
Diagnosis, pharmacologic management, non-pharmacologic management, and other considerations

This material is provided by UCSF Weill Institute for Neurosciences as an educational resource for health care providers.
A Healthcare Provider’s Guide To HIV-Associated Neurocognitive Disorder (HAND):
Diagnosis, pharmacologic management, non-pharmacologic management, and other considerations

Diagnosis

Definition
People living with a detectable or suppressed viral load of HIV may develop several types of cognitive problems collectively known as HIV-associated neurocognitive disorder (HAND). The more common form of HAND is mild neurocognitive disorder (MND), which may include behavioral changes; difficulty in making decisions; and learning, attention, concentration, and memory difficulties with mild interference with everyday function. In its most severe form, HAND can manifest as HIV-associated dementia (HAD). Dementia is a clinical syndrome defined as a cognitive or behavioral decline that leads to an inability to complete daily tasks independently. Patients with a third form of HAND, asymptomatic neurocognitive impairment (ANI), show impaired performance on neuropsychological tests but are able to perform everyday functions.

Etiology
Although advances in antiretroviral therapy from the past two decades have decreased the severity of HAND, symptoms persist in 30–50% of people living with HIV. Before the arrival of combination anti-retroviral therapy (a.k.a. cART and sometimes referred to as HAART) in the second half of the 1990s, HAD, the most severe form of HAND, was a frequent finding in late-stage disease. More recently, experts have estimated that less than 5 percent of people on cART develop HAD, although many more suffer from mild changes that can affect daily living.

Course
There is no “typical” course of HAND. Several groups have described daily fluctuation in function. Most of the time, HAND remains relatively mild in patients with suppressed viral load. HAND may be severe or progress rapidly. Some people experience only cognitive disturbances or mood shifts, while others struggle with a combination of mental, motor, and behavior changes. How much these changes disrupt a person’s daily life differs from one individual to the next and from one stage of the disease to another. Cognitive problems are often—although not always—the first to become apparent to a person with HAND and their family members, friends, caregivers, and health care providers. Motor and behavioral changes, if they occur, frequently become evident in later stages of the syndrome.

Differential Diagnosis
Depression and psychiatric disorders should be ruled out. For patients not on cART, opportunistic infections typical in patients with advanced HIV may cause similar symptoms to HAND.

Diagnostic Criteria
The National Institute of Mental Health and the National Institute of Neurological Diseases and Stroke directed a working group to develop a standardized diagnostic classification of HAND. The results were published in 2007.

1. HIV-associated asymptomatic neurocognitive impairment
If there is a prior diagnosis of ANI, but currently the individual does not meet criteria, the diagnosis of ANI in remission can be made.

   a. Acquired impairment in cognitive functioning, involving at least two ability domains, documented by performance of at least 1.0 standard deviations (SD) below the mean for age-education-appropriate norms on standardized neuropsychological tests. The neuropsychological assessment must survey at least the following abilities:
verbal/language; attention/working memory; abstraction/executive; memory (learning; recall); speed of information processing; sensory-perceptual, motor skills.

b. The cognitive impairment does not interfere with everyday functioning.

c. The cognitive impairment does not meet criteria for delirium or dementia.

d. There is no evidence of another preexisting cause for ANI.
   i. If the individual with suspected ANI also satisfies criteria for a major depressive episode or substance dependence, the diagnosis of ANI should be deferred to a subsequent examination conducted at a time when the major depression has remitted or at least 1 month after cessation of substance use.

2. HIV-1-associated mild neurocognitive disorder (MND)

If there is a prior diagnosis of MND, but currently the individual does not meet criteria, the diagnosis of MND in remission can be made.

a. Acquired impairment in cognitive functioning, involving at least two ability domains, documented by performance of at least 1.0 SD below the mean for age-education-appropriate norms on standardized neuropsychological tests. The neuropsychological assessment must survey at least the following abilities: verbal/language; attention/working memory; abstraction/executive; memory (learning; recall); speed of information processing; sensory-perceptual, motor skills. Typically, this would correspond to an MSK scale stage of 0.5 to 1.0.

b. The cognitive impairment produces at least mild interference in daily functioning (at least one of the following):
   i. Self-report of reduced mental acuity, inefficiency in work, homemaking, or social functioning.
   ii. Observation by knowledgeable others that the individual has undergone at least mild decline in mental acuity with resultant inefficiency in work, homemaking, or social functioning.

c. The cognitive impairment does not meet criteria for delirium or dementia.

d. There is no evidence of another preexisting cause for the MND.
   i. If the individual with suspected MND also satisfies criteria for a severe episode of major depression with significant functional limitations or psychotic features, or substance dependence, the diagnosis of MND should be deferred to a subsequent examination conducted at a time when the major depression has remitted or at least 1 month after cessation of substance use.

3. HIV-1-associated dementia (HAD)

If there is a prior diagnosis of HAD, but currently the individual does not meet criteria, the diagnosis of HAD in remission can be made.

a. Marked acquired impairment in cognitive functioning, involving at least two ability domains; typically the impairment is in multiple domains, especially in learning of new information, slowed information processing, and defective attention/concentration. The cognitive impairment must be ascertained by neuropsychological testing with at least two domains 2 SD or greater than demographically corrected means. (Note that where neuropsychological testing is not available, standard neurological evaluation and simple bedside testing may be used, but this should be done as indicated in algorithm; see below). Typically, this would correspond to an MSK scale stage of 2.0 or greater.

b. The cognitive impairment produces marked interference with day-to-day functioning (work, home life, social activities).

c. The pattern of cognitive impairment does not meet criteria for delirium (e.g., clouding of consciousness is not a prominent feature), or, if delirium is present, criteria for dementia need to have been met on a prior examination when delirium was not present.

d. There is no evidence of another, preexisting cause for the dementia (e.g., other central nervous system (CNS) infection, CNS neoplasm, cerebrovascular disease, preexisting neurologic disease, or severe substance abuse compatible with CNS disorder).
   i. If the individual with suspected HAD also satisfies criteria for a severe episode of major depression with significant functional limitations or psychotic features, or substance dependence, the diagnosis of HAD should be deferred to a subsequent examination conducted at a time when the major depression has remitted or at least 1 month has elapsed following cessation of substance use. Note that the consensus was that even when major depression and HAD occurred together, there is little evidence that pseudodementia exists and the cognitive deficits do not generally improve with treatment of depression.

Pharmacologic Management

Medications to Use

The primary pharmaceutical intervention is cART to decrease viral load and bolster the cluster of differentiation 4 (CD4) count. Lack of treatment is the biggest risk factor for cognitive decline. Review expected and realistic goals of treatment (e.g., treatment
is for symptomatic improvement and not a cure or reversal of disease). Expected benefