



v23 n3 Summer 2008

FOCUS

A Guide to AIDS Research and Counseling

Cognitive Disorders in the Era of Combination HIV Antiviral Treatment

Thomas D. Marcotte, PhD

Since the beginning of the HIV epidemic, researchers and clinicians have known that HIV can enter the central nervous system early in the course of the disease and, over time, may cause changes in thinking, emotions, and behaviors. Among these changes are “cognitive impairments”: problems with processing, learning, and remembering information. “Dementia,” in which a person has severe cognitive impairments that markedly affect activities of daily living, was the most frightening and obvious cognitive consequence of HIV. Yet less severe impairments were even more common, including difficulties in remembering things (such as appointments), problems in doing more than one task at a time, and slowed thinking. The advent of triple combination HIV antiviral treatment in 1996 led to a dramatic decrease in both HIV-related medical conditions and deaths. But what impact have these treatments had on the cognitive effects of HIV infection?

Prior to 1996, cognitive impairments occurred in approximately 30 percent of HIV-positive people who had no medical symptoms of HIV disease and in 55 percent of people who had AIDS-defining illnesses.¹ At that time, the incidence of dementia was estimated at 7 percent per year in people who developed AIDS. Since 1996, the incidence of severe dementia has declined substantially, with one study finding it reduced by 50 percent.² However, HIV-associated neurocognitive problems have not been eliminated. Preliminary data from CHARTER, a large, six-site study funded by

the National Institutes of Health, suggest that even in the era of combination anti-retroviral therapy, between one-third and one-half of HIV-positive individuals may have some form of cognitive impairment. It is not clear whether the continued presence of these disorders reflects an increase in the incidence of milder forms of impairment or the fact that people with impairments are living longer. Regardless, even these milder forms may affect medication adherence, vocational abilities, and complex activities of daily living such as financial management and automobile driving.^{3,4}

This article reviews some of the ways that HIV disease affects the brain, the current diagnostic criteria for HIV-related cognitive disorders, and how HIV antiviral treatment affects the progression of these disorders. The focus is on the impact of HIV infection on the central nervous system, although the role of opportunistic infections and other cofactors in cognitive impairment is also addressed.

Cognitive Manifestations

HIV-associated cognitive disorders most commonly affect learning, motor abilities, attention, memory, how fast information is processed, and executive functioning (planning, weighing options, and making decisions). However, the virus affects different parts of the brain in different people. For example, researchers at the San Diego HIV Neurobehavioral Research Center (HNRC) examined patterns of impairment in 320 HIV-positive study participants who were impaired in at least two areas of cognitive functioning. While learning, attention, and working memory were the most frequent individual impairments, the researchers found 164 different patterns of impairment, with the most common pattern occurring in only 11 cases.

Editorial: The Current State of Mind

Michelle Cataldo, LCSW, Clinical Editor

Several months ago, a colleague in a clinical discussion group mentioned seeing a client who was living with progressive multifocal leukoencephalopathy (PML). The part of the story that surprised me was that the client had been stable with this diagnosis for years. While I haven't provided direct services to people with HIV for three years, I remembered the sense of helplessness and devastation that a diagnosis of PML brought patients, caregivers, and, often, providers. People with this diagnosis declined sharply and died quickly.

This experience made me wonder what HIV-related cognitive impairment looks like today. With so many HIV treatment advances, which cognitive impairments are most prevalent now? This issue of *FOCUS* begins to answer these questions.

In his article, Thomas Marcotte, PhD, discusses the ways HIV affects the brain, reviews the current diagnostic criteria for HIV-associated neurocognitive disorders, and helps explain the complex relationship between HIV disease, HIV treatment, and cognitive impairment.

Also in this issue, Lawrence McGlynn, MD, and Maggie Chartier, MPH, MS, discuss the differential diagnosis of cognitive impairment, and briefly review some of the medical and nonmedical interventions that can support clients with these conditions.

In areas with easy access to HIV antiviral therapies, both the frequency and severity of many of these conditions have diminished. Yet, as Marcotte notes, between one-third and one-half of the participants in a recent research study of HIV-positive individuals had neurologic impairment—reminding us that, despite treatment advances, these conditions continue to challenge patients, caregivers, and providers. ■

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It has always been the case that individuals with mild impairment did not necessarily progress to more severe forms of impairment. It appears that this is even more true in the era of improved HIV treatment. While most people remain stable as either cognitively normal or impaired, a significant subset (perhaps 20 percent) experiences fluctuations in cognitive functioning. This means that a person who is impaired at one time may not necessarily be impaired at another time. It is not yet clear whether this is due to a failure of the HIV antiviral treatment regimen, poor adherence to the medication regimen, or other factors.

Diagnostic Criteria

Diagnostic criteria for HIV-related neurocognitive disorders have evolved over the past 15 years. The most commonly used criteria are those outlined by the American Academy of Neurology (AAN) Task Force.⁵ However, in 2006, the National Institute of Mental Health and the National Institute of Neurological Disorders and Stroke organized a meeting (the Frascati Working Group) to revisit and modify the AAN criteria.⁶ Consistent with the classification in use at the San Diego HIV Neurobehavioral Research Center, this group excluded the social, personality, and emotional deficits that were included in the original AAN criteria. Such noncognitive conditions can have many sources and may

not always reflect HIV-related changes in brain function. In fact, there is preliminary evidence that focusing purely on the neurocognitive changes yields diagnoses that are more strongly correlated with brain alterations seen at autopsy.

The Frascati Working Group coined the term HIV-associated neurocognitive disorders (HAND) to cover impairments ranging from mild to severe. The working group defined three diagnostic categories, and for each one the clinician must exclude non-HIV causes (including neurologic disorders such as head injury, diseases, and severe substance use) and delirium (acute confusional state) as the source of the cognitive impairment.

Asymptomatic Neurocognitive Impairment (ANI). This diagnosis requires that performance on cognitive tests must be at least one standard deviation below the mean of demographically adjusted normative scores (in other words, the person's performance is lower than 85 percent of the people in the normative group) in at least two cognitive domains. In order to adequately evaluate HIV-related neurocognitive functioning, at least five of the following domains should be assessed: attention and information processing, language, abstraction and executive functioning, complex perceptual motor skills, memory (including learning and recall),

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simple motor skills, or sensory perceptual abilities.

For this diagnosis, the impairments must not affect everyday functioning. However, there is evidence that they are still meaningful because they predict brain pathology. Therefore, it may be important for physicians to track individuals with asymptomatic neurocognitive impairment closely. If there is cognitive decline, the physician may want to modify the patient's medication regimen—even when viral loads are low.

Mild Neurocognitive Disorder (MND). This diagnosis implies that the person now has a “disorder,” in that the impairments are at least having mild impact on his or her everyday functioning. The criteria regarding impaired performance on neu-

ropsychological tests are the same as with asymptomatic neurocognitive impairment. The impairment cannot meet criteria for dementia as outlined below.

HIV-Associated Dementia (HAD). This diagnosis requires acquired moderate-to-severe cognitive impairment that is at least two standard deviations below demographically corrected normative means (in other words, performing worse than 97.5 percent of the normative group). At least two different cognitive areas must be affected, and the dementia must cause marked difficulty in activities of daily living.

Also of note, because of the fluctuating nature of neurocognitive impairment in some individuals, the Frascati Working Group included “in remission” as a qualifier for all three diagnostic categories. Since the working group's criteria for HIV-associated neurocognitive disorders have not been widely used, the group recommended that the criteria continue to be applied in research settings before being adopted into clinical practice.

Disease Status and Cognitive Function

Historically, HIV-associated cognitive disorders were found in individuals with lower CD4+ cell counts and higher viral loads. With the advent of highly active HIV anti-

viral treatment, however, this relationship has become less clear. Raising the CD4+ cell count alone does not always protect against cognitive impairment. Once a rare occurrence, full-blown dementia is now more commonly identified in individuals with CD4+ cell levels greater than 200. In fact, it appears that there is a stronger relationship between the lowest CD4+ cell count a person has experienced (known in the research literature as the “nadir”) and his or her current cognition, suggesting that brain alterations occurred when the disease was most advanced.

The amount of time a person has spent at low CD4+ cell levels may be an even better predictor of the development of neurologic damage, but researchers have yet to fully explore this theory.

Since individuals with viral loads below the level of detection can still experience impairment, it could be that permanent damage occurred earlier in the disease progression, or perhaps that an ongoing neuroinflammatory response continues despite minimal viral presence. Another possibility is that, in some cases, immune recovery may start an inflammatory response in the central nervous system; this supposition has yet to be demonstrated, however.

These findings and theories suggest that clinicians should remain alert to potential cognitive problems, even in the context of current immune competence, and should consider earlier HIV antiviral treatment, or regimen modifications, for those who develop cognitive impairment. Patient reports can sometimes be unreliable, and a person's complaints regarding cognition may reflect mood disturbances (for example, depression) more than actual cognitive problems. Neuropsychological testing thus serves as an important diagnostic tool in establishing cognitive status.

McArthur, Brew, and Nath have suggested four distinct patterns of impairment.⁷ These are: a subacute, progressive decline in untreated patients with severe dementia; chronic, active, slowly progressive impairments in patients on antiviral treatment who

Since 1996, the incidence of severe impairments has declined substantially, but HIV-related cognitive disorders have not been eliminated.

have incomplete virological control; chronic inactive impairments in people on antiviral treatment who have achieved virological suppression and who have had some neurocognitive recovery and are neurologically stable; and, finally, reversible impairment in treated patients who initially suffered progressive impairments that are reversed with effective virological suppression.

A number of studies have shown that cognitive functioning can improve with HIV antiviral therapy, and that reduction in the amount of HIV in the fluid surrounding the brain and spinal cord (cerebrospinal fluid) may correlate with cognitive improvement. The amount of HIV in the fluid may serve as a surrogate marker for the amount of virus in the brain itself. Unfortunately, many HIV antiviral treatments, including protease inhibitors, do not penetrate the blood-brain barrier well and thus may not be as effective in attacking the virus in the central nervous system (CNS) as they are in fighting the virus in the blood. Researchers at the HIV Neurobehavioral Research Center have developed a way to categorize the degree to which HIV antiviral medications penetrate into the brain and the spinal cord—the “CNS Penetration-Effectiveness” (CPE) rank—which takes into account a drug’s chemical properties, its concentrations in the cerebrospinal fluid, and its effectiveness in the central nervous system as demonstrated by clinical studies.⁸ In a large cohort, people whose HIV antiviral regimens had better CPE ranks had lower HIV levels in their cerebrospinal fluid.⁸ The clinical utility of this score is still under investigation, but it may ultimately help physicians and patients make medication choices that better treat HIV in the brain.

CNS Opportunistic Infections

Prior to HIV antiviral treatment, opportunistic infections of the central nervous system were common and contributed significantly to cognitive impairment. These often occurred at very low CD4+ cell counts. The rates of nearly all of these conditions have declined significantly among individuals taking improved antiviral treatments.

The incidence of cryptococcal meningitis, for example, decreased almost tenfold between 1992 and 2000, and patients with the illness are living longer. Whereas a diagnosis of progressive multifocal leukoencephalopathy (PML) once meant death within months, survival has significantly

improved, and up to 50 percent of patients now remain stable. There is a concern, however, that in some cases immune reconstitution may itself trigger PML. The incidence of a type of brain cancer, primary central nervous system lymphoma, has also declined,⁹ and patients are living longer. While there has been a reduction in the incidence of central nervous system toxoplasmosis, this reduction appears to be smaller than it is for other central nervous system opportunistic infections, and it still remains prevalent. Despite these improvements, these opportunistic infections continue to plague individuals for whom HIV antiviral therapy has failed and people who live in areas without access to antiviral therapy.

Other Factors

As individuals with HIV live longer and healthier lives, other conditions may affect the emergence of HIV-related neurocognitive disorders. For example, there is growing evidence that hepatitis C infection, which is particularly common in HIV-positive people who have injected drugs, may cause cognitive impairments beyond those associated with poor liver function. Drugs, including methamphetamine, may have a direct impact on cognitive functioning and share some common pathways with HIV in damaging the brain. Advancing age may also be a risk factor for developing HIV-related cognitive disorders or perhaps even early Alzheimer’s disease. Autopsy studies have demonstrated an increase in amyloid deposits in the brains of HIV-positive individuals (though the nature and localization of the amyloid may differ from that in Alzheimer’s disease), and some neuropsychological studies have found older individuals with HIV to have increased impairment compared to younger persons with HIV.¹⁰ To date, most studies have not had access to large numbers of people with HIV over the age of 59, so this hypothesis is preliminary.

All of these conditions can increase the likelihood of cognitive impairments, either in an additive or interactive manner, and make it harder to diagnose cognitive dysfunction accurately in people with HIV. Cumulative “hits” on brain function may diminish a person’s “cognitive reserve,” making it more likely that their symptoms will become apparent earlier.

