychiatric consultation during her second admission when she reported new-onset visual hallucinations. One month earlier, Ms. A had been admitted for evaluation of pain on swallowing (odynophagia), weakness, wasting, and weight loss. She was found to have esophageal candidiasis, a CD4 of 2, and a viral load of >750,000. Ms. A was treated for candida and started on antiretrovirals shortly after her discharge. On her second admission she reported seeing frightening faces. Her fever and abnormal chest x-ray were due to *Mycobacterium avium* pneumonia.

Ms. A had a psychiatric presentation of a medical illness, visual hallucinations due to cytomegalovirus retinitis, and encephalitis. Her visual hallucinations resolved when she was treated with gancyclovir.

Case Vignette 1.2: Outpatient HIV Clinic Psychiatric Consultation: Psychiatric Complication of Medical Illness or Treatment

Ms. B is a 52-year-old unemployed former administrative assistant with HIV and a CD4 of 317. She also had ulcerative colitis, osteoarthritis, and hypertension. She presented with depression and suicidal ideation after being started on efavirenz, a non-nucleoside reverse transcriptase inhibitor. Ms. B was found to have PTSD due to early childhood trauma, and major depressive disorder, recurrent. She responded well to psychotherapy, antidepressants, and discontinuation of efavirenz as well as her other antiretroviral medications. She has been adherent to psychiatric and medical care and understands that she may need to resume ART.

Ms. B had a psychiatric complication of her medical treatment, developing neuropsychiatric side effects secondary to efavirenz, with an improvement of symptomatology when efavirenz was discontinued and depression and PTSD were treated.

Case Vignette 1.3: Outpatient HIV Clinic Psychiatric Consultation: Psychological Response to Medical Illness

Ms. C is a 31-year-old unemployed teacher's assistant with HIV and a CD4 of 1,024 who presented with depression and anxiety. Ms. C felt isolated and alone because she was unable to disclose her diagnosis. She withdrew from friends, did not tell family members, and feared being seen attending the HIV clinic. Ms. C felt that she would never again be able to date anyone because she feared rejection if she disclosed her HIV serostatus. In psychotherapy, she was able to work through her fears of rejection and to some extent was able to come to terms with the embarrassment about her diagnosis in psychotherapy. Ms. C returned to work and responded to suggestions to join an HIV-positive social group.

Ms. C had a psychological response to medical illness related to the stigma of HIV infection.

Case Vignette 1.4: Inpatient General Care Psychiatric Consultation: Medical Presentation of Psychiatric Illness

Mr. D is a 29-year-old unemployed actor and former Walt Disney World Donald Duck character who was admitted to medicine unit of a general hospital with weight loss, cough, night sweats, and fever and gave a history of PCP and AIDS. A psychiatric consultation was requested when his history of PCP and AIDS could not be verified and he refused HIV testing. He was living in New York City–supported housing for persons with AIDS and had fabricated his history to pursue his acting career in New York and obtain both housing and entitlements.

Mr. D was malingering with AIDS in order to obtain entitlements and housing to further his acting career by establishing a home and support in New York City (Cohen, 1992).

Case Vignette 1.5: Outpatient HIV Clinic Psychiatric Consultation: Multimorbid Medical and Psychiatric Illness

Mr. E is a 58-year-old disabled lawyer with chronic obstructive pulmonary disease (oxygen-dependent), rheumatic heart disease, HCV, and HIV (CD4 count of 1,384 and undetectable viral load) who was referred for depression with suicidal ideation since his diagnosis of HIV infection. Mr. E was found to have major depressive disorder, recurrent, and a history of opioid dependence in full, sustained remission on agonist therapy for 30 years. He responded well to long-term psychodynamic psychotherapy and antidepressants but became intermittently depressed and suicidal until specific goals were established and family members were involved in his care.

Mr. E had multimorbid medical and psychiatric illness that responded to psychiatric care including psychodynamic and meaning-centered psychotherapy, family therapy, and antidepressants.

THE MULTIPLE DISPARITIES OF HIV AND AIDS

RACIAL, ETHNIC, AND SOCIOECONOMIC DISPARITIES

Racial, ethnic, and socioeconomic disparities have been observed and documented in all aspects of the United States healthcare system (Agency for Healthcare Research

and Quality, 2005a). The overall HIV death rate of African Americans was found to be 10.95 times higher than that of whites (Agency for Healthcare Research and Quality, 2005b), and racial disparities have been shown to contribute to increased HIV incidence and inadequate access to medical and psychiatric care (CDC, 2006a). U.S. correctional facilities and urban drug epicenters may be seen as microcosms of discrimination. Correctional facilities may also be instrumental in perpetuating the HIV epidemic both inside and outside of prison walls (Blankenship et al., 2005; CDC, 2006b; Fullilove, 2011; Golembeski and Fullilove, 2005; Hammett et al., 2002).

It would be difficult to calculate the true impact of these disparities on persons with HIV. In addition to the incalculable distress, suffering, and anguish (Cohen et al., 2002), persons with HIV/AIDS have multimorbid medical and psychiatric illnesses, all of which are also found among those who experience disparities in care (Cohen, 1996; Cohen et al., 1991; Kolb et al., 2006).

PSYCHIATRIC DISPARITIES

Psychiatric factors take on new relevance and meaning as we near the end of the fourth decade of the HIV pandemic. In a multisite study (n = 1,061), Blank and colleagues (2014) sought to highlight the HIV prevalence and associated risk factors among persons receiving care in various psychiatric treatment settings. After administering rapid HIV testing to this patient population, their results showed that the rate of HIV infection was four times the base rate for the general public in Baltimore and Philadelphia. Although the majority of patients (76%) were already aware of their HIV diagnosis, the new diagnoses discovered through screening patients in a mental health setting likely reflect a failure in the public and mental health care system. This study showed that patients with more severe symptoms of mental illness were at higher risk for being HIV-infected, and also that issues such as homelessness were linked to a higher prevalence of HIV.

Risk factors for infection in patients with severe mental illness are similar to risk factors in the general population (Blank et al., 2014). Untreated psychiatric disorders can be exacerbated by HIV stigma to make persons with HIV and AIDS especially vulnerable to suicide (Alfonso and Cohen, 1997; Marzuk et al., 1988; McKegney and O'Dowd, 1992; Perry et al., 1990). Psychiatric treatment with individual (Cohen, 1987; Cohen and Alfonso, 1998, 2004; Cohen and Weisman, 1986), group (Alfonso and Cohen, 1997), and family therapy can alleviate suffering, improve adherence (Gwadz et al., 2015; Pyne et al., 2011), and prevent suicide.

ISSUES OF PREVENTION AND ADHERENCE

Since the development of effective ART, the life expectancy of persons with HIV has increased, and for persons with access and adherence to care, the incidence of the opportunistic infections and cancers previously associated with AIDS has decreased (Huang et al., 2006). However, persons with untreated psychiatric disorders may lack access to care because severe mental illness is associated with nonadherence to care. Persons with severe mental illness may have difficulty getting to medical appointments, taking medications regularly, or obtaining laboratory tests and follow-up care. As a result, persons with HIV and untreated psychiatric disorders may present with AIDS-related illnesses not usually encountered in countries with access to care since the introduction of effective ART in 1996.

Harm reduction is an innovative and significant approach to care that has become an increasingly popular treatment paradigm to target patient populations at risk for HIV infection. Harm reduction is rooted in the goal of decreasing harm to the individual and self without requiring abstinence from the unwanted behavior. Although this multidisciplinary approach originated in prevention of addiction, the harm reduction model has been applied to various high-risk or unwanted behaviors over time. The harm reduction approach to HIV care gained momentum in the early to mid-1980s in response to the crisis of HIV and AIDS, the main focus being on decreasing transmission that occurred through intravenous drug use. When considering sexual transmission, the number one factor in sexual risk reduction is the knowledge of HIV status (Marlatt et al., 2012). Worldwide, 54% of persons with HIV (19 million of the 36.7 million persons with HIV) are unaware of their serostatus (UNAIDS, 2016). Therefore, harm reduction programs that encourage behavioral changes to reduce risk of sexual transmission are crucial, particularly when a large proportion of the population may not be aware of their HIV status. Behavioral change achieved over the past 10 years accounts for a very significant increase in awareness worldwide, with the number of persons HIV unaware of their serostatus decreasing from 90% (Kamya et al., 2007) to 54% (UNAIDS, 2014).

Prevention strategies that have shown promise include those that target specific sexual acts (e.g., decreasing sex acts that involve an exchange of bodily fluids), address sexual partner concerns (e.g., negotiating condom use or decreasing number of overall partners), and address intrapersonal and situational antecedents of risky sexual behaviors (e.g., intimate partner violence) (Marlatt et al., 2012). Although some critics state that harm reduction enables high-risk behavior, research has shown that harm reduction programs do not undermine treatment efforts or exacerbate high-risk behavior such as drug use. In fact, the World Health Organization (WHO) and the United Nations (UNAIDS) support harm reduction as best practice and crucial for decreasing HIV infection, particularly for persons who inject drugs (WHO, UNODC, UNAIDS, 2013). The use of PrEP and PEP represent a very important harm reduction approach when used in conjunction with counseling and barrier contraception.

BIOMEDICAL PREVENTION WITH PRE- AND POST-EXPOSURE PROPHYLAXIS

Strategies have been developed for communication to best address prevention of HIV transmission, improvement of

adherence to risk reduction and medical care, addressing healthcare disparities, and amelioration of stigma. These strategies include the National HIV/AIDS Strategy: Updated to 2020 (White House Office of National AIDS Policy, 2015), the 2015 Blueprint to Eliminate AIDS in New York State (New York State Department of Health, 2015), and the World Health Organization Guidelines (WHO, 2016b). Key prevention strategies for all patients are presented in Table 1.2.

Persons who are thought to be the most substantially vulnerable to HIV infection include HIV-negative members of serodiscordant couples and HIV-negative persons who inject drugs. An HIV-negative member of a serodiscordant couple may take PrEP to prevent infection. PrEP and PEP with antiretroviral medications such as tenofovir together with emtricitabine in combination with safe sex, barrier contraception, and safe injecting drug practices can prevent HIV transmission in serodiscordant couples. The evidence for the effective use of PrEP and PEP in serodiscordant couples is strong (Beaten et al., 2012; Cohen et al., 2011; Grant et al., 2010; White House Office of National AIDS Strategy, 2015; Thigpen et al., 2012).

PrEP may also be an effective measure in persons with HIV who inject drugs. In 2014 and 2015, both the Centers for Disease Control and Prevention and WHO included persons who inject drugs in their endorsement of PrEP as an HIV prevention method. Much of the evidence for the efficacy of PrEP in injecting drug users was derived from the Bangkok Tenofovir Study, which showed a 48.9% reduction in HIV infections (Choopanya et al., 2013). Ongoing PrEP demonstration projects have included persons who inject drugs in their participant pool, but data concerning overall awareness, uptake, and engagement in persons who inject drugs are limited. A summary of recommendations for prevention and pre- and post-exposure prophylaxis is provided in Table 1.3. With adequate support, empowerment, and education, people are more likely to make more positive health choices. See Chapter 31 for a more detailed discussion of PrEP and PEP.

Table 1.2. KEY HIV PREVENTION STRATEGIES FOR ALL PSYCHIATRIC PATIENTS

- **Routine HIV testing is now recommended for all persons from 13 to 64 years of age and for persons of any age with risk behaviors (CDC, 2015)**
- **Consider encouraging and offering routine HIV testing as part of initial comprehensive psychiatric assessment (Smith et al., 2014)**
- **Provide education for HIV prevention and make condoms available in psychiatric inpatient and outpatient facilities**
- **Assess for risk behaviors and encourage barrier contraception, treatment for substance use disorders, and safe injecting drug use**
- **Prevention or diminution of HIV risk behaviors can prevent transmission**
- **Treatment of substance use and other psychiatric disorders can prevent HIV transmission**
- **Early treatment with antiretrovirals, within the first 72 hours after exposure to HIV, can prevent both HIV infection and development of independent reservoirs for HIV in the brain (Heaton et al., 2011)**
- **Initiation of antiretroviral therapy in early asymptomatic HIV infection, regardless of CD4 count, improves outcomes and can prevent development of independent CNS reservoirs for HIV (CDC, 2016; Heaton et al., 2011)**

Table 1.3 SUMMARY OF RECOMMENDATIONS FOR PREVENTION AND PRE- AND POST-EXPOSURE PROPHYLAXIS

- **Persons with risk behaviors for sexual transmission can be encouraged to take PrEP alone or in combination with barrier contraception.**
- **Persons with HIV who inject drugs can take PrEP in combination with barrier contraception and safe injecting practices**
- **Following an unanticipated, unplanned or forced unsafe sexual encounter, any person can be encouraged to take tenofovir and emtricitabine for PEP after unsafe sex (Smith et al., 2014)**
- **PEP is no longer for occupational exposure to HIV only**

PEP, post-exposure prophylaxis; PrEP, pre-exposure prophylaxis.

In addition, among persons who are adherent to care, there has been an increase in the prevalence of endocrine, pulmonary, cardiac, gastrointestinal, renal, and metabolic disorders, some of which may be multimorbid and unrelated to HIV, while others may be related to HIV or to its treatments. Persons with HIV who are adherent to care and are virally suppressed are living longer, and aging accounts, in part, for the high prevalence of medical multimorbidities. The life expectancy of persons with HIV who have access to care and are treated with ART is similar to that of the general population (Manfredi, 2004a, 2004b).

Morbidity and mortality due to non-AIDS-related events has surpassed that due to AIDS-related events among HIV-infected persons in developed countries (Marin et al., 2009; May et al., 2014; Samji et al., 2013). The majority of non-AIDS-defining deaths are due to liver disease, non-AIDS-defining malignancies, cardiovascular disease, and non-AIDS defining infections (Antiretroviral Therapy Cohort Collaboration, 2010; Data Collection on Adverse Events of Anti-HIV Drugs [D:A:D] Study Group, 2010; Marin et al., 2009; Neuhaus et al., 2010; Samji et al., 2013). Other non-AIDS-related causes of death include renal disease, respiratory disease, suicide, homicide, drug overdose, and accidents. A number of non-AIDS-related multimorbidities are more common among HIV-infected persons and occur at a younger age than in the general population, including cardiovascular disease, diabetes mellitus, renal disease, and bone fractures, and multimorbidity is more common (Guaraldi et al., 2011).

Sackoff and colleagues (2006) and Aberg (2006) have recommended a paradigm shift in the care of persons with AIDS from a primary focus on HIV prevention and care to a more comprehensive approach to medical and mental health. The complexity and severity of the multiple medical and psychiatric illnesses prevalent in persons with HIV and AIDS are important in the psychiatric assessment and substantiate the need for a comprehensive and compassionate biopsychosocial approach that takes into account the full range of medical,

psychiatric, social, and cultural factors and their synergistic implications relevant to patient care (Cohen, 1987, 1992; Cohen et al., 2010; Cohen and Gorman, 2008; Cohen and Weisman, 1986, 1988; Deuchar, 1984).

AN INTEGRATED BIOPSYCHOSOCIAL APPROACH TO HIV AND AIDS

In the summer of 1981, one of the authors of this chapter (MAC) began to respond to her first psychiatric consultations requested for persons with AIDS. She described finding her AIDS patients' rooms inadequately cleaned, often with very sticky floors that made her shoes stick to them when entering (Cohen, 2008; Cohen and Gorman, 2008). Many patients were young, severely cachectic, and withdrawn, and some had their sheets drawn over their heads.

The "sticky-floor syndrome" joined the "sheet sign" as one of the early unique responses to the AIDS pandemic, with frequent spills as a result. It was clear that only a hospital-wide, multidisciplinary program and education for every level of staff on all shifts would improve the care of persons with AIDS, diminish stigma and discrimination, and help to alleviate fear, anxiety, and stigma in caregivers. In 1983, the infectious disease director, a social worker, and Dr. Mary Ann Cohen developed a multidisciplinary AIDS program at the hospital to provide coordinated, integrated, and comprehensive care for persons with AIDS and to provide education for hospital staff as well as medical students and their faculty. This program was the first of its kind to be described in the literature as a response to the epidemic (Cohen and Weisman, 1986; Deuchar, 1984). Deuchar, a British medical student on an elective in HIV psychiatry on the consultation-liaison psychiatry service in 1983, wrote an article about the psychosocial aspects of AIDS in New York City. He described this multidisciplinary program as a means of providing coordination of care and communication among the multiple subspecialties and disciplines involved in the care of persons with AIDS (Deuchar, 1984). He characterized the program as a "comprehensive program" with a "bio-psycho-social approach" that "maintains a view that each individual is a member of a family and community and deserves a coordinated approach to medical care and treatment with dignity." He wrote: "The programme includes maintenance of a multidisciplinary treatment team, provision of ongoing psychological support for patients and families, and education and support for hospital staff. As such, it is clearly a good example of consultation-liaison psychiatry." Since Deucher's description, an integrated biopsychosocial approach to the care of persons with HIV and AIDS has proved to improve treatment entry, engagement, retention, and adherence (Gwadz et al., 2015; Pyne et al. 2011; Thompson et al., 2012) and decrease morbidity and mortality (Mugavero et al., 2014).

Psychiatrists make ideal HIV educators. General psychiatrists who work in the areas of inpatient and outpatient psychiatry settings, private offices, addiction psychiatry, geriatric psychiatry, child and adolescent psychiatry, correctional facilities, and long-term care facilities are all in a prime position to provide education, help prevent transmission of HIV, suggest or provide condoms and information about safe sex, and suggest or offer HIV testing to lead toward early diagnosis and treatment. Psychiatrists take detailed sexual and drug histories and work with patients to help them change behaviors. The significance of taking a detailed sexual history was especially evident in a population-based study of men in New York City. This study revealed discordance between sexual behavior and self-reported sexual identity; nearly 10% of straight-identified men reported at least one sexual encounter with another man in the previous year (Pathela et al., 2006). Most psychiatrists form long-term, ongoing relationships with their patients and work with patients toward achieving gratification in long-term, intimate-partner relationships. All of these characteristics can be of major importance in primary prevention as well as early diagnosis and treatment of HIV infection.

There are some overlapping skill sets that mental health professionals and other HIV clinicians share, and there are therapeutic modalities that integrated psychiatrists can both utilize and teach to other clinicians in HIV clinics. Motivational interviewing (MI) was developed in the early 1980s as a counseling strategy to promote behavioral change in patients abusing alcohol or substances. It is a patient-centered approach with the goal of promoting intrinsic motivation for change and exploring ambivalence. While an estimated 50–70% of HIV patients take their antiretroviral medications as prescribed (Krummenacher et al., 2011), MI has been explored as a possible tool to further increase adherence as well as decrease high-risk HIV behaviors. HIV care professionals have been found to unknowingly utilize MI skills more often than not when counseling patients with high-risk behaviors for HIV transmission (Flickinger et al., 2013). Therefore, it is a reasonable and promising intervention for psychiatrists and other HIV clinicians to consider using that has shown efficacy in reducing risky sex and substance-using behaviors (Parsons et al., 2013), but it requires further study in its utility as a strategy to increase antiretroviral medication adherence (Hill and Kavookjian, 2012).

Psychosomatic medicine psychiatrists and HIV psychiatrists are in a unique position to provide psychiatric care for persons with HIV, from the time of infection to the time of death and its aftermath, with provision of support for partners and families. Most HIV psychiatrists rarely have the chance to take care of their patients until they are they are diagnosed with HIV. However, Ruiz (2000) provided a detailed description of his care of a patient that begins prior to the diagnosis of HIV and continues throughout the course of illness and progression to end-stage AIDS and the end of his life. In his article, Ruiz also described his attendance at the memorial service and his support of the patient's family during their time of loss and grief. HIV psychiatrists can provide colocated psychiatric services, education and support for trainees, and support and leadership for the multidisciplinary teams of physicians, nurses, social workers, other health professionals, and staff. It is especially gratifying to work as part of a dedicated and compassionate team of clinicians who are providing comprehensive care for persons with HIV and AIDS. There is growing evidence

that integrating HIV and mental health services leads to fewer emotional and psychological difficulties, a decrease in alcohol and substance use, and an increased likelihood of receiving antiretrovirals and adequate psychotropics, when needed (Whetten et al., 2006; Winiarski et al., 2005). When persons with HIV have delayed, declined, or discontinued ART, behavioral interventions can improve medical outcomes (Gwadz et al., 2015) and decrease morbidity and mortality (Mugavero et al., 2014). Furthermore, advances such as rapid HIV testing hold great promise for integrating routine HIV testing into mental health services in a variety of different clinical settings (Blank et al., 2014).

CONCLUSIONS

Comprehensive, coordinated care by a multidisciplinary team including HIV psychiatrists can provide an integrated approach that is supportive to patients, families, and clinicians. Integrated care can lead to full viral suppression and diminishes both suffering and discrimination (Crowley et al., 2015; Gwadz et al., 2015; Mugavero et al., 2014; Pyne et al., 2011; Thompson et al., 2012). Integrated care has public health implications and diminishes HIV transmission (Satcher et al., 2015). Psychiatric interventions are valuable in every phase of infection, from identification of risk behaviors to anticipation about HIV testing; from exposure and initial infection to confirmation with a positive HIV antibody test; from entry into systems of care engagement and retention in care and adherence to an antiretroviral regimen; from being healthy and seropositive to the onset of first HIV-related or unrelated illness; from severe illness to late stage and death. AIDSism, stigma, discrimination, criminalization, and fear, in conjunction with denial and lack of awareness, complicate and perpetuate the HIV pandemic. The creation of supportive, nurturing, nonjudgmental, integrated healthcare environments can help combat AIDSism and provide comprehensive and compassionate care (Cohen, 1996). HIV psychiatrists and other mental health professionals need to be integrated closely into clinical, academic, and research aspects of HIV prevention and treatment. In order for persons with HIV to live more comfortable lives, with preservation of independence and dignity, it is important to establish special nurturing, supportive, and loving healthcare environments. Such environments can enable persons with HIV, their loved ones, and caregivers to meet the challenges of HIV with optimism and dignity (Cohen and Alfonso, 2004). Such environments may also result in the concept of HIV/AIDS as the "great magnifier of maladies" receding into history.

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2.

HIV/AIDS IN THE FOURTH DECADE

ORIGINS, EPIDEMIOLOGY, CLINICAL MANIFESTATIONS, AND TREATMENT

*Michael J. Mugavero and J. Michael Kilby**

Acquired immunodeficiency syndrome (AIDS) appeared nearly four decades ago and mystified doctors and scientists alike as it became one of the worst plagues in human history. Currently, an estimated 36.7 million people are living worldwide with human immunodeficiency virus (HIV) infection (UNAIDS, 2016; WHO, 2016b). The last decade has witnessed dramatic scientific advances in HIV prevention and treatment and the intersection of the two. Moreover, there has been a sizeable scale-up of combination antiretroviral therapy (ART), with an estimated 17 million people on treatment as of June 2016. New infections decreased by 35% from 2000 to 2010 but have not declined in adults since then, while AIDS-related deaths have declined by 45% after peaking in 2005 (UNAIDS, 2016; WHO, 2016e). Despite these considerable advances, formidable challenges remain. The HIV "treatment cascade," also referred to as the "care continuum," depicts steps following HIV acquisition including diagnosis, linkage to care, retention in care, and ART receipt and adherence to achieve viral suppression (Bradley et al., 2014; Gardner et al., 2011; White House Office of National AIDS Policy, 2015; WHO, 2016c). Globally, a minority of persons living with HIV have achieved viral suppression, largely attributable to undiagnosed infection, failure to engage in sustained longitudinal medical treatment, and/or failure to consistently access ART, with varying contributions of these steps across geographic regions. While effective prevention and treatment options have expanded substantially, a cure or protective vaccine remains elusive. Accordingly, global efforts to further thwart the HIV pandemic have focused on enhanced and more efficient implementation of proven behavioral and biomedical prevention and treatment modalities. Achieving ambitious targets for serostatus awareness via HIV testing, widespread ART treatment, and near universal viral suppression to maximize individual and population health outcomes will essentially require integrated care responsive to the complex comorbid medical and psychiatric illnesses often seen among persons living with HIV.

ORIGINS AND PATHOBIOLOGY

A BRIEF HISTORY OF HIV

Human immunodeficiency virus type 1 (HIV-1), the agent causing AIDS, is a lentivirus genetically closely related to SIVcpz, found in chimpanzees (Keele et al., 2006). HIV-2 is less pathogenic than HIV-1 and likely originated from macaques and sooty mangabeys. Analysis of the phylogenetic relationships between circulating human and simian immunodeficiency viruses (SIV) suggests that multiple, independent cross-species transmission events occurred between nonhuman primates and humans, resulting in the present circulating HIV-1 strains. The HIV strains that spread around the world belong predominantly to HIV-1 group M, whereas HIV-1 group N, HIV-1 group O, and HIV-2 have a more restricted geographic distribution (e.g., Western and Central Africa). HIV-1 group M comprises nine major clades that differ in frequency and global distribution: 50–55% of all infections are due to subtype C (Thomson and Najera, 2005). In this text, use of the acronym *HIV* refers to HIV-1 unless otherwise specified.

Estimates suggest that HIV-1 was introduced into humans in the first decades of the past century but remained rare and unrecognized for several decades (Korber et al., 2000). The earliest time point that HIV infection could be documented retrospectively in humans is 1959 (Zhu et al., 1998). Case reports of opportunistic infections in people without clear reason for immune suppression indicate sporadic occurrence throughout the 1950–1970s, with HIV-specific genetic materials being detected in retrospect in some of the preserved tissues (Zhu et al., 1998).

It was not until 1981 that HIV/AIDS first emerged as a public health issue, after a clustering of unusual opportunistic infections and cancers were reported in men who have sex with men, in New York and San Francisco (Centers for Disease Control and Prevention, 1981). It was hypothesized that the men were suffering from a common syndrome; a report from the Centers for Disease Control and Prevention

* Posthumously; in honor of a brilliant scientist and physician, and a dedicated and loving husband and father.

(CDC) suggested that the disease might be caused by a sexually transmitted infectious agent (CDC, 1982a). The disease was initially associated with men who have sex with men, despite the fact that similar clinical cases had been reported in injecting drug users, hemophiliacs, and newborns and infants receiving blood transfusions (CDC, 1982b). In 1982, the acronym *AIDS* was coined to describe this syndrome of unknown origin, which was associated with a variety of opportunistic infections and unusual tumors, in persons with the risk behaviors described here as well as in persons with hemophilia and in newborns who had received blood transfusions (CDC, 1982b). HIV, initially designated HTLV-III (human T-lymphotropic virus III), was isolated from AIDS patients in subsequent years by several research groups (Barre-Sinoussi, 1996; Barre-Sinoussi et al., 1983; Popovic et al., 1983). Soon after, an HIV-1 antibody screening test was developed, which allowed for the diagnosis of HIV prior to the development of clinically apparent end-stage immunodeficiency (Popovic et al., 1984; Sarngadharan et al., 1984). This was pivotal not only for gaining a better understanding of the extent of the epidemic and the course of infection, but, most importantly, for allowing screening of blood and blood products.

THE VIRUS AND THE CELL

The manipulation and hijacking of cellular processes is an essential viral survival strategy, since viruses rely on the cell machinery of the infected host for their replication. An impressive 8% of the human genome is composed of sequences of viral origin, suggesting that humans and viruses share a lengthy common history (Lander et al., 2001). Humans have evolved sophisticated defenses in the form of innate and acquired immunity (Stevenson, 2003). The HIV pandemic illustrates that the virus has found efficient ways to evade innate and adapted immunity and to silence essential components of the intrinsic immune system (Simon et al., 2006).

Lentiviruses, which include HIV, are small, enveloped retroviruses that package their genome in the form of two RNA copies. The name is due to the slow and chronic nature of diseases associated with these viruses. Like all retroviruses, they encode for a unique enzyme that allows the virus to reverse transcribe their (RNA) genome into DNA with subsequent insertion into the host chromosomes, thereby becoming an integral part of the cell's chromosomal DNA. Reverse transcription generates a swarm of related but distinct viral variants (known as viral quasi-species), since the viral enzyme reverse transcriptase (RT) is prone to error (Coffin, 1995). Every transcribed viral genome, therefore, differs from one another on average by one nucleotide. HIV replication in vivo is very dynamic, with more than 10 billion viruses being produced per day in an untreated, chronically infected patient (Coffin, 1996; Simon and Ho, 2003). The high replication rate, together with the high error rate of reverse transcription, is at the root of the extensive HIV sequence diversification that complicates treatment interventions and vaccine development.

The HIV life cycle can be divided into early and late phases, with integration indicating the mid-point of infection and irreversibly rendering the cell infected. The virus enters the target cell through binding with a high-affinity interaction between its envelope gp120 protein and the CD4 receptor on the T cells, followed by gp120 interaction with a co-receptor, usually the chemokine receptors CCR5 or CXCR4. Once internalized, the viral core disassembles as proviral DNA is generated by the viral reverse transcriptase incorporated into the incoming core. The double-stranded proviral DNA ultimately integrates into the host genome. Host and viral factors drive transcription of viral proteins, which are assembled into new virions adjacent to the cell membrane. Immature viral particles are released from the infected cells in a noncytolytic manner. Lastly, infectious HIV-1 is generated when the viral Gag protein is cleaved by the viral enzyme protease (PR). Essential viral proteins, including the viral envelope, reverse transcriptase, protease, and integrase, have been major targets for the development of antiretroviral drugs.

EPIDEMIOLOGY

GLOBAL BURDEN OF DISEASE

The most recent estimates (2016) suggest that 71% of the 36.7 (34.0–39.8) million people living with HIV/AIDS worldwide live in sub-Saharan Africa (UNAIDS, 2016). Globally, women account for 17.4 (16.1–20.0) million HIV infections, with children (<15 years old) representing 2.6 (2.4–2.8) million infections. The first decade of the pandemic was characterized by a restricted distribution of HIV infection in (a) industrialized countries where risk behaviors included unprotected sexual contact among men who have sex with men (MSM) and sharing of contaminated needles and drug paraphernalia by injecting drug users, and (b) central, east, and West Africa and the Caribbean where the virus spread in the general population through heterosexual transmission. The second decade witnessed the rapid spread of HIV to almost every part of the world, along with increasing viral subtype diversity. There was an explosive increase of HIV in sub-Saharan Africa. In the third and fourth decades, sub-Saharan Africa remains the epicenter of the pandemic and accounts for 71% of all new HIV infections worldwide (UNAIDS, 2016). Heterosexual transmission continues to be the dominant route of transmission worldwide, while injection drug use accounts for almost one-third of all new infections outside of sub-Saharan Africa. This is particularly notable in the Eastern Europe and Central Asia region, which has witnessed a 30% increase in new HIV infections between 2000 and 2014, a time period during which most other global regions witnessed sizeable declines in new infections (UNAIDS, 2015).

Please see Chapter 3 of this textbook for a more detailed discussion of global HIV and AIDS.

THE EPIDEMIC IN THE UNITED STATES

In the United States there have been long-standing disparities in HIV infection, with higher rates observed among African Americans and Latinos; in 2013 the rates were (per 100,00

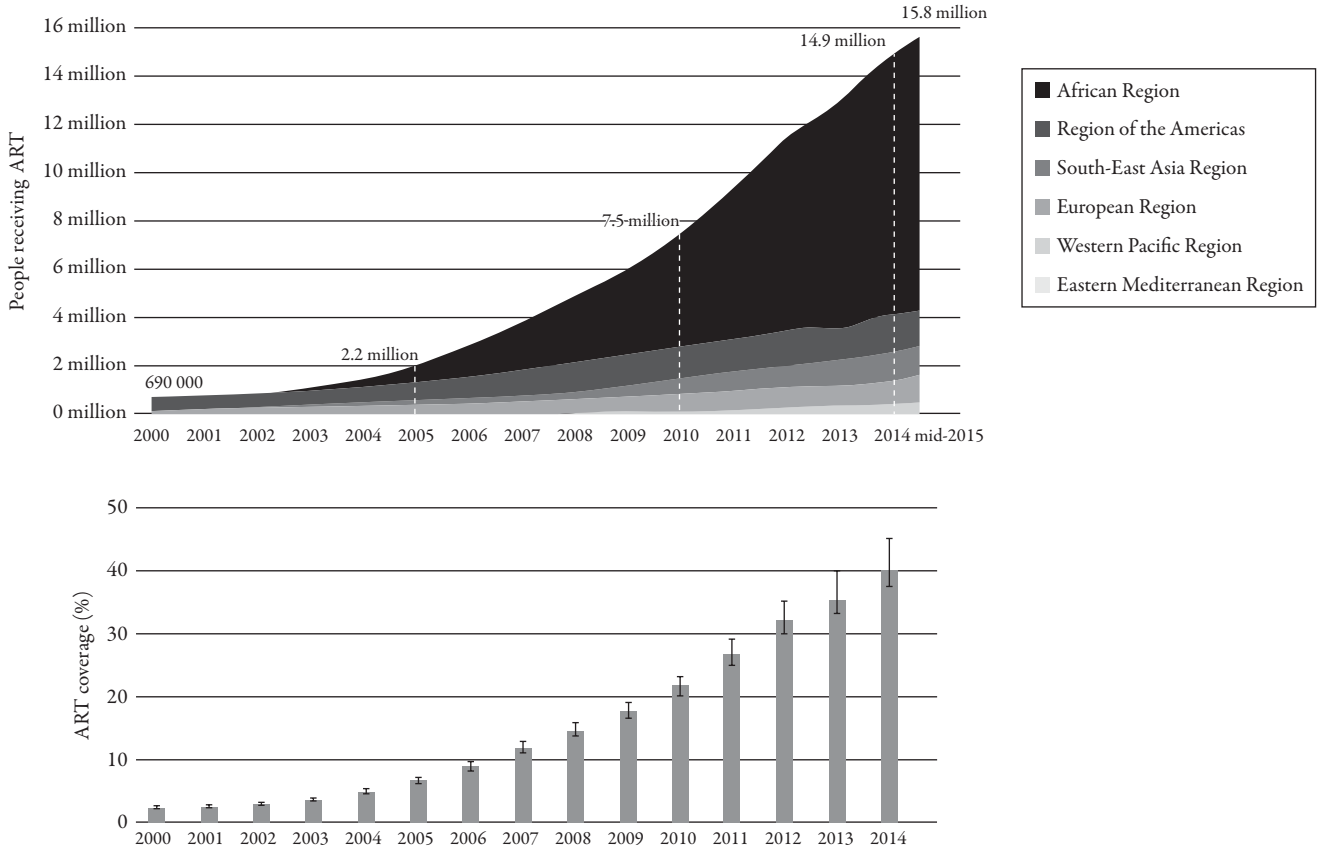

Figure 2.1 Estimated number of persons receiving antiretroviral therapy (ART) globally and by World Health Organization (WHO) region, and percentage of HIV-infected persons covered globally, 2000–2015 (WHO, 2015).

population) 55.9 for African Americans and 18.7 for Latinos, compared to 6.6 for whites; these disparities are particularly magnified among women (CDC, 2015). Moreover, similar racial/ethnic disparities are observed for mortality, even among persons living with HIV with access to ART (Lesko et al., 2015). In the United States, the majority of infections are observed among men who have sex with men (68%), with recent epidemiological trends demonstrating young men who have sex with men of color being particularly impacted (CDC, 2015). Indeed, a sobering report from the CDC suggests that the lifetime risk of acquiring HIV is 1 in 2 for African American men who have sex with men and 1 in 4 for Latino men who have sex with men at current infection rates (Hess et al., 2016).

THE TREATMENT CASCADE

The depiction of the treatment cascade united and galvanized providers, researchers, advocates, and policymakers (Gardner et al., 2011; White House Office of National AIDS Policy, 2015; WHO, 2016c). A simple bar graph showing the steps following acquisition of HIV infection, including diagnosis (via HIV testing), linkage to care, retention in care, receipt of ART, and adherence to ART to achieve viral suppression, provided a foundation on which to evaluate where the greatest challenges exist, at a population level, to achieving universal viral suppression. Globally, an estimated 17.1 million persons living with HIV do not know they have the virus and need to be reached by HIV testing services (UNAIDS, 2015). Moreover, late diagnosis remains a challenge throughout the world, with a high proportion of persons with HIV having severely depleted CD4 counts at the time they become aware of their status (Lesko et al., 2013; Siedner et al., 2015). Taken together, these data indicate the importance of more widespread HIV testing to allow for enhanced serostatus awareness and more timely diagnosis of HIV infection, with implications for improved individual and population health outcomes.

Despite dramatic scale-up of ART since 2000, worldwide, a minority of HIV-infected persons in need of treatment are receiving therapy (Figure 2.1). Whereas 41% (38–46%) of adults living with HIV were accessing ART in 2014, only 32% (30–34%) of children were accessing treatment, a notable treatment gap.

In response to these sobering global statistics and HIV diagnosis and treatment, UNAIDS has developed a fast-track approach to achieve ambitious 90-90-90 goals by 2020: 90% serostatus awareness among persons living with HIV through testing services, 90% ART access among persons diagnosed with HIV, and 90% viral suppression among those on ART.

In the United States, the greatest challenge on the treatment cascade is the step of engagement in care, with over 50% of persons diagnosed with HIV not receiving regular medical care (Figure 2.2). Beyond the deleterious impact on individual health, persons with HIV not receiving regular

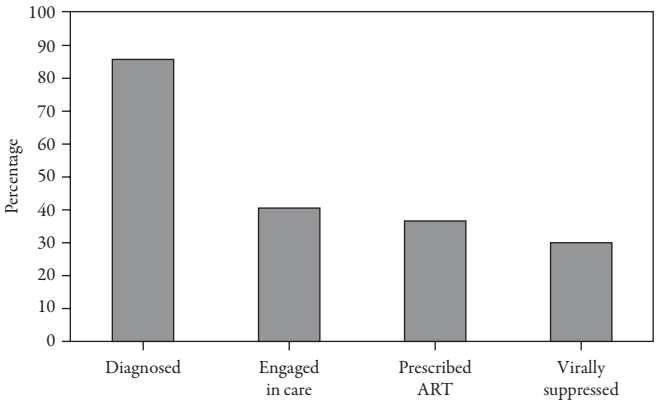

Figure 2.2 United States treatment cascade, 2011 (Bradley et al., 2014).

medical care account for an estimated 61% of new HIV cases, with an additional 30% attributable to those living with HIV who are undiagnosed, estimated to represent 14% of persons living with HIV in the United States (Bradley et al., 2014; Skarbinski et al., 2015). Taken together, these data suggest that less than 10% of new infections in the United States are attributable to persons diagnosed with HIV and engaged in care, a majority of whom are on ART and virally suppressed.

BEYOND THE TREATMENT CASCADE: THE IMPACT OF MISSED CLINIC VISITS

While the treatment cascade has provided a powerful tool to measure and monitor success in achieving universal viral suppression, it represents a static image at the population level and does not capture the dynamic and often bidirectional journey individuals living with HIV face when navigating these steps over time. At an individual level, missed clinic visits are common and easily measured in real time. Moreover, missed clinic visits have been associated with a threefold increased mortality risk—a magnitude equivalent to having a CD4 count <200, indicative of immunological AIDS (Mugavero et al., 2009). Similar findings have been observed across the globe, with dramatic implications for morbidity, mortality, and prevention of new infections (Brennan et al., 2010; Zhang et al., 2012). As psychological and psychiatric factors have been linked with missed HIV clinic visits, integrated programs to screen for and treat such comorbidities are essential to reducing the likelihood and untoward consequences of missed visits. Moreover, effective interventions amenable to implementation in a wide range of settings are available and may be proactively implemented to prevent missed visits rather than reactively attempting to identify and re-engage those who are lost to medical care, which has proven time and resource intensive (Gardner et al., 2014; Thompson et al., 2012).

CLINICAL MANIFESTATIONS

THE VIRUS AND THE INFECTED PATIENT

The hallmark of HIV infection is the slow depletion of naïve and memory CD4+ T lymphocytes, cell populations that are crucial for effective humoral and cellular immune responses. Expansion in CD8+ T-cell numbers and dysregulation of CD8+ T-cell functions are also seen throughout most of the disease.

Upon sexual transmission, HIV first replicates in the epithelium and the local lymphoid organs such as the draining lymph nodes. T lymphocytes, macrophages, and dendritic cells located in the lamina propria of the vaginal, cervical, and rectal epithelium are probably among the first infected target cells (Shattock and Moore, 2003). Local amplification and migration of infected cells and/or virions throughout the body via the bloodstream lead to the very high levels of circulating virus in the plasma compartment associated with acute HIV-1 infection. According to experimental infections of rhesus macaques with SIV, viral dissemination occurs within days following exposure (Haase, 2005). Most infected humans develop HIV-specific CD8+ cytotoxic T lymphocytes (CTL) within 6 weeks of infection, whereas seroconversion with HIV-specific antibodies is generally observed after 1–3 months (see Figure 2.3).

The mounting of an HIV-specific immune response (e.g., CTL) is temporally correlated with a reduction in the peak of viremia, as determined by the quantity of viral RNA copies per milliliter of plasma, to a level that is maintained over years in the untreated individual. This association suggests that cell-mediated immunity plays a role in controlling replication, although this control is incomplete. The established level of viral RNA in the plasma, termed the *viral set point*, differs between patients and predicts disease progression (Mellors et al., 1997). Thus, CD8+-mediated cellular immune responses initially reduce viral replication, but the rapid selection of viral CTL escape mutants limits the long-term efficacy during chronic infection (Lichterfeld et al., 2005).

It is important to note that although symptoms may be mild in the first years of disease (so-called latent/dormant phase), HIV continuously replicates in the vast majority of those infected until the replacement of CD4+ cells cannot keep pace with the loss of these cells. The time from infection to the point when CD4+ T cells fall below a critical circulating level needed to prevent opportunistic infections varies among individuals (e.g., 10 to 15 years). Genetic factors have been identified to account for some of the observed variation, including HLA haplotypes, and mutations in CCR5 co-receptor gene/promoter or co-receptor ligands (O'Brien and Nelson, 2004).

DIAGNOSIS

Many commercially available kits enable the detection of HIV-specific antibodies. The availability of simple and rapid antibody detection systems have allowed for broader screening and earlier identification of infected individuals (Branson et al., 2006). More recently, fourth-generation antigen/antibody testing technology that detects p24 antigen as well as HIV-specific antibodies has enabled better detection of early infections. These serological tests fail to provide a reliable diagnosis in newborns and infants born to HIV-infected mothers who bear maternal antibodies and in the setting of acute infection

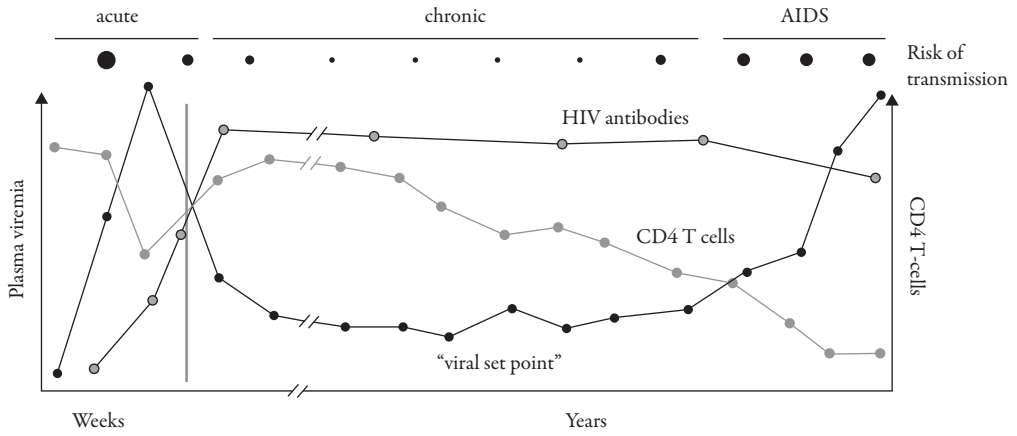

Figure 2.3 The natural course of HIV infection as depicted by the surrogate markers plasma viremia and CD4+ T-cell counts. Primary infection can be associated with clinical symptoms. During the first weeks of infection the risk of transmission is high, while HIV antibodies are still absent. Viremia stabilizes after the first month of infection, reaching an individual viral set point. Opportunistic diseases and certain HIV-associated malignancies define the stage of clinically apparent immunodeficiency (AIDS). Reproduced with permission from *Nature Reviews Microbiology*, Simon V, and Ho DD (2003). HIV-1 dynamics in vivo: implications for therapy. 1(3):181–190, copyright 2003, Macmillan Magazines Ltd.

when antibodies are still absent. In these clinical scenarios, only the direct detection of viral nucleic acids establishes a diagnosis, via quantification of the plasma HIV viral load.

SIGNS AND SYMPTOMS

The natural course of HIV infection can be divided into three phases: acute, chronic, and immunodeficiency stages (see Figure 2.1). During primary infection, flu-like symptoms with rash and fever may occur (acute retroviral syndrome). The probability of transmission has been linked to the level of viral replication (Quinn et al., 2000). Since the plasma viral loads are highest during acute infection, in the late stages of HIV disease and during concurrent sexually transmitted infections, these are considered high-risk periods for transmission. Therefore, the risk of transmission may be high during relatively asymptomatic periods of infection. Newly infected individuals are often unaware of their serostatus and thus inadvertently may expose others to a very high risk of HIV acquisition.

In the chronic phase of infection, the number of absolute and relative CD4 T cells is maintained and eventually gradually decreases. However, patients are generally free of major symptoms until CD4+ T-cell depletion reaches a certain level (e.g., $<200/mm^3$) and the immunodeficiency becomes clinically apparent. A variety of pathogens, such as viruses, bacteria, fungi, or protozoa, may cause opportunistic diseases (Benson et al., 2005). Infections with *Pneumocystis carinii* (e.g., pneumonia), *Toxoplasma gondii* (e.g., cerebral manifestation), cytomegalovirus (CMV) (e.g., generalized CMV, encephalitis), and *Mycobacterium avium* complex, and neoplastic diseases such as Kaposi sarcoma and non-Hodgkin lymphoma were common AIDS-defining events in patients in North America and Europe during the pre-ART era. In other geographic settings (e.g., sub-Saharan Africa) mycobacterium tuberculosis or wasting syndrome takes a more prominent role as an AIDS-defining disease.

STAGING SYSTEMS

In the first decade of the pandemic, classifications systems (Walter Reed, CDC classification) served as important tools in predicting disease progression and initiating clinical interventions such as preemptive prophylactic treatments (e.g., *Pneumocystis carinii* prophylaxis). In the era of ART, HIV/AIDS disease is staged on the basis of CDC classification from 1993, which combines CD4+ cell counts (categories 1–3) and clinical manifestation of certain opportunistic infections or tumors (CDC, 1993). Its relevance for daily management of the disease is somewhat reduced, since the single most important determinant of disease progression, the level of virus replication as measured in the plasma, is not part of the classification. Additionally, ART increases CD4+ T cells to near-normal levels, drastically reducing the risk of opportunistic infections. But backstaging from a more advanced CDC category is not a part of current staging. In resource-limited regions, infrastructure may not allow sophisticated laboratory testing, and clinical symptoms are the only available criteria on which to base treatment decisions. The World Health Organization (WHO) has therefore developed a classification system based solely on clinical presentations (clinical stages 1–4) (WHO, 2006).

BASIC PRINCIPLES OF TREATMENT AND PREVENTION

ANTIRETROVIRAL MEDICATIONS

Since 1996, combination antiretroviral therapy has been the mainstay of treatment for HIV infection. Heralded as one of the greatest biomedical and population health advances, combination ART transformed a uniformly fatal illness into a manageable chronic disease for persons with consistent access and adherence to treatment. Over the two decades following the advent of combination ART, pharmacological advances

in medications have allowed for treatment regimens with fewer pills, daily dosing, better tolerability, and lower toxicity, which have translated to improved adherence and higher rates of viral suppression among persons on treatment (Althoff et al., 2012; Nachega et al., 2014). As of 2016, numerous antiretroviral medications, including fixed-dose combination and single-tablet regimens, belonging to a wide range of classes acting on varying drug targets were approved for the treatment of HIV infection (Table 2.1) (WHO, 2016a, 2016d). Ongoing research is evaluating injectable, long-acting antiretroviral medications, which may become a potential alternative to daily oral medications.

ANTIRETROVIRAL TREATMENT PRINCIPLES

While there is considerable global variability in recommendations of what medications to start as recommended therapy, consensus has been achieved on when to start. Past guidance on starting therapy when the CD4+ count falls below a specified threshold has been abandoned, with global treatment guidelines now recommending ART treatment for all persons after HIV diagnosis, regardless of CD4 count (WHO, 2016a, 2016d). This shift in treatment paradigm is largely attributable to a large cohort study and subsequent clinical trial demonstrating the treatment benefits of immediate versus delayed initiation of ART, with reduction in morbidity and mortality when ART is initiated at higher CD4+ counts (INSIGHT START Study Group, 2015; Kitahata et al., 2009). Once antiretroviral treatment is initiated, uninterrupted therapy is recommended. The Strategies for Management of Antiretroviral Therapy (SMART) randomized trial demonstrated an elevated risk of opportunistic infections and mortality among participants treated with episodic ART guided by CD4+ count compared to risk for those on continuous treatment with a goal of achieving sustained viral suppression (SMART Study Group, 2006). Moreover, once continuous treatment was instituted in the episodic ART arm, attenuated, but persistent risk for clinical events was observed, suggesting propagated deleterious effects of the prior intermittent treatment strategy, despite the institution of continuous ART to achieve sustained viral suppression (SMART Study Group, 2008).

LIMITATIONS OF ANTIRETROVIRAL TREATMENT

The success of ART is limited by virological, biological, and behavioral factors. The selection of viral variants with reduced drug susceptibility, the limited penetration of drugs in biological compartments (e.g., brain), the presence of long-lived cells that harbor the virus, and short- and long-term toxicities are some of the obstacles that need to be overcome before a long-lasting cure becomes available. Furthermore, successful response to combination ART requires rigorous individual adherence to a daily regimen indefinitely. Emergence of drug resistance in the setting of nonadherence limits the efficacy of antiretroviral medications. Different classes of antiretroviral medications have varying genetic barriers to resistance, such that some agents are more forgiving in terms of the emergence of resistance in the setting of nonadherence.

On a cellular level, there are reservoirs in the body where the virus is integrated in the genome but the cell does not produce viral proteins or infectious virus. These reservoirs, however, can be induced to produce virus. These latent reservoirs may be quite longed-lived and remain a challenge for an ultimate cure (Blankson et al., 2002). Viral reservoirs comprise anatomical sanctuaries such as the central nervous system, the testis, and the kidney, as well as a small pool of circulating latently infected, long-lived memory T lymphocytes (Blankson et al., 2002; Finzi et al., 1999). These quiescent cell populations are inaccessible to current combination antiretroviral treatments that only work on active virus replication. Furthermore, they are not recognized by the immune system and therefore elude the goal of total eradication. A number of strategies are under active investigation to eradicate these latent pools and allow for potential cure.

PROPHYLACTIC INTERVENTIONS AGAINST OPPORTUNISTIC INFECTIONS

Chemotherapeutic prophylaxis for *Pneumocystis carinii, Mycobacterium avium* complex, and *Toxoplasma gondii* (for antibody-positive patients) is recommended once CD4+ cell counts drop below a certain level (e.g., 200/mm^3 for *Pneumocystis carinii*). Secondary prophylaxis may prevent recurrence of an opportunistic manifestation such as *Cryptococcus neoformans* encephalitis or cerebral toxoplasmosis (Panel on Antiretroviral Guidelines for Adults and Adolescents, 2016; U.S. Department of Health and Human Services, 2006). These interventions depend on an assessment of an individual's immune status, which currently is based largely on the stable measurement of CD4+ helper T cells. Most of the primary and secondary prophylaxis for opportunistic infections can be stopped in patients who have had sustained recovery of CD4+ cells in response to ART (Benson et al., 2005).

PRIMARY HIV PREVENTION

Dramatic scientific advances have changed the landscape of primary HIV prevention, the prevention of HIV infection among HIV-uninfected persons. Pre-exposure prophylaxis (PrEP), the daily ingestion of certain antiretroviral medications among high-risk HIV-negative persons has proven efficacious in reducing the risk of acquiring HIV infection (Grant et al., 2010). The biomedical prevention toolkit has also been bolstered by studies demonstrating the efficacy of topical microbicides in reducing the risk of new HIV infections. The CAPRISA004 study documented a 50% reduction in HIV acquisition among women randomized to an intravaginal antiretroviral microbicide (vs. placebo) applied within 12 hours before and 12 hours after sex (Abdool Karim et al., 2010). Studies evaluating these biomedical prevention tools have consistently observed that efficacy is associated with adherence, with one trial comparing PrEP and a topical microbicide observing no prevention benefit to

Table 2.1 APPROVED ANTIRETROVIRAL MEDICATIONS FOR TREATMENT OF HIV INFECTION, 2016

ANTIRETROVIRAL DRUG CLASS (ABBREVIATION)	GENERIC NAME (ABBREVIATION)	U.S. FDA APPROVAL DATE
Nucleoside reverse transcriptase inhibitor (NRTI)	Abacavir (ABC)	December 17, 1998
NRTI	Didanosine (ddI)	October 9, 1991
NRTI	Emtricitabine (FTC)	July 2, 2003
NRTI	Lamivudine (3TC)	November 17, 1995
NRTI	Stavudine (d4T)	June 24, 1994
NRTI	Tenofovir disoproxil fumarate (TDF)	October 26, 2001
NRTI	Zidovudine (AZT, ZDV)	March 19, 1987
Non-nucleoside reverse transcriptase inhibitor (NNRTI)	Efavirenz (EFV)	September 17, 1998
NNRTI	Etravirine (ETR)	January 18, 2008
NNRTI	Nevirapine (NVP)	June 21, 1996
NNRTI	Rilpivirine (RPV)	May 20, 2011
Protease inhibitor (PI)	Atazanavir (ATV)	June 20, 2003
PI	Darunavir (DRV)	June 23, 2006
PI	Fosamprenavir (FPV)	October 20, 2003
PI	Indinavir (IDV)	March 13, 1996
PI	Nelfinavir (NFV)	March 14, 1997
PI	Ritonavir (RTV)	March 1, 1996
PI	Saquinavir (SQV)	December 6, 1995
PI	Tipranavir (TPV)	June 22, 2005
Fusion inhibitor	Enfuvirtide (T-20)	March 13, 2003
Entry inhibitor	Maraviroc (MVC)	August 6, 2007
Integrase inhibitors		
Integrase inhibitor	Dolutegravir (DTG)	August 13, 2013
Integrase inhibitor	Elvitegravir (EVG)	September 24, 2014
Integrase inhibitor	Raltegravir (RAL)	October 12, 2007
Pharmacokinetic enhancer	Cobicistat (COBI)	September 24, 2014
Fixed-dose combination antiretroviral medications	Abacavir and lamivudine (ABC/3TC)	August 2, 2004
	Abacavir, lamivudine, and dolutegravir (ABC/3TC/DTG)	August 22, 2014
	Abacavir, lamivudine, and zidovudine (ABC/3TC/ZDV)	November 14, 2000
	Atazanavir and cobicistat (ATV/COBI)	January 29, 2015
	Darunavir and cobicistat (DRV/COBI)	January 29, 2015
	Emtricitabine, tenofovir disoproxil fumarate, and efavirenz (FTC/TDF/EFV)	July 12, 2006

(*continued*)

Table 2.1 CONTINUED

ANTIRETROVIRAL DRUG CLASS (ABBREVIATION)	GENERIC NAME (ABBREVIATION)	U.S. FDA APPROVAL DATE
	Emtricitabine, tenofovir alafenamide fumarate, elvitegravir, and cobicistat (FTC/TAF/EVG/COBI)	November 5, 2015
	Emtricitabine, tenofovir disoproxil fumarate, elvitegravir, and cobicistat (FTC/TDF/EVG/COBI)	August 27, 2012
	Emtricitabine, tenofovir alafenamide fumarate, and rilpivirine (FTC/TAF/RPV)	March 1, 2016
	Emtricitabine, tenofovir disoproxil fumarate, and rilpivirine (FTC/TDF/RPV)	August 10, 2011
	Emtricitabine and tenofovir alafenamide fumarate (FTC/TAF)	April 4, 2016
	Emtricitabine and tenofovir disoproxil fumarate (FTC/TDF)	August 2, 2004
	Lamivudine and zidovudine (3TC/ZDV)	September 27, 1997
	Lopinavir and ritonavir (LPV/r)	September 15, 2000

either approach, attributable to low adherence to study drugs (Marrazzo et al., 2015). Indeed, as with HIV treatment, the efficacy of biomedical prevention of HIV is directly linked to adherence—behavior fuels biology in both realms.

ANTIRETROVIRAL TREATMENT AS PREVENTION

A dose–response relationship between plasma viral load and risk for sexual HIV transmission among serodiscordant couples was identified in a landmark study conducted prior to the availability of combination ART in a cohort in Rakai, Uganda (Quinn et al., 2000). This observational study provided a scientific foundation for the principle of HIV treatment as prevention, positing that suppression of plasma viral load via combination ART could render a person living with HIV virtually noninfectious. Ecological studies at a population level provided further evidence suggesting that expansion of ART uptake in a geographic region could lead to a decrease in newly diagnosed HIV cases via decreased community viral load, suggesting a population health benefit to treatment as prevention (Montaner et al., 2010). The HIV Prevention Trials Network 052 randomized clinical trial provided definitive scientific evidence of the efficacy of HIV treatment as prevention. A 96% reduction in paired HIV transmission among serodiscordant couples was observed when the HIV-positive partner was randomized to immediate versus deferred ART based on CD4+ thresholds for treatment initiation aligned with treatment guidelines in place at the time of the study (Cohen et al., 2011). Beyond benefits to the individual, the population health and prevention benefits of ART are part of the rationale for global treatment guidelines now recommending ART initiation and treatment for all persons following HIV diagnosis, regardless of CD4+ count. Please see Chapters 29 and 31 of this textbook for a more detailed discussion of prevention measures and treatment as prevention.

CONCLUSIONS

In the fourth decade of the global HIV pandemic, it remains as dynamic as ever. However, scientific breakthroughs in treatment and prevention, and substantial investment in global ART scale-up have resulted in some degree of stabilization of a maturing epidemic in many regions of the world, many of which have witnessed dramatic declines in the number of new cases annually since 2000 (UNAIDS, 2015; WHO, 2016c). Indeed, while a preventative vaccine and long-lasting cure do not appear to be on the horizon, the expansion of the treatment and prevention armamentarium, and the intersection of the two, provide a scientific foundation and basis on which to further hasten and halt the scourge of HIV/AIDS on society. Considerable work lies ahead to address the large gaps on the treatment cascade, most notably, serostatus awareness via HIV testing and engagement in care to allow for uninterrupted ART access and adherence, to sustain viral suppression at an individual and population level. Moreover, as behavior fuels biology, beyond financial resources, the collective global success of HIV treatment and prevention will ultimately be dictated by adherence to testing, prevention, and treatment guidelines, biomedical, and behavioral tools. Achieving success in this realm will essentially require integrated care that is responsive to the complex comorbid psychiatric illnesses often seen among persons living with HIV, as these are among the most critical determinants of adherence, which ultimately will be a critical determinant in our global effectiveness.

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3.

EPIDEMIOLOGY OF PSYCHIATRIC DISORDERS ASSOCIATED WITH HIV AND AIDS

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For persons with HIV, mental health problems can occur as risk factors for HIV infection, coincidentally with HIV infection, or as a result of HIV infection and its complications. Psychiatric disorders are associated with HIV transmission, poor prognosis, and inadequate adherence to antiretroviral regimens (Cournos et al., 2005). The majority of individuals with HIV will experience a diagnosable psychiatric disorder (Stoff et al., 2004), as the prevalence of these disorders among those living with HIV is many times greater than in the general population (Blank et al., 2002, 2014; Lyketsos et al., 1996). Further, HIV infects the brain, and a variety of central nervous system (CNS) complications can result. These complications are detailed in Chapter 26. Psychiatric and neurocognitive aspects of HIV disease are expected to become more prominent and important for addressing the continuum of care in the coming years (Wainberg et al., 2014). Despite the move toward preexposure prophylaxis, and until a widely available and highly effective vaccination to prevent HIV infection or a cure for HIV is developed—neither of which is anticipated in the near future—the HIV epidemic will not be adequately controlled without greater attention to co-occurring psychiatric disorders along the entire continuum of care.

Given the high rates of psychiatric disorders among people with HIV, psychiatrists and other mental health care clinicians are squarely in charge of treatment decisions that affect the course of patients' illness, the quality of their lives, and, ultimately, containment of the epidemic. Most psychiatric disorders comorbid with HIV are highly treatable, but they offer a challenge to clinicians in terms of differential diagnosis and management. An understanding of the epidemiology of comorbid psychiatric disorders can help clinicians conduct a differential diagnosis and intervene in ways that minimize further spread of the virus and its devastating effects on the brain and body. *Epidemiology* refers to the incidence, distribution, and control of disease in a population. With respect to HIV, incidence studies of psychiatric disorders are rare, so for our purposes we will focus on the distribution of psychiatric conditions (i.e., their prevalence) across the populations in which they have been studied.

This chapter focuses on rates of psychiatric disorders among adults with HIV infection. All prevalences cited in this chapter were derived from U.S. studies unless otherwise stated. We discuss commonly seen psychiatric disorders among people with HIV infection in the United States. We begin with HIV-associated neurocognitive disorders resulting from the direct effects of HIV on the central nervous system (CNS) and then follow with a discussion of alcohol and other substance use disorders; depressive disorders; anxiety disorders; posttraumatic stress disorder (PTSD); mania; psychosis; and personality disorders. We also describe what is known about rates of HIV infection among people with psychiatric disorders. We briefly mention how psychiatrists and other healthcare professionals can help to contain the epidemic and to improve care to their patients.

Consistent with the diagnostic approaches of both the *Diagnostic and Statistical Manual of Mental Disorders*, fifth edition (DSM-5) and the World Health Organization's *International Classification of Diseases* (ICD), we use the terms *mental disorders* and *psychiatric disorders* to include alcohol/substance-related diagnoses, other mental illnesses, and HIV-related neurocognitive impairment. Almost all of the U.S. studies we cite here used DSM-IV nomenclature. However, we have organized the chapter so that it is consistent with how disorders are now classified in the DSM-5. Most relevant to this chapter, in the DSM-5 the term *mood disorders* has been eliminated and depressive and bipolar disorders are in separate categories; PTSD has been separated from anxiety disorders and is now classified as part of the new category of stress disorders; and disorders of alcohol and other drug (AOD) use are differentiated on a continuum of intensity and duration of use, and the terms *abuse* and *dependence* have been eliminated.

In this discussion we have moved away from the concept of risk groups, because anyone who engages in risky sexual and drug use behaviors can potentially acquire or transmit HIV. Use of the concept of risk groups has been stigmatizing and falsely reassuring to persons who may not be members of the groups or countries affected early in the epidemic (Cohen, 1988). Nonetheless, it remains true that most countries currently have epidemics that are concentrated in vulnerable populations. Vulnerable populations include the economically disadvantaged, racial and ethnic minorities, the uninsured, adolescents and younger adults and the elderly, homeless people, and those with other chronic health conditions, including severe mental illness. It may also include rural residents, who often encounter barriers to accessing healthcare services. In vulnerable populations, health and

Table 3.1. SUBSTANCE USE AND OTHER MENTAL HEALTH DISORDERS IN CONCENTRATED HIV EPIDEMICS

- **Injection drug users: high rates of addictive and other psychiatric disorders**
- **Men who have sex with men: elevated rates of alcohol/substance use disorders and depression**
- **Sex workers: high rates of childhood sexual abuse; elevated rates of addictive disorders and post-traumatic stress disorder**

healthcare problems intersect with social determinants of health, including substandard and unstable housing, food insecurity, and low education (*American Journal of Managed Care*, 2006). Among the most vulnerable to HIV infection are men who have sex with men (MSM), people who inject drugs (PWID), and sex workers (SWs), all three of whom have elevated rates of specific psychiatric disorders (see Table 3.1) that may in part be related to their disenfranchisement from the dominant culture, to the corresponding stigma and legal and other sanctions, and to inadequate access to prevention services. Each of these factors is associated with increased risk behaviors (Acuff et al., 1999; Cournos et al., 2005).

Underlying the daunting task of preventing the spread of HIV within and beyond vulnerable populations are numerous structural factors, including social discrimination, political indifference or oppression, poverty, and violence. Fundamental changes in behavior within entire populations need to occur, and mental health must become part of the fabric of public health initiatives to accomplish this task. Models of behavior change need to be incorporated into prevention initiatives to understand what motivates people to engage in risky behavior, what incentives are available to change such behavior, and what skills are needed to implement and maintain safer practices. In addition, detecting, understanding, and treating behavioral and psychiatric problems that interfere with safer practices or even promote unsafe practices must be a priority. It is our hope that the information presented in this chapter will contribute to these efforts.

RATES OF PSYCHIATRIC DISORDERS AMONG PEOPLE LIVING WITH HIV INFECTION

Accuracy of available prevalence estimates is unclear because most studies of psychiatric disorders among people with HIV infection used convenience samples, often of the historic risk groups, had small sample sizes, or were confined to specific geographic areas.

OVERVIEW: POPULATION-BASED STUDIES

Population-based estimates of psychiatric disorders among HIV-positive people are scarce, and the occasional study that had a larger and more representative sample may not represent current trends. Most notably, the landmark HIV Cost and Services Utilization Study (HCSUS) administered a brief, structured psychiatric instrument that screened for major depression, dysthymia, generalized anxiety disorder, panic disorder, heavy drinking, and drug dependence in a large, nationally representative probability sample of adults receiving medical care for HIV in the United States in early 1996 (N = 2,864: 2,017 men, 847 women) (Bing et al., 2001). Elevated rates of probable mental disorders were found, which are discussed in this chapter under specific diagnoses. However, the baseline study was not set up to make definitive psychiatric diagnoses. Subsequently, a follow-up study using the original screen, followed shortly thereafter by a full diagnostic interview, in a subsample of patients estimated lower rates of psychiatric disorders. For many psychiatric disorders these rates nonetheless remained higher than general population estimates (Orlando et al., 2002). It is also of note that 1996 marked the year that more effective treatments for HIV infection became available in the United States, significantly modifying the outcomes of HIV infection and potentially changing the pattern of psychiatric comorbidities. In addition, HCSUS did not obtain rates of PTSD, psychosis, bipolar disorder, and most alcohol and substance use disorders as they were then defined in DSM-IV. Another important aspect of the HCSUS study to note is that people with HIV infection who are receiving medical care may be different from those not receiving medical care in terms of underlying comorbidities and their impact on illness progression.

Hospital admissions for AIDS-related illnesses decreased soon after the introduction of effective antiretroviral therapy (ART), but a study of hospitalizations of 8376 patients in six U.S. HIV care sites showed that among patients hospitalized at least once, the third most common admission diagnosis after AIDS-defining illnesses (21%) and gastrointestinal disorders (9.5%) was a mental illness (9%) (Betz et al., 2005). This study also found that, compared with Caucasians, African Americans had higher admission rates for mental illnesses but not for AIDS-defining illnesses. The relatively large number of mental illness admissions highlights the need for comanagement of substance use disorders and other psychiatric illnesses among people with HIV Infection.

One probability sample study was conducted using South Carolina hospital discharge data from all of the state's 68 hospitals: among 378,710 adult cases of discharge from all hospitalizations and emergency room visits during 1995, 422 had a diagnosis of HIV/AIDS and mental illness (using ICD-9 criteria), 1,353 had a diagnosis of HIV/AIDS alone, and 67,092 had a diagnosis of mental illness alone. People with a mental illness, regardless of race, gender, or age, were 1.44 times as likely to have HIV/AIDS as people without a mental illness (Stoskopf et al., 2001). In this study, two categories of mental illness—alcohol/drug abuse and depressive disorders—were found to have relative risks significantly associated with HIV infection.

A population sample of all persons who resided in Stockholm County, Sweden, as of December, 31, 2012 (N = 2,212,435; with HIV N = 3,031) found that HIV-positive men had a 3- to 4-fold higher age-adjusted odds of being diagnosed with depression and a 3-fold higher odds of anxiety disorders. HIV-positive women had a 1.6- to 2-fold

higher age-adjusted odds of depression and anxiety disorders than males and females in the general population, respectively (Jallow et al., 2015).

The 2004–2005 National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) Wave 2, a large nationally representative sample of U.S. adults (N = 34,653), also reported on how HIV status was associated with 12-month prevalence of psychiatric disorders (Lopes et al., 2012), but the HIV sample size was quite small (N = 149 HIV-positive people: 79 women, 70 men). Consistent with previous reports (Bing et al., 2001; Galvan et al., 2002; McDaniel et al., 1995), psychiatric disorders were common among HIV-positive adults: 64% of the men and 38% of the women had a psychiatric disorder, respectively. Rates of psychiatric disorders were significantly higher in HIV-positive men than in their HIV-negative counterparts. By contrast, HIV-positive women were not significantly more likely than HIV-negative women to have psychiatric disorders.

Many studies of psychiatric disorders among people with HIV infection do not include data on neurocognitive disorders. However, such data have been collected in a number of large clinical trials focused on HIV treatment. Most of the psychiatric disorders that we discuss here are explored in greater detail in other sections of this textbook.

HIV-ASSOCIATED NEUROCOGNITIVE DISORDERS

HIV is a neurotropic virus that enters the CNS at the time of initial infection and persists there, causing neurocognitive syndromes that can vary from subtle impairments to profoundly disabling dementia (Ho et al., 1985, Navia et al., 1986). HIV-associated dementia (HAD) confers an increased risk for early mortality, independent of other medical predictors, and is more frequently seen in advanced stages of HIV disease but can occur even in individuals with otherwise medically asymptomatic HIV infection (Cournos et al., 2005, Heaton et al., 2011). In untreated HIV infection, symptoms are predominantly subcortical and include decreased attention and concentration, psychomotor slowing, reduced speed of information processing, executive dysfunction, and, in more advanced cases, verbal memory impairment. However, this pattern of brain injury and the nomenclature used to describe it has evolved with earlier detection of HIV infection and treatment advances. The use of effective ART has seen the neuropsychiatric complications of HIV evolve from a predominantly subcortical disorder to one that now prominently includes the cortex, with volumetric loss and ventricular enlargement (Cohen et al., 2010). Finally, increased life expectancy of HIV patients may add cerebrovascular or degenerative CNS diseases to the clinical presentation of HIV neurocognitive disorders (Cournos et al., 2005). Although early neurocognitive complications are usually mild and survival is not compromised (Sevigny et al., 2007, Tozzi et al., 2007), they may over time negatively affect quality of life (Tozzi et al., 2007), employment, independence in daily activities, including driving, and adherence to treatment and safer sex practices (Heaton et al., 2004).

Since 2007, the term *HIV-associated neurocognitive disorder* (HAND) has been established to capture the wide spectrum of HIV-related neurocognitive deficits and encompasses three conditions: asymptomatic neurocognitive impairment (ANI) without significant impact on day-to-day functioning, mild neurocognitive disorder (MND) with mild to moderate impairment, and debilitating HAD (Antinori et al., 2007). The research diagnostic criteria of HAND require comprehensive neuropsychological evaluation to detect ANI and MND. Such testing is seldom available in clinical settings, even in high-income countries (Butters et al., 1990, Cherner et al., 2007). Clinical assessment or brief screening tools are the norm, although their validity is still being evaluated (Simioni et al., 2010).

The introduction of effective ART in the mid-1990s and the widespread use of primary prophylaxis against opportunistic infections have dramatically decreased the incidence of the most common HIV-related opportunistic diseases affecting the brain (Kaplan et al., 2000; Sacktor et al., 2001; Sonneville et al., 2011). However, neurological complications of HIV infection still cause considerable morbidity and mortality, and more than 50% of patients develop neurological disorders, even in the ART era (d'Arminio at al., 2000; Power, et al., 2009; Sonneville et al., 2011). Conservative estimates from resource-rich countries suggest that the number of individuals of all ages living with HIV neurocognitive disorders will increase 5- to 10- fold by 2030 (Cysique et al., 2011).

Prior to effective ART, HAD prevalence estimates were approximately 15–20% in persons with AIDS (McArthur et al., 1993; Simpson, 1999), whereas more recent estimates are less than 5–10% (Dore et al., 1999; Heaton et al., 2010; Sacktor et al., 1999). Among HIV-positive patients who received ART, the proportion of HAD as a percentage of all AIDS-defining illnesses rose from 4.4% to 6.5% between 1995 and 1997, a time period that marked the introduction of more effective HIV treatment (Dore et al., 1999). This shift was thought to reflect the decrease in rates of other AIDS-defining conditions, thereby leading to the relative rise in HAD cases. Even though some initial studies reported a decrease in incidence of HAD from 21.1/1,000 person years in 1990–1992 to 14.7/1,000 person years in 1995–1997 (Dore et al., 1999; Sacktor et al., 1999), others reported HAD incidence irrespective of the use of ART (McArthur, 2004)

While the prevalence of HAD decreased considerably in the era of ART, HAND continues to occur, with a high prevalence of 28–50%, although mostly in mild forms (Ances and Ellis, 2007; Dore et al., 2003; Heaton et al., 2011; Letendre et al., 2009; Levine et al., 2012; Sacktor et al., 2002). Longitudinal studies among ART-treated patients have documented high persisting rates of mild-to-moderate neurocognitive impairment (Heaton et al., 2011; McArthur and Brew, 2010; Tozzi et al., 2007) even with undetectable HIV RNA in plasma (Sacktor et al., 2016; Simioni et al., 2010). However, the majority of HAND-diagnosed ART-treated patients with systemic virological suppression do not experience HAND progression over 3 to 4 years of follow-up (Brouillette et al., 2016; Sacktor et al., 2016).

Possible explanations for the lack of response of HAND to ART include incomplete viral suppression in the CNS due to poor antiretroviral (ARV) CNS penetration, presence of drug-resistant viral strains, neurotoxicity of ARV drugs, metabolic abnormalities, neurovascular pathology, or the neurocognitive effects of comorbid conditions such as syphilis or chronic hepatitis (Cournos et al., 2005; Heaton et al., 2011; Letendre et al., 2009). Hepatitis C virus (HCV) is highly comorbid with HIV, and HCV can create its own neuropsychiatric problems as well as exacerbate those caused by HIV. Screening for HCV is simple, and treatment advances have revolutionized the tolerability and cure rates associated with HCV treatment, including among those with HIV infection (Bichoupan et al., 2014). Approximately 100 million people worldwide are infected with HCV, yet it has been estimated in resource-rich countries that less than 30% of people with HCV know they are infected (National Institutes of Health, 1997). HCV is an important diagnosis of exclusion in the evaluation and treatment of the neuropsychiatric complications of HIV. A full discussion of HCV in persons with HIV can be found in Chapter 43 of this textbook.

Asymptomatic neurocognitive impairment may be found in 22–30% of otherwise asymptomatic patients with HIV infection (White et al., 1995). Before effective ART, the prevalence of MND (which was classified as minor cognitive motor disorder prior to 2007) was estimated at 20–30% for HIV-asymptomatic patients and 60–90% for HIV late-stage patients (Goodkin et al., 1997). Following effective ART, these rates have remained fairly constant for patients with late-stage disease, but fortunately earlier use of ART has meant that fewer patients reach this stage. At the same time, following the introduction of ART, the prevalence of HAND increased for HIV asymptomatic patients by about 20% in most studies (Gisslén et al., 2011) up to a total of 52% in this population (Neuenburg et al., 2002; Simioni et al., 2010). Testing for ANI raises important ethical issues as well as diagnostic and therapeutic implications by categorizing patients who don't have any symptoms as neurocognitively impaired (Gisslén et al., 2011). This research definition should not be used to establish a clinical diagnosis, especially in patients with ongoing effective ARV treatment, as there is currently no evidence that patients with ANI are at increased risk to develop more severe impairment or need any specific intervention (Gisslén et al., 2011).

Please see Chapters 16 and 26 for more comprehensive and detailed discussions of HIV-associated neurocognitive disorders.

ALCOHOL-RELATED, DRUG-RELATED, AND ADDICTIVE DISORDERS

Among HIV-infected individuals with or without hepatitis B or C, heavy drinking predicts HIV end-stage disease and mortality (DeLorenze et al., 2011; Joshi et al., 2011; Rosenthal et al., 2009). Prior to ART, the Multicenter AIDS Cohort Study found no association between alcohol use and HIV disease progression (Kaslow et al., 1989). However, post-ART availability, in one study of people living with HIV infection who had current or past alcohol problems and were prospectively assessed for up to 7 years, among individuals who were not on ART, heavy alcohol consumption was associated with a lower CD4 cell count but not with higher HIV viral load (Samet et al., 2007). In another study, among women who were on ART, heavy alcohol consumption was not associated with a lower CD4 cell count or higher HIV viral load (Ghebremichael et al., 2009). A patient's visit time, high viral load, and drug use were found to be predictors of alcohol use in women with HIV, which in turn was associated with depression and then HIV disease progression (Ghebremichael et al., 2009). Bing et al. (2001) found that patients in medical care for HIV had a rate of heavy drinking of 8%, almost twice that found in the general population.

The prevalence of current alcohol-related disorders among people with HIV infection has been estimated to range from 3% to 12% (Brown et al., 1992; Burnam et al., 2001; Dew et al., 1997; Ferrando et al., 1998; Galvan et al., 2002; Lopes et al., 2012; Rabkin et al., 1997; Sullivan et al., 2008), which is similar to the estimated 5–10% prevalence of current alcohol use disorders in the general population (Kessler et al., 1994; Regier et al., 1990).

Recreational drug use was found among 50% of people in medical care for HIV in the HCSUS study (Bing et al., 2001). Turning to the prevalence of current drug use disorders among HIV-infected individuals, the estimates vary from 2% to 19% (Bing et al., 2001; Brown et al., 1992; Dew et al., 1997; Ferrando et al., 1998; Lopes et al., 2012; Rabkin et al., 1997). The prevalence rate of current drug use disorder in the general population is about 2–3.6% (Kessler et al., 1994; Regier et al., 1990).

The HCSUS study also screened participants for the most severe form of drug use disorder: drug dependence. Here the rate was 2.6% in the previous 12 months. Specific drugs for which dependence had developed were not reported.

On the basis of these studies, it appears that the prevalence of current alcohol and other drug-related disorders is not different for people living with HIV compared with general-population estimates; however, lifetime prevalence for both alcohol- and other drug-related disorders does appear to be higher. Across studies, the lifetime prevalence of alcohol-related disorders for people with HIV was 22% to 64% (Dew et al., 1997; Ferrando et al., 1998; Rabkin, 1996) compared with a general-population prevalence of 14% (Regier et al., 1990) to 24% (Kessler et al., 1994). Similarly, the lifetime prevalence of drug-related disorders for people with HIV was 23% to 56% (Dew et al., 1997; Ferrando et al., 1998; Rabkin, 1996), whereas for the general population it was 6% (Regier et al., 1990) to 12% (Kessler et al., 1994). In a study of adults aged 50 and older, HIV was associated with a 20% rate of drug-related disorders in the past year (Beatie et al., 2015), which is consistent with previous reports of older adults with HIV infection (Justice et al., 2004).

Please see Chapter 14 for a more comprehensive and detailed discussion of addictive disorders in persons with HIV.

DEPRESSION, ANXIETY, AND STRESS DISORDERS

Depression, anxiety, and stress disorders are seen throughout the course of HIV infection with considerable comorbidity among them (McDaniel and Blalock, 2000). There is an increased likelihood of the emergence of symptoms during pivotal disease points (such as HIV antibody testing, declines in immune status, and occurrence of opportunistic infections). These common mental disorders are much more prevalent in people living with HIV infection than in the U.S. general population (Kessler et al., 1994). There may also be gender differences. Among the 70 men and 79 women with HIV infection in the NESARC study (Lopes et al., 2012), HIV-positive men had significantly greater odds of having any mood disorder (7.17) and any anxiety disorder (3.45) than HIV-positive women. Comparing prevalence of psychiatric disorders among those HIV infected with that of their HIV-negative counterparts, HIV-positive men had significantly greater odds of having any mood disorder (6.10), major depressive disorder/dysthymia (3.77), and any anxiety disorder (4.02). By contrast, HIV-positive women were not significantly more likely than HIV-negative women to have psychiatric disorders. As noted previously, however, this study had a very small sample size.

DEPRESSION

Depression, and more specifically major depression and persistent depressive disorder (dysthymia), is the most common reason for psychiatric referral among people with HIV infection (Strober et al., 1997) and the most common mental disorder among patients with HIV infection, with estimates of its current prevalence ranging from 7% to 67% (Bing et al., 2001; Ickovics et al., 2001; Kacanek et al., 2010; Lopes et al., 2012; McDaniel and Blalock, 2000; Morrison et al., 2002; Pence et al., 2006, 2012). Its prevalence is always greater than the general-population rate of 6–10% (Kessler, et al., 1994; Regier et al., 1990). Up to 85% of HIV-seropositive individuals report some depression symptoms (Stolar et al., 2005).

In the HCSUS study the baseline rate for a 12-month diagnosis of probable major depression using a brief screening instrument (the Composite International Diagnostic Interview-Short Form [CIDI-SF]) was 36%. At the first follow-up interview, using the same screening instrument, conducted approximately 8 months later the 12-month rate of probable major depression in the sample had dropped to 27% (Orlando et al., 2002). Full diagnostic interviews (CIDI) conducted shortly after the first follow-up on a subsample of patients, however, showed a 12-month rate of major depression of 19%, suggesting that the screen overestimated major depression rates. For dysthymia the rates were 27% on the baseline screen, 21% on the follow-up screen, but only 4% with a full diagnostic interview (Orlando et al., 2002). This study makes clear that some brief screening tools give much higher estimated rates of depressive disorders than those established by using more thorough diagnostic interviews.

A recent study examined the excess burden of depression among a nationally representative sample of more than 4,000 HIV-infected people receiving medical care in the United States and compared these rates to those for the general U.S. population (Do et al., 2014). Among people with HIV infection 12.4% had current major depression and 13.2% had other depression diagnoses, yielding 25.6% with any current depression. This was almost three times greater than rates in the general population, where 4.1% had major depression and 5.1% had other depression diagnoses for a 9.1% rate of any current depression (Do et al., 2014). This finding was replicated in data collected about active members of the U.S. Armed Services from 2001–2011 (Mirza et al., 2012). This study compared 1906 active service members with HIV and/or HSV2 infection to 19,060 service members who had neither of these infections (the referent group). Active service members with HIV infection were 2.9 times more likely to have a depression diagnosis than veterans who had neither HIV nor HSV2 infection (Mirza et al., 2012).

Risk factors that have been cited for depression among persons with HIV include female gender, prior history of depression, comorbid psychiatric disorders/problems (e.g., substance abuse, PTSD, generalized anxiety disorder, and lifetime attempted suicide), family history of psychiatric disorder, psychosocial impairment, unemployment, food insecurity, use of avoidance coping strategies, lack of social support, increasing negative life events, multiple losses, and HIV-related physical symptoms (Bradley et al., 2008; Cournos et al., 2005; Goodkin, 1996). Depression rates tend to be lower among community-based HIV-positive samples and are highest among people who inject drugs and among women.

But as already noted, and in striking departure from patterns of depression seen in the general population and in some of the other studies of HIV-positive populations, the NERSAC Wave 2 study found that HIV-positive men had significantly greater odds of having any mood disorder compared to HIV-positive women (7.17) or HIV-negative men (6.10) (Lopes et al., 2012).

Rates of depression may be higher among patients with more advanced HIV disease, particularly those hospitalized for medical illness. Thus clinicians working with patients with HIV/AIDS must consider underlying medical causes for depression, such as medication side effects, opportunistic disorders of the CNS, and endocrine disorders. A 2-year prospective study comparing men living with HIV infection to uninfected same risk-group controls found that the 2-year cumulative rate of a major depressive episode was about 40% in persons with symptomatic advanced illness compared to about 20% for asymptomatic individuals and for same risk-group controls (Atkinson et al., 2008), which was also higher than in the epidemiological community surveys, in which 6- to 12-month rates ranged from 6% to 10% (Kessler et al., 1994; Regier et al., 1990). In this same study neither HIV disease progression during 2-year follow-up nor the baseline presence of neurocognitive impairment, clinical brain imaging abnormality, or marked life adversity predicted a later major depressive episode (Atkinson et al., 2008). Rather, prior psychiatric history was the strongest predictor of future vulnerability.

The authors concluded that symptomatic HIV disease, but not HIV infection itself, increases intermediate-term risk of major depression. However, in other studies, while people with HIV infection were almost twice as likely as those who were HIV negative to be diagnosed with major depression, depression was equally prevalent in people with symptomatic and asymptomatic HIV infection (Chander et al., 2006; Ciesla and Roberts, 2001; Treisman et al., 1998, 2001).

Studies have shown that untreated depressive disorders increase HIV transmission risk behaviors (Bradley et al., 2008; Kelly et al., 1993), decrease immune status (Ickovics et al., 2001; Leserman et al., 2007), and decrease adherence to ART (Chesney, 2003; Horberg et al., 2008; Kacanek et al., 2010), which may result in decreased clinical effectiveness of ART and potential development of drug resistance (Bangsberg, 2008; Kozal et al., 2005). Thus, depression poses challenging barriers to effective medical care at multiple points along the continuum of care engagement and treatment (i.e., "HIV treatment cascade") (Pence et al., 2012). Untreated depression has been associated with a lower likelihood of receiving antiretrovirals (Nilsson Schönnesson et al., 2007; Wagner, 2002), with poor adherence (Ammassari et al., 2004; Kelly et al., 1993), and with increased morbidity (Bouhnik et al., 2005; Cook et al., 2004; Hartzell et al., 2008; Ironson et al., 2005) and mortality (Ickovics et al., 2001). Depression is a predictor of clinical progression independent of nonadherence behaviors (Bouhnik et al., 2005). Depression is frequently underdiagnosed and even when recognized is often poorly treated, particularly in primary medical settings where HIV/AIDS patients receive care (Asch et al., 2003; Cournos et al., 2005). Mounting evidence suggests that effectively treating depression in patients with HIV may reap benefits for their HIV treatment retention, ART adherence, and virological suppression and, therefore, for community viral load (Pence et al., 2012).

Please see Chapter 15 for a detailed discussion of depression in persons with HIV.

ANXIETY

Estimates of the prevalence of anxiety disorders in patients with HIV/AIDS range from almost negligible to as high as 40% (Blalock et al., 2005; Dew et al., 1997; Rabkin et al., 1997). In a study of adults aged 50 and older, HIV was associated with a 32% rate of anxiety disorders (Beatie et al., 2015), which is consistent with previous reports for older adults with HIV infection (Justice et al., 2004).

The rates vary for numerous reasons, including a host of psychosocial correlates and because anxiety frequently coexists with depression and substance use problems. Higher rates generally are seen as HIV illness progresses, and the presence of anxiety symptoms may increase HIV fatigue and physical functional limitations (Barroso et al., 2010).

Despite the wide range of prevalence estimates, a pattern emerged in the late 1990s: several studies showed a point prevalence of anxiety disorders in HIV-seropositive patients not significantly different from that of HIV-seronegative clinical comparison groups, even though lifetime rates are higher in the HIV clinical population than in the general population (Dew et al., 1997; Rabkin et al., 1997; Sewell, et al., 2000).

Using a brief screen (CIDI-SF), the HCSUS estimated the 12-month rate of generalized anxiety disorder (GAD) at 16%, a follow-up rate approximately 8 months later of 11%, and the rate using a full diagnostic interview (CIDI) shortly after the first follow-up of 4%. For panic disorder these rates were 13% at baseline, 11% at first follow-up, and 9% for the full diagnostic interview. The authors note that the brief screening instrument overestimated GAD but did well in providing an accurate 12-month rate for panic disorder (Orlando et al., 2002).

The NERSAC Wave 2 study found that HIV-positive men had a 12-month prevalence of 33% for any anxiety disorder, compared to 24% among HIV-positive women; HIV-negative men and women had 11% and 21% 12-month prevalence for any anxiety disorder, respectively (Lopes et al., 2012). The rate of panic disorder did not appear to be elevated above community norms. Mirza et al.'s study (2012) found that active service members of the U.S. Armed Forces who had HIV infection were twice as likely to have an anxiety disorder than active service members with neither HIV nor HSV2 infection.

Please see Chapter 18 for a detailed discussion of anxiety in persons with HIV.

POSTTRAUMATIC STRESS DISORDER

PTSD is a stress disorder that has received substantial attention from HIV researchers. The rate of PTSD among individuals infected with HIV varies across studies for reasons similar to those for other mental disorders (e.g., varying assessments, diagnostic criteria, symptomatology, sample size and characteristics) (Delahanty et al., 2004; Kelly et al., 1998; Safren et al., 2003). Diverse definitions of qualifying traumatic events or trauma indices (Breslau and Kessler, 2001), the traumatic histories of many of the most vulnerable groups affected by HIV, and the variability of traumatic events that surround those infected with HIV make establishing PTSD prevalence and comparison rates to the general populations a complex determination.

PTSD may precede an HIV diagnosis because of previously experienced traumatic events, or it may emerge post-HIV diagnosis as a result of the stress of being diagnosed with a life-threatening illness (Breslau and Kessler, 2001; Martin and Kagee, 2011) or subsequent challenges over the course of the HIV disease trajectory. Stresses include fears and worries about access to appropriate treatment, the welfare of dependents, stigma, discrimination, possible isolation, dying, traumatic events, loss of employment, and physical decline and disability (Carr and Gramling 2004; Kagee, 2008; Poindexter, 1997; Safren et al., 2003). As with HIV-negative populations, the level of PTSD among people living with HIV infection also has been found to be positively correlated with the total number of traumatic life events experienced (Katz and Nevid, 2005; Martinez et al., 2002). Further, PTSD comorbid with other mental disorders such as schizophrenia, schizoaffective disorder, and bipolar disorder can be an important predictor of HIV infection (Essock et al., 2003). Among people living

with HIV infection, greater psychological trauma and PTSD have been associated with several adverse health outcomes, including AIDS-defining illnesses or mortality, substance use, high-risk behaviors, and decreased medication adherence (Kalichman et al., 2002; Mugavero et al., 2007; Whetten et al., 2006).

Available studies suggest that the lifetime prevalence of PTSD among people living with HIV infection ranges from 30% to 64% (Brief et al., 2004; Cohen et al., 2002; Kelly et al., 1998; Kimerling et al., 1999; Martinez et al., 2002; Safren et al., 2003) and is higher than in the general population, 7.8% (5–6% in males and 10–11% in females), in the United States (Breslau et al., 1991; Kessler et al., 1995).

Please see Chapter 17 for a detailed discussion of PTSD in persons with HIV.

BIPOLAR DISORDER

Cases of mania were reported in the context of severe HIV-associated neurocognitive impairment early in the HIV epidemic in the United States, and such cases are still being documented in sub-Saharan Africa (Nakimuli-Mpungu et al., 2009). This has often been referred to as *secondary mania* (Nakimuli-Mpungu et al., 2009). Such cases are less common in the United States now that earlier and more effective treatment for HIV is available.

There are few studies documenting rates of bipolar disorder among people living with HIV infection in the United States. In one study conducted with data collected about active service members in the U.S. Armed Forces from 2001 to 2011, those with HIV infection were 3.27 times as likely to have bipolar disorder as service members who were not HIV infected (Mirza et al., 2012). In the handful of other studies, the prevalence of bipolar disorder among HIV-infected persons ranged from 2.6% to 9.1% (Atkinson et al., 2005; Druss et al., 2007; Robins et al., 1988).

Bipolar disorder affects approximately 2% of the general population [Merikangas et al., 2007). Therefore, bipolar disorder and HIV infection co-occur at higher rates than would be expected in the general population. The prevalence of HIV is particularly elevated among persons with bipolar disorder, perhaps approaching 10% Beyer et al., 2005, 2007; Cournos and McKinnon, 1997; Evans and Charney, 2003; Walkup et al., 1999).

Please see Chapter 15 for a detailed discussion of bipolar disorder in persons with HIV.

PSYCHOSIS

An overview of the literature suggests that the pathophysiology of psychosis in HIV infection is complex, and a multifactorial etiology of psychotic symptoms is likely in many cases. Psychotic symptoms may be part of a major depressive disorder, schizophrenia, mania, obsessive-compulsive disorder (OCD), or medication side effects or may be secondary to drug or alcohol use, CNS complications, medications, or a wide array of systemic physical illnesses. There are many reports of psychotic symptoms in HIV-infected persons in the absence of concurrent harmful substance use, iatrogenic causes, evidence of opportunistic infection or neoplasm, or detectable cognitive impairment. A common clinical feature of new-onset psychosis in HIV-infected patients is the acute onset of symptoms. Estimates of the prevalence of new-onset psychosis in HIV-infected patients vary widely, from less than 0.5% to 15% (Boccellari and Dilley, 1992; Halstead et al., 1988; Harris et al., 1991; Navia et al., 1986; Prier et al., 1991); post-ART studies indicate a prevalence closer to 3% for new-onset psychosis (Alciati et al., 2001; de Ronchi et al., 2000). New-onset psychotic disorder is found most often in late stages of the disease, particularly in subjects with neurocognitive disorders (Gallego et al., 2011; Sewell, 1996; Walkup et al., 1999). The NERSAC Wave 2 study found that HIV-positive men had a 12-month prevalence of 9.2% compared to 3.4% among HIV-positive women for any psychotic disorder in the last 12 months; HIV-negative men and women had a 0.6% 12-month prevalence for any psychotic disorder (Lopes et al., 2012). In one study, HIV/AIDS was the leading cause of death among young semirural New York patients experiencing their first hospitalization for a psychotic episode (Susser et al., 1997). Among active service members in the U.S. Armed Forces from 2001–2011, those with HIV infection were 6.22 times as likely to have schizophrenia or another psychotic disorder as service members who were not infected with HIV or HSV2 (Mirza et al., 2012).

Please see Chapter 19 for a detailed discussion of psychosis in persons with HIV.

PERSONALITY DISORDERS

Personality disorders can be detected in up to 30% of HIV-positive persons (Perkins et al., 1993). Borderline, antisocial, dependent, histrionic, and disorders not otherwise specified are, in this order, the most frequent personality disorders among HIV-positive individuals (Gallego et al., 2011; Jacobsberg et al., 1995; Johnson et al., 1995; Perkins et al., 1993). Evidence suggests that the presence of pathological personality traits or disorders may potentiate risk of HIV infection and transmission, adversely affect adherence to HIV treatments, and contribute to disease progression (Disney et al., 2006; Hansen et al., 2009). The NERSAC Wave 2 study found that, among a small sample of HIV-positive people, HIV-positive men had significantly greater odds of having any personality disorder (2.66) than HIV-positive women: a 43% 12-month prevalence among men compared to 19% for women. Comparing prevalence among those HIV infected with their HIV-negative counterparts, HIV-positive men had significantly greater odds of having any personality disorder (2.50), whereas an increased prevalence was not found among HIV-positive women; HIV-negative men and women had 23% and 20% 12-month prevalence for any personality disorder, respectively (Lopes et al., 2012). With regard to specific diagnoses, HIV-positive men and women had the following 12-month prevalence rates: schizotypal (16% vs. 8%), schizoid (14% vs. 7%), paranoid (15% vs. 6%), borderline (19% vs. 9.8%), narcissistic (15% vs. 7%), and avoidant (13% vs. 11%) (Lopes et al., 2012).

Please see Chapter 20 for a detailed discussion of personality disorders in persons with HIV.