Why do some HIV-positive people develop HIV-related neurocognitive disorders, while

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others do not? Recently, researchers have focused on “host” (the person with HIV) and “viral” (the type of HIV a person has) factors that might determine these outcomes. On the host side, genetic variations may affect both how HIV disease progresses, including in the brain,¹¹ and how one’s body responds to HIV antiviral treatments. As a virus, HIV, too, is diverse, and there are different subtypes (or “clades”) of HIV throughout the world. Most HIV-related neurological research has focused on North American and Western European populations, where clade B predominates. Early data from other regions suggest that other HIV subtypes might affect the brain differently.

Conclusion

The advent of combination HIV antiviral therapy has had a significant impact

on the illness and death associated with HIV disease. The incidence of severe dementia, as well as central nervous system opportunistic infections, has also declined during this era. However, milder forms of HIV-related neurocognitive disorders remain prevalent and can have a significant impact on the quality of life of people with HIV.

Although we continue to learn more about the causes of these disorders, there is still much to learn regarding the factors that put individuals at risk for cognitive impairments. As HIV has become a “chronic” disease for many individuals, additional factors—advancing age, coinfection with hepatitis C virus, and substance use—may have an increasing effect on the cognitive function of people living with HIV. ■

HIV-Associated Cognitive Impairment: Key Issues for Providers

Lawrence McGlynn, MD, and Maggie Chartier, MPH, MS

HIV researchers now have access to ever-improving clinical data about the brain. These data create a better understanding of HIV-associated central nervous system disorders, ultimately leading to better diagnosis and treatment. This article explores some of the remaining challenges of diagnosing HIV-associated cognitive impairment today, and describes how medical providers can treat and support patients with this disability.

Differential Diagnosis

The damage that HIV causes to the central nervous system is one cause of cognitive impairment, but to make this diagnosis, many other causes must be ruled out. For example, suppose a 39-year-old patient with AIDS and a history of methamphetamine abuse presents with depressed mood, complaints of memory changes, and an inability to concentrate. When given a mental status examination, he shows significant psychomotor retardation, a symptom commonly associated not only with HIV-associated cognitive dysfunction, but also with major depressive disorder and with methamphetamine withdrawal.

In addition to these differential diagnoses, opportunistic infections, sexually transmit-

ted diseases (such as neurosyphilis), vascular incidents (such as stroke), malignancies (such as lymphoma), metabolic derangement (hypothyroidism or electrolyte imbalance), and medication side effects could be clouding the patient’s cognition. As an example, many patients use zolpidem (Ambien), which can itself cause amnesia and confusion. If a patient is taking zolpidem regularly, and the provider has not yet definitively diagnosed cognitive impairment, the patient should slowly taper off zolpidem prior to diagnosis. Some HIV antiviral medications, particularly efavirenz (Sustiva), may also contribute to confusion and have central nervous system effects.

The provider must differentiate between HIV-associated cognitive impairments and these other diagnoses, which are not the result of HIV acting directly on the brain. This often necessitates specialty medical testing, including both imaging tests (such as computerized tomography [CT] or magnetic resonance imaging [MRI] tests and lab tests (such as an analysis of cerebrospinal fluid, metabolic and thyroid tests, urine toxicology tests, and syphilis, cryptococcal, and toxoplasmosis tests, among others). These tests may be supplemented with a battery of neuropsychological testing.

While neuropsychological testing is readily available in some communities, it is prohibitively expensive or virtually nonexistent in others, often because of limitations imposed by insurance companies and long waiting lists. Thus, many provid-

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ers use brief screening instruments such as the Mini-Mental State Examination to diagnose cognitive impairment in people with HIV. Unfortunately, research shows that this test is ineffective in detecting cognitive impairment in this population.¹ An alternative is the HIV Dementia Scale. This test can also be quickly administered and is better at detecting cognitive impairment, but it also lacks the sensitivity and specificity of a full neuropsychological battery.²

Medical Treatment

If the provider has ruled out other causes and believes the impairment to be HIV-associated, bringing viral load down through the use of HIV antiviral therapy is the chief way to decrease injury to the brain. In the presence of an opportunistic infection, however, medications (such as trimethoprim/sulfamethoxazole [Bactrim or Septra] for toxoplasmosis) may be used. Other medical interventions can treat the symptoms of cognitive impairment—such as depression, agitation, cognitive slowing, mania, and paranoia—but not the cause. Antiviral therapy and stimulant medications such as methylphenidate (Ritalin) often improve cognitive functioning.^{3,4} Unfortunately, insurance companies may decline to cover the cost of treatment with stimulants if the client is a current or past stimulant user.