RATES OF HIV INFECTION AMONG PEOPLE LIVING WITH PSYCHIATRIC DISORDERS

RATES OF HIV INFECTION AMONG PEOPLE WITH ALCOHOL AND OTHER SUBSTANCE USE DISORDERS

The extent to which addiction fuels injection drug use is the most obvious link between psychiatric disorders and HIV transmission. Kral et al. (1998) estimated an overall HIV infection rate among American who inject drugs of 13%, with wide geographic variability between cities in the East (where rates exceeded 40%) and in the Midwest and West (where rates generally were under 5%). Yet many studies of this population did not obtain alcohol and other drug (AOD) use disorder diagnoses, so summarizing across studies to generalize rates of HIV infection for specific diagnostic groups is methodologically problematic. People discharged from general hospitals who had documented AOD use disorders were twice as likely to be HIV infected as those without AOD use disorders (Stoskopf et al., 2001). Studies of people admitted to treatment for primary alcohol abuse or dependence reported HIV infection rates of 5% to 10.3% (Avins et al., 1994; Mahler et al., 1994; Woods et al., 2000), and these rates are 10 to 20 times higher than those among the general population (McQuillan et al., 1997).

More recent studies of AOD use disorders among people with HIV are scarce, although DeLorenze et al. (2011) investigated mortality after diagnosis of psychiatric disorders and co-occurring substance use disorders among HIV-infected patients in the Kaiser Permanente Northern California (KPNC) health plan over a 12-year period. Among the 9,757 HIV-infected patients in the study sample, 25.4% (n = 2,472) had received a psychiatric diagnosis, and 25.5% (n = 2,489) had been diagnosed with substance use disorder; 1,180 (12.1%) patients had received both psychiatric and substance use problem diagnoses. The prevalence of specific psychiatric disorders among the 2,472 patients who received a psychiatric diagnosis was major depression (81.1%), panic disorder (17.1%), bipolar disorder (14.2%), and anorexia/bulimia (8.1%). Multiple drug dependence/abuse (41.0%) and alcohol alone (32.7%) were the most prevalent substance use diagnoses in the subpopulation with substance use disorders. Other single substance use diagnoses included cannabis (8.5%), amphetamines (7.7%), cocaine (3.9%), opioids (1.9%), alcohol or drug psychoses (1.8%), and unspecified (18.8%); 47.6% had a single substance use diagnosis. In contrast, a study of the KPNC general health plan membership found that 10.8% were diagnosed with depression and 2.1% were diagnosed with a substance use disorder, based on medical records (Satre et al., 2010).

Please see Chapter 14 for a detailed discussion of addictive disorders in persons with HIV.

RATES OF HIV INFECTION AMONG PEOPLE WITH SEVERE MENTAL ILLNESS

Most studies of rates of HIV infection in psychiatric populations focus on people with severe mental illness (SMI). *Severe mental illness* is a term used to describe a heterogeneous group of psychiatric conditions, most commonly including schizophrenia, bipolar disorder, and major depression with psychotic features (Lagios and Deane, 2007) that are characterized by acute or persistent duration, functional disability, and, typically, a significant history of hospitalization and/or maintenance medication (McKinnon and Rosner, 2000).

Among adults in treatment for such conditions in the United States, infection with HIV has been documented in seroprevalence studies at rates of 0% to 29% (Table 3.2). Rates found in seroprevalence studies where blood was drawn for HIV antibody testing generally are more reliable than those found in prevalence studies that relied on patient knowledge of their HIV status or on what had been recorded in the medical record; still, generalizability of seroprevalence to other patient populations is limited.

Another study documented a 1.2% HIV infection rate among adult patients attending a system of psychiatric outpatient clinics (N = 11,284 individuals), approximately four times the occurrence of HIV infection in the general adult population of the United States at the time (Beyer et al., 2007). The major psychiatric diagnostic categories with a high prevalence of HIV infection were substance abuse disorders (5%), personality disorders (3.1%), bipolar disorders (2.6%), and PTSD (2.1%) (Beyer et al., 2007). Patients with unipolar depressive disorders had a HIV prevalence of 1.4%. The authors estimated that those with personality disorders ($p < 0.001$), bipolar disorder ($p < 0.001$), PTSD ($p < 0.05$), or depressive disorders ($p < 0.05$) had significantly higher risk of HIV infection than the general psychiatric population (and even greater risk than the general adult U.S. population). One assumption is that HIV rates in personality and bipolar disorders would be elevated because of the impulse-control problems involved in the diseases, whereas depression and PTSD rates may be elevated because of factors involved in HIV exposure or the disease itself. Alternatively, it is possible that these diseases may "self-select" for comorbid infections, since the risk of substance abuse has long been noted to be high in these disorders and substance use is in turn associated with increased risk for a variety of infections, including HIV. However, the impact of substance abuse was different in each of these categories. Patients with bipolar disorder, PTSD, and personality disorders had a much lower substance abuse/HIV risk ratio (1.7, 2.6, and 3.1, respectively) compared with the full sample. This suggests that comorbid substance abuse, though still a significant risk factor, was less important in these conditions than in other psychiatric diagnoses. The highest risk ratio (6.4) was for depressive disorders, which suggests that, in this group, substance abuse comorbidity played a much more significant role in HIV risk.

Taken together, available studies provide an evidence base regarding differences in HIV infection among those with SMI

Table 3.2. HIV SEROPREVALENCE AMONG PSYCHIATRIC PATIENTS IN THE UNITED STATES

STUDY	TESTING METHOD	U.S. REGION	SAMPLE	*N*	RATE OF HIV INFECTION
Clair et al., 1989	Blood	South Carolina	Psychiatric facility inpatients	1,228	0.3%
Hatem et al., 1990	Blood	Massachusetts	Psychiatric facility inpatients	163	1.8%
Cournos et al., 1991	Blood	New York City	Acute-care inpatient	451	5.5%
Volavka et al., 1991	Blood	New York City	Psychiatric hospital inpatients	515	8.9%
Lee et al., 1992	Blood	New York City	Psychiatric inpatient unit of hospital	135	16.3%
Sacks et al., 1992	Blood	New York City	Inpatient	350	7.1%
Empfield et al., 1993	Blood	New York City	Inpatients homeless psychiatric unit	203	6.4%
Meyer et al., 1993	Blood	New York City	Long-stay psychiatric inpatient unit	199	4.0%
Susser et al., 1993	Blood	New York City	Homeless men's shelter psychiatric program	62	19.4%
Cournos et al., 1994	Blood	New York City	Psychiatric facility inpatients	971	5.2%
Silberstein et al., 1994	Blood	New York City	Municipal hospital dual-diagnosis inpatients	118	22.9%
Stewart et al., 1994	Blood	Baltimore, Maryland	Psychiatric hospital inpatient/outpatient new admissions	533	5.8%
Meyer et al., 1995	Blood	New York City	Inpatients homeless psychiatric unit	87	5.8%
Schwartz-Watts et al., 1995	Chart	Columbia, South Carolina	Forensic inpatient unit for pretrial detainees	220	5.5%
Doyle and Labbate, 1997	Chart	National	Military hospital new-onset psychosis	246	0
Susser et al., 1997	Chart	Suffolk County, New York	First-admission psychiatric inpatients referred from 12 hospitals	320	3.8%
Krakow et al., 1998	Blood	New York City	Municipal hospital dual-diagnosis unit inpatients	113	19.0%
Rosenberg et al., 2001	Blood	Connecticut, Maryland, New Hampshire, North Carolina	Inpatient/outpatient treatment recipients in public mental health systems or VA	931 CT = 158 MD = 133 NH = 288 NC (VA) = 185	3.1%
Blank et al., 2002	Chart	Philadelphia, Pennsylvania	Medicaid and welfare recipients with schizophrenia spectrum disorder or major affective disorder	391,454	1.8%

(*continued*)

Table 3.2 CONTINUED

STUDY	TESTING METHOD	U.S. REGION	SAMPLE	*N*	RATE OF HIV INFECTION
Klinkenberg et al., 2003	Blood	St. Louis, Missouri	Homeless outpatient with SMI+SUD	172	6.2%
Beyer et al., 2005	chart	Durham, North Carolina	Outpatient psychiatric clinic patients with bipolar disorder	1,379	2.8%
Pirl et al., 2005	Chart	Boston, Massachusetts	Psychiatric hospital inpatients	62	29.0%
Beyer et al., 2007	Chart	Durham, North Carolina	General hospital psychiatric outpatients	11,284	1.2%
Himelhoch et al., 2007	Chart	National	Inpatient/outpatient veterans with versus without SMI	SMI: 191,625 No SMI: 67,965	SMI: 1.0% No SMI: 0.5%
Rothbard et al., 2009	Chart and blood	Philadelphia, Pennsylvania	Inpatient psychiatric units	588	10.0%
Walkup et al., 2010	Chart	California, Florida, Georgia, Illinois, New Jersey, New York, Ohio, Texas	Medicaid and Medicare claims from recipients with schizophrenia	1,000,000+	1.8%
Himelhoch et al., 2011	Blood	Baltimore metro area, Maryland	Outpatients in public mental health treatment settings with SMI+SUD	153	6.1%
Jackson-Malik et al., 2011	Saliva	Philadelphia, Pennsylvania	Veterans with a history of mental health and substance abuse diagnoses, residing in assisted living facilities	64	3.1%
Walkup et al., 2011	Chart	California, Florida, Georgia, Illinois, New Jersey, New York, Ohio, Texas	Medicaid beneficiaries with schizophrenia treated for HIV	Not reported	1.6%
Prince et al., 2012	Chart	California, Florida, Georgia, Illinois, New Jersey, New York, Ohio, Texas	Medicaid beneficiaries who were without HIV in 2001 but diagnosed with HIV 2002–2004	6,417,676 SMI: 443,994 SMI+SUD: 72,752 MDD: 130,788 BPD: 55,582 SCH: 184,872	SMI: 0.7% SMI+SUD: 2.0% MDD: 0.6% BPD: 0.6% SCH: 0.5%
Blank et al., 2014	Saliva	Philadelphia, Pennsylvania and Baltimore, Maryland	University-based inpatient psychiatric units (287), intensive case-management programs (273), community mental health centers (501)	1,061	4.8% Inpatient = 5.9% ICM = 5.1% CMHC = 4.0% Baltimore = 5.9% Philadelphia = 3.9%

BPD, bipolar disorder; CMHC, community mental health center, ICM, intensive case management; MDD, major depressive disorder; SCH, schizophrenia; SMI, severe mental illness; SUD, substance use disorder; VA, Veterans Affairs.

that are based on geographic location, subpopulation characteristics, and risk behaviors. For instance, HIV rates generally are lower among veterans than among homeless populations and those who have injection-drug use histories. A summary of rates among different subpopulations, some of which are overlapping, is presented next.

Geographic location. One study directly compared HIV infection rates among those with SMI in urban versus other locations, with rates varying from 1.7% in rural areas to 5% in metropolitan areas (Brunette et al., 1999; Rosenberg et al., 2001). Many environmental factors associated with a greater prevalence of HIV/AIDS risk behaviors and infection, including poverty, unstable housing, and injection drug use, are more common in some urban neighborhoods (Carey et al., 1997; McKinnon et al., 2002; McKinnon and Rosner, 2000).

Treatment setting. Psychiatric inpatients and outpatients compared in one study showed different HIV infection rates, with inpatients infected at higher rates than those in intensive case-management programs or community mental health centers (Blank et al., 2014).

Forensic. One study among pretrial detainees showed a 5.5% rate of HIV infection (Schwartz-Watts et al., 1995).

Homeless. In one study homeless people with concurrent SMI and substance use disorders had a 6.2% HIV rate (Klinkenberg et al., 2003). Among homeless people with severe mental illness who may or may not have also had a secondary substance use disorder, rates of HIV have ranged from 5.8% to 19.4% (Empfield et al., 1993; Meyer et al., 1993; Susser et al., 1993).

Veterans. HIV prevalence among American veterans with SMI is 1% (compared to veterans without SMI whose infection rate is 0.5%) (Himelhoch et al., 2007). In a study of veterans with a history of mental health and substance abuse diagnoses who are residing in assisted living facilities, the rate of HIV infection was 3.1% (Jackson-Malik et al., 2011).

Men who have sex with men. Approximately one in four of those with a history of male–male sex were HIV positive (Cournos and McKinnon, 1997).

Dual diagnosis. The highest rates of infection are among those dually diagnosed with SMI and substance-related disorders, with rates ranging from 6.1% to 22.9% (Himelhoch et al., 2011; Krakow et al., 1998; Prince et al., 2012; Silberstein et al., 1994).

First-episode/onset psychosis. Two studies examined rates of HIV infection among people having their first episode of psychosis or first psychiatric hospitalization, with rates of 0 to 3.8% (Doyle and Labbate, 1997; Susser et al., 1997).

These studies provide dramatic evidence that a main driver of the HIV epidemic among people with SMI is substance use, even for sexual transmission, so prevention of HIV infection among people with SMI, half of whom are likely to develop substance use disorders, should start with the onset of the first disorder (Table 3.3) by ensuring adequate treatment and appropriate prevention of the secondary disorder.

Table 3.3. **SUBSTANCE USE AND OTHER MENTAL DISORDER COMORBIDITY ESTIMATES FROM THE U.S. NATIONAL COMORBIDITY STUDY**

- **51% of people with lifetime alcohol or other drug (AOD) use disorders met criteria for at least one other lifetime mental disorder, and vice versa.**
- **15% of people with a mental disorder in the past year also met criteria for an AOD disorder in the past year.**
- **43% of people with an AOD in the past year also met criteria for another mental disorder in the past year.**

RESPONDING TO COMORBIDITIES AMONG PEOPLE AFFECTED BY HIV

More often than not, HIV is syndemic with additional medical conditions such as hepatitis C and other parenterally or sexually transmitted infections. These medical conditions can be associated with neuropsychiatric complications. Other psychiatric comorbidities are also common and multiple psychiatric disorders may be present.

The National Comorbidity Study (Kessler et al., 1996) showed that substance use disorders are highly comorbid with other psychiatric disorders (e.g., bipolar disorder, depression, psychotic disorders, anxiety disorders, and antisocial and borderline personality disorders). Possible explanations for this have been propounded, including that one disorder is a marker for the other disorder, that mental illness leads to self-medication with alcohol and other drugs, and that substance use or withdrawal leads to symptoms of mental illness. Often it is impossible to know which disorder came first or is primary, although onset of non–substance use mental disorders appears to occur at a younger age than that for addictive disorders (Kessler et al., 1996). In clinical settings of any kind it is prudent to screen patients with one type of disorder for the other type of disorder.

Those individuals with dual psychiatric and alcohol/substance use disorders may be at higher risk for HIV infection than those with either disorder alone (Ferrando and Batki, 2000), and these disorders are likely to be found together across populations of HIV-infected people. The HCSUS study established estimates of the prevalence of co-occurring psychiatric symptoms and either or both drug dependence symptoms or heavy drinking: 13% of their sample had co-occurring psychiatric symptoms and either or both drug dependence symptoms or heavy drinking (Galvan et al., 2003). Sixty-nine percent of those with a substance-related condition also had psychiatric symptoms; 27% of those with psychiatric symptoms also had a substance-related condition.

In the United States, as in most other places in the world, psychiatric disorders are common and undertreated in HIV patients and health disparities are common. For instance, in the HCSUS sample significant disparities were found between African Americans and others in the prescription of medication for depression (Table 3.4).

The rates of mental disorders encountered by HIV/AIDS care clinicians warrant our attention if we are to strengthen both the evidence base from which treatment and prevention

Table 3.4. **HIV COST AND SERVICES UTILIZATION STUDY: PSYCHOTROPIC MEDICATIONS AMONG 1,489 HIV-POSITIVE MEDICAL PATIENTS**

- **27% took psychotropic medication:**
  - **21% antidepressants**
  - **17% anxiolytics**
  - **5% antipsychotics**
  - **3% psychostimulants**
- **About half of patients with depressive disorders did not receive antidepressants; African Americans were overrepresented.**

planning can be sustainably implemented and the quality of care individuals receive for their comorbid conditions. Addressing mental disorders as part of HIV care and treatment must be seen in the larger context of the mental health treatment gap—the proportion of persons who need but do not receive care. This gap is large for both severe and common mental disorders worldwide (Lopez et al., 2006; Prince et al., 2007). The diagnosis and treatment of mental disorders has been largely absent despite the fact that the World Health Organization has issued numerous reports documenting that mental illnesses are among the world's most disabling illnesses and account for 13% of the total global burden of disease (Chander et al., 2006; Demyttenaere et al., 2004). In the United States and other high-income countries there is a 35–50% treatment gap for mental disorders.