Depression often occurs in people with cognitive impairment, sometimes due to decreases in dopamine activity. Dopamine-stimulating antidepressants such as bupropion (Wellbutrin) are often effective treatments. In general, antidepressants should be started at lower doses, and increased more gradually in people with HIV than in others, due to potential drug interactions, or metabolic issues related to kidney or liver impairment. People with advancing AIDS and cognitive impairment may also be more sensitive to the anticholinergic side effects of tricyclic antidepressants, including confusion, impaired memory, blurred vision, and dizziness, so providers should prescribe these with caution.

Agitation, psychosis (sometimes including paranoia), and mania may appear in people with severe cognitive dysfunction. Low doses of atypical neuroleptics such as olanzapine (Zyprexa) may reduce these symptoms. Mood stabilizers such as valproic acid are also used to treat mania, although these may cause patients liver and hemato-

logic problems. Benzodiazepines are usually not recommended because they may cause further cognitive impairment, problematic drug interactions, excessive sedation, disinhibition, and addiction, particularly for current and former substance abusers.

Insomnia is common both in people with cognitive dysfunction and in people with HIV—and at higher rates in those who have both.⁵ Low doses of sedating antidepressants such as mirtazapine (Remeron) or trazodone (Desyrel) may treat this problem successfully. As in the cases of agitation and psychosis, low doses of atypical neuroleptics may be helpful to treat insomnia.

Supporting Cognitively Impaired Patients

As cognitive impairment worsens, patients may participate less in the day-to-day decisions about their lives, while providers and others assume a greater role. At each stage of the process, providers can make interventions that offer patients, caregivers, and other team members a greater sense of support and continuity.

Testing. Providers should discuss the process and possible outcomes of neuropsychological testing with patients and the people in their support systems in advance, because a diagnosis of cognitive impairment is life-changing. The distress of an additional diagnosis, and fears about loss of independence, disability, and death are common, and some patients respond by becoming withdrawn, depressed, and even suicidal. In addition, the process of testing itself can be demoralizing, as many clients may know or suspect that they are performing poorly. Providers can prepare patients by letting them know that the tests are quite challenging, and that they should expect to make some errors.

Mild to Moderate Impairment. The early stages of cognitive impairment may include

Comments and Submissions

We invite readers to send letters responding to articles published in *FOCUS* or dealing with current AIDS research and counseling issues. We also encourage readers to submit article proposals. Send correspondence to rob.marks@ucsf.edu or to Editor, *FOCUS*, UCSF AIDS Health Project, Box 0884, San Francisco, CA 94143-0884.

symptoms such as slowed thinking and movement, memory problems, balance and coordination difficulties, irritability, apathy, and depression.⁶ Providers can respond by helping patients to anticipate changes and make gradual adaptations.⁷ Frequent appointments can enhance the patient's sense of continuity. Educational, social, and practical interventions can facilitate this process. Helping patients establish routines and teaching about the use of pillboxes and posted notes, lists, and calendars can help patients stay organized and maintain a sense of independence. The more providers can encourage patients with milder impairments to adapt and compensate the better.⁷

A multidisciplinary team approach, including primary care, mental health, and other professionals, benefits both

patients and providers. It is also advisable for providers to engage the patient's informal support network early, if one is available. This network may include family members, friends, and volunteers. Network members can assist the patient in planning for the future and also help patients create legal documents such as wills or trusts, durable powers of attorney for health care and finances, since it is crucial that they do so while they are still considered mentally competent.⁷ In addition to medical and practical interventions, providers should also consider recommending psychotherapy, which can help patients to make healthier behavior choices and process the grief and trauma of HIV disease and cognitive losses.

Moderate to Severe Impairment. As impairment progresses, patients may weaken, and movement and responses further slow. They may become incontinent, spastic, and bedridden.⁶ Members of the patient's support system must take a more active caregiving role, and caregivers and providers experience added stress and the risk of burnout. Respite care and caregiver sup-

port groups can ease some of this stress. Since patients can no longer adapt and compensate as they once could, helping clients and caregivers make changes in the patient's routine and environment is crucial.⁷ Interventions include physical therapy, assistive medical devices, removing clutter that may cause falls, and helping clients save energy (for example, by sitting down to brush their teeth).⁸ Likewise, psychotherapists of clients in these later stages of impairment should move toward a more pragmatic and directive approach that can help clients make sense of their thoughts and their world.⁷

Provider-patient relations are often strained during this time. The provider is often forced to deliver unpleasant news, with implications for the patient's identity, freedom, and future. The provider's suggestion that the patient allow additional professionals into the home may be met with resistance and apprehension. Patients with memory loss forget why such profes-

sionals are necessary. Patients with paranoia are especially difficult to work with because the patient has no insight into his or her faulty beliefs, and reassurances by the provider are usually ineffective.