Historically, service delivery systems (medical care, mental health care, alcohol and other substance use treatment) were structured to work separately (due to different funding streams), and efforts to navigate multiple systems failed (Messeri et al., 2002; Satriano et al., 2007; Staab and Evans, 2001). In our rapidly changing healthcare environment, the current focus on integrated care, including under the U.S. Affordable Care Act, is now shifting more toward integrating both mental health care and HIV care into larger primary care systems. Time will tell how effective these changes will be for people living with HIV infection.

CONCLUSIONS

Although the rates vary, the bulk of the available evidence shows that people living with HIV infection in the United States have rates of mental disorders that are considerably higher than for the general population, and that mental disorders are associated with a multitude of negative outcomes. Despite incredible scientific advances, the absence of a strong focus on mental disorders remains a glaring omission in our progress on HIV prevention, care, and treatment, especially for the special populations that most need these services. Attention to mental disorders has always been a struggle to achieve in healthcare, but advocacy efforts have led to some improvements in this domain, and further progress is both necessary and achievable. Taking the lead from the subspecialty of psychosomatic medicine (previously consultation-liaison psychiatry), the field of HIV medicine is more advanced than many other branches of medicine in integrating mental health care into healthcare, but mental health professionals have valuable insights, expertise, and experiences to contribute to larger efforts to integrate mental health care into primary care for people living with HIV.

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4.

GLOBAL ASPECTS OF THE HIV PANDEMIC

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While HIV/AIDS is a global epidemic, the nature of the illness and its effects on the people living with it varies across regions and is deeply affected by the stigma of HIV and its associated risk behaviors, socioeconomic and gender inequalities, the reach and capacity of local health systems, and cultural factors, among other influences. This chapter explores the current state of the epidemic in four regions: sub-Saharan Africa, Asia-Pacific, Europe, and the Americas.

The chapter begins with an exploration of HIV/AIDS in the hardest-hit region of the world, sub-Saharan Africa, which bears a disproportionate share of the global burden with more than two-thirds of all people living with HIV globally (Figure 4.1). Even within sub-Saharan Africa, the disease burden and epidemiological characteristics differ across countries, heavily concentrating in southern and eastern Africa. Encouragingly, much progress has been made in recent years, with the rate of new HIV infections decreasing in 25 sub-Saharan African countries by 50% between 2001 and 2011. However, HIV has still continued to spread faster than its treatment in this part of the world, and despite the achievements in the past decade, many challenges remain.

At the same time, there have been tremendous advances in access to antiretroviral treatment (ART) in sub-Saharan Africa, especially in the past decade, with more than 12 million people having received life-saving ART in Africa. In general, scale-up of ART has resulted in improved life expectancy in HIV-positive individuals in sub-Saharan Africa, as well as reduced secondary sexual transmission and reduced HIV incidence. Moreover, scale-up of prevention of mother-to-child transmission (PMTCT) has resulted in a dramatic decrease in vertical transmission. Besides ART scale-up, efforts to focus on prevention, including male circumcision, pre-exposure prophylaxis (PrEP), and vaginal microbicides, are also on the rise in sub-Saharan Africa, although these efforts have shown slower progress than increasing access to ART. The authors of this section stress the need for ART rollout and HIV prevention programs to be critically scaled up among key populations in Africa, in particular men who have sex with men (MSM), sex workers, vulnerable youth, and people who inject drugs (PWID).

The remaining challenges in Africa are strongly related to more general systemic problems in this part of the world, namely poverty and inequity, including transportation barriers, health worker shortages, and lack of access to viral load testing. Also, new challenges for African clinicians and health systems result from the changing face of the epidemic due to increasing survival on ART and aging of the HIV population, with its associated multimorbidities. Finally, the burden of HIV is not limited to the effects of the illness itself. Mental illness and comorbid chronic diseases are as much a concern in the African epidemic as in other parts of the world. With the many advances in controlling the HIV epidemic in Africa come many challenges, some old and some new. Political will, sufficient funding, health system improvements, and more effective ways of overcoming stigma will be needed to cope with the current and emerging challenges associated with the HIV epidemic in this region of the world.

In contrast, the epidemic in the Asia-Pacific region seems to be in a dynamic equilibrium that is rapidly evolving, with increases in numbers of people living with HIV in the region and decreases in newly infected individuals. However, these aggregate statistics obscure the considerable variation that exists subregionally. A more accurate perspective is gained from dividing the region into five subregions, one with a declining epidemic, one with a maturing epidemic, one with an expanding epidemic, one with a latent epidemic, and one a low-prevalence area. In this area, the epidemic is most concentrated in particular groups, including transgender individuals, MSM, female sex workers, and PWID. To further complicate things, large countries in the region, including China, India, and Indonesia, show considerable variations in the nature and prevalence of the epidemic even within their own borders.

Stigma is the major barrier to HIV prevention and treatment, as is lack of proper linkages to care and community-based HIV treatment. Many countries in this region still depend heavily on international donors to fund HIV treatment programs, although rapid economic development in places such as China has altered this profile slightly. More work is needed not only to understand the nuanced barriers

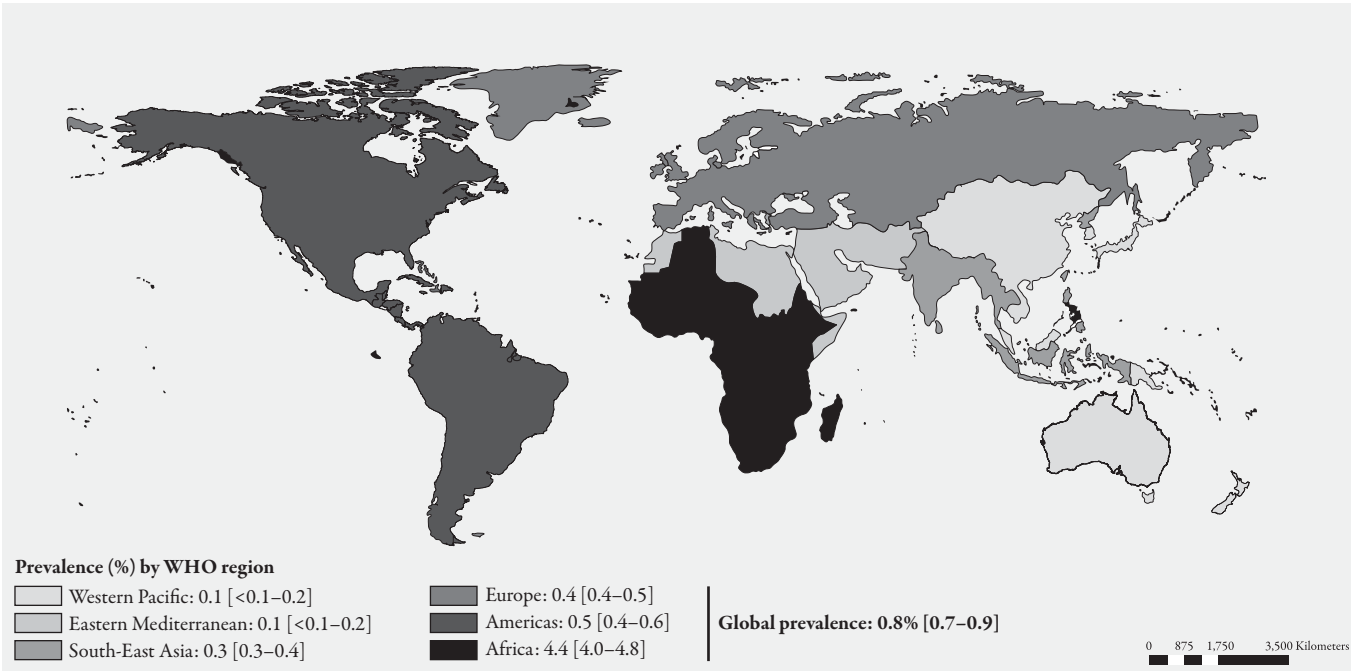

Figure 4.1. Adult HIV prevalence (15–49 years) 2015, globally, by WHO region.
SOURCE: http://www.who.int/gho/hiv/hiv_013.jpg?ua=1. Accessed January 3, 2017.

and challenges in different subpopulations within the very large and diverse Asia-Pacific region but also to strengthen health systems and reduce stigma and discrimination to ensure that at-risk individuals are receiving the prevention and treatment services they need.

In Europe, the epidemic is as diverse as the population with a clear division between Eastern and Western European countries. Although ART has led to great advances in health in this region, late identification of illness is a ubiquitous problem across all the countries of the European Union, particularly in the East. Stigma and discrimination makes it difficult for MSM to seek treatment, especially in Eastern Europe. Of particular relevance, migrant populations from high–HIV endemic countries are a significant part of the European epidemic, and migrants face inequity, stigma, and increasing barriers to access health care. The authors of this section note the considerable mental health challenges for vertically infected HIV-positive adolescents in Europe, who represent a small, albeit significant, group.

The epidemic in the United States has changed a lot over time, and the country is faced with a situation in which rates of new HIV infection have dropped among certain groups but continue to rise among others. In particular, African Americans and, to some extent, other minority groups as well as MSM, are key vulnerable populations. Given the increasing availability and efficacy of treatment for HIV, the number of people living with HIV in the United States continues to grow, and is now estimated at 1.2 million. The high prevalence of the infection creates an increased opportunity for transmission, making prevention and testing key strategies to reduce incidence. Addressing disparities in access to healthcare, increased attention to targeted prevention, and attending to the social determinants of health remain vital strategies in controlling the epidemic in the United States.

In Canada, the number of PLHIV has increased over the last few years, as advances in treatment have led to longer lifespans for PLHIV. Overall, the incidence of new HIV infections has decreased over the last 30 years, although some vulnerable populations, particularly the Aboriginal population, experience higher rates of HIV infection.

The epidemic is also extremely varied across Latin American, South American, and Central American countries. Some countries, such as Mexico, have experienced significant declines in rates of new infections in recent years, while others, such as Brazil, have seen increases. Once again, in these regions, the impact of the epidemic varies across demographic groups, with MSM, sex workers, and transgender people showing the highest rates of new infection.

While the HIV epidemic and its accompanying mental health issues are incredibly diverse across and within regions examined in this chapter, it is also important to recognize some striking similarities that cross cultural and geographic lines. Almost universally, HIV-positive individuals face serious stigma and discrimination that can make access to treatment difficult. In addition, while ART has been the most significant factor in the reduction of HIV-related deaths, too little attention is paid to preventive efforts as well as to the social circumstances associated with the illness across the globe. A global effort that simultaneously recognizes the common, underlying problems still facing HIV-positive individuals worldwide and takes into account the nuances in the different manifestations of the epidemic in different regions and populations around the world is absolutely essential to make progress against this disease.

HIV AIDS IN AFRICA

Emilio Letang and Francine Cournos

THE BURDEN OF HIV/AIDS IN SUB-SAHARAN AFRICA

Since the first AIDS cases were reported in California 36 years ago (Centers for Disease Control and Prevention [CDC], 1981), HIV has relentlessly spread, to become one of the worst epidemics in human history. All areas of the globe have been affected, but the burden of disease has dramatically concentrated among the poorest countries in the world, particularly those in sub-Saharan Africa (SSA). Despite the efforts made in the last decade, which have resulted in a stabilization of the epidemic in the region, SSA continues to bear a disproportionate share of the global HIV burden (UNAIDS, 2016).

Declines in new HIV infections among adults have slowed alarmingly in recent years, with the estimated annual number of new infections among adults remaining nearly static at about 2.1 million [1.8 million–2.4 million] in 2015. In 2015, an estimated 36.7 million (34.0 million–39.8 million) people were living with HIV (PLHIV) worldwide, with more than half—51.2%, or 19.0 million (17.7 million–20.5 million)—in sub-Saharan Africa (UNAIDS 2016). HIV prevalence in SSA in 2015 was higher than in any other area of the world, including the Caribbean, Asia, Eastern Europe, Western and Central Europe, and North America (UNAIDS, 2016). New infections and AIDS-related deaths were also disproportionately concentrated in SSA in 2012, accounting for 69% (1.8 million) of the 2.3 million new infections and 70% (1.2 million) of the 1.7 million AIDS-related deaths (UNAIDS, 2013a).

The epidemics in SSA differ greatly among countries, with southern Africa most heavily affected. Thirty-four percent of all people living with HIV worldwide reside in 10 southern African countries: Angola, Botswana, Lesotho, Malawi, Mozambique, Namibia, South Africa, Swaziland, Zambia, and Zimbabwe (UNAIDS, 2013a). South Africa has experienced one of the fastest growing epidemics globally, and in 2012 it was home to 6.4 million PLHIV in a population of approximately 52 million, up from an estimated 4 million in 2002 (Shisana, 2013; Stats-SA, 2010, 2013; UNAIDS, 2010, 2013a; United Nations, Population Division, 2015). In turn, Nigeria had 3.4 million PLHIV, Kenya 1.6 million, Tanzania 1.5 million, Uganda and Mozambique 1.4 million each, Zimbabwe 1.2 million, and Zambia and Malawi 1 million each, whereas Ethiopia (790,000), Ghana (230,000), and Lesotho (320,000) had considerably smaller numbers of PLHIV (UNAIDS, 2013a).

Encouragingly, the overall growth of the epidemic appears to have stabilized worldwide as well as in most of the countries in southern and eastern Africa. The rate of new HIV infections decreased in 25 sub-Saharan African countries by 50% between 2001 and 2011, with further declines in 2012, including all countries mentioned except for Lesotho and Angola, where the epidemic remains stable (UNAIDS, 2013b). In addition, the remarkable scale-up of ART in resource-limited settings (RLS) has resulted in a reduction of AIDS-related annual mortality in the region during the last decade. In the world's most affected region, eastern and southern Africa, the number of people on treatment has more than doubled since 2010, reaching nearly 10.3 million people. AIDS-related deaths in the region have decreased by 36% since 2010 (UNAIDS, 2016).

However, HIV has continued to spread faster than its treatment, and in 2010 it was estimated that for every two patients who started ART, five to six new infections occurred (World Health Organization [WHO], 2010a). Also, new infections outnumber AIDS-related deaths as a result of increased life expectancy on ART, so the number of PLHIV in Africa has increased by nearly one third (31%) in the last decade (UNAIDS, 2013a). Many challenges persist as HIV infection continues to be associated with high rates of morbidity and mortality, and HIV incidence remains unacceptably high (UNAIDS, 2013a). In a model using South African data, it was estimated that, if incidence rates were maintained constant at the rates reported in 2008, 40–50% of 15-year-olds would become HIV infected by age 60 (Johnson et al., 2012). Importantly, the consequences of this epidemic extend beyond the individual level and include impacts on education, industry, agriculture, transport, human resources, and the economy in general, with decades of economic development having been rolled back (Dixon et al., 2002; Urassa et al., 2001).

ART SCALE-UP PROGRAMS IN SUB-SAHARAN AFRICA AND IMPACT

The HIV epidemic has mobilized a tremendous political, financial, and human response, both globally and in SSA. Important initiatives include the World Bank Multi-Country AIDS program (1999); the United Nations Millennium Declaration (United Nations [UN], 2000) in 2000 and corresponding goals report in 2010 (UN, 2010; UNAIDS, 2016); the UN General Assembly Special Session on AIDS in 2001; the creation of the Global Fund to Fight AIDS, Tuberculosis, and Malaria (GFATM) in 2002; the adoption by the U.S. government of the President's Emergency Plan for AIDS Relief (PEPFAR) in 2003; and the 3 by 5 initiative launched in 2003 by the World Health Organization (WHO) and the Joint United Nations Program on HIV/AIDS (UNAIDS; WHO, 2003). Global expenditures for the HIV epidemic increased from 3.8 billion U.S. dollars in 2001 to 18.9 billion U.S. dollars in 2012 (UNAIDS, 2013a). Between 2000 and 2011, 51.6 billion U.S. dollars from development assistance for health (DAH) resources have been spent in HIV programs in low- and middle-income countries (Institute for Health Metrics and Evaluation, 2014).

Before ART became available in SSA, HIV infection resulted in premature death for most infected people (Morgan and Whitworth, 2001). Increased international funding, coupled with a dramatic reduction in ART prices about a decade ago (Badri et al., 2006), has resulted in previously unimaginable access to ART, prevention services, and evidence-based care interventions for PLHIV in Africa (Reynolds and Quinn, 2010). At the end of 2015, more than 15 million people were