One of the most challenging moments in the provider-patient relationship occurs when providers must take action to substantially limit their patients' freedom, such as suspending driving privileges. Patients often see providers, rather than their cognitive impairment, as responsible for taking away their independence. Reactions such as fear, desperation, and rejection may be especially intense among people with HIV, who may have already experienced significant relationship ruptures and stigma.

It is crucial that providers not only continue to assist the patient and support system during these difficult later stages, but also stay attuned to their own reactions, including stress and the possibility of burnout. The support of a multidisciplinary approach, consultation with other providers on difficult cases, and personal stress management methods such

When patients can no longer adapt and compensate as they once could, helping patients and caregivers make changes in the patient's routine and environment is crucial.

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FOCUS is a free, quarterly, digital-only publication of the AIDS Health Project, affiliated with the University of California, San Francisco. It is published and distributed with the support of the Office of AIDS of the California Department of Public Health and of the California Department of Mental Health.

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ISSN 1047-0719



as exercise and relaxation techniques can all ease stress and counter burnout.⁷

Conclusion

Despite the presence of HIV antiviral therapy, HIV-associated cognitive impairments continue to devastate patients, affecting multiple domains including thought, emotion, and behavior. Once providers diagnose such

impairments, HIV antiviral therapy can reduce viral damage to the brain. Other medications can reduce the psychological and behavioral symptoms of cognitive impairment. An integrated, multidisciplinary approach allows providers to not only help patients with cognitive impairment and their support systems achieve the best possible outcomes, but also to maintain their own balance. ■

Related Resources

Resources include caregiving fact sheets, an online caregiver group, and trainings for both professional and informal caregivers.

Journal Articles

Letendre SL, Cherner M, Ellis RJ, et al. The effects of hepatitis C, HIV, and methamphetamine dependence on neuropsychological performance: Biological correlates of disease. *AIDS*. 2005; 19(3 Suppl.): S72-S78. This cross-sectional study found that HIV infection, hepatitis C infection, and methamphetamine dependence were each independently associated with poorer performance on neuropsychological tests. Higher hepatitis C levels in plasma were associated with neurocognitive impairment, supporting a link between brain injury and hepatitis C virus replication. Hepatitis C virus was also associated with higher levels of proteins known to be neurotoxic or strongly associated with HIV-related dementia.

Vance DE, Struzick TC. Addressing risk factors of cognitive impairment in adults aging with HIV: A social work model. *Journal of Gerontological Social Work*. 2007; 49(4): 51-77. Uses the concepts of “cognitive reserve,” (the cognitive resources an individual has, which can be diminished by illness, substance use, and other factors) and “neuroplasticity” (the brain’s ability to form new connections and maintain old ones) to provide a framework for the interventions social workers can use to help prevent and address cognitive impairment in older adults with HIV.

Web Sites

Family Caregiver Alliance: <http://www.caregiver.org/caregiver/jsp/home.jsp>. This organization offers local, state, and national programs to assist people caring for a loved one, including those who are caring for someone with HIV-related dementia.

National Institute of Neurological Disorders and Stroke: Neurological Complications of AIDS Fact Sheet. http://www.ninds.nih.gov/disorders/aids/detail_aids.htm. This 2007 online resource describes the diagnosis, effects, and treatment of several of the key HIV-related neurological disorders, including HIV encephalopathy, central nervous system lymphomas, cryptococcal meningitis, cytomegalovirus, herpes virus, neurosyphilis, and others. ■

Next Issue

At the recent XVII International AIDS Conference in Mexico City, the rallying cry was “Universal Action Now!” One of the many challenges participants identified in taking effective action was the difficulty in anticipating the shifting shape of the global pandemic.

In the Fall 2008 issue of *FOCUS*, Columbia University Associate Professor **Quarraisha Abdool Karim, PhD**, discusses the evolving pandemic and how emerging trends should influence prevention and treatment efforts.

Also in the Fall issue, **Patrick Sullivan, DVM, PhD**, Associate Professor of Epidemiology at Emory University, explores the HIV epidemic in the United States, and sheds light on the newly revised Centers for Disease Control and Prevention (CDC) HIV incidence numbers that are fueling debate not only about the accuracy of HIV surveillance, but also the effectiveness of current prevention and treatment efforts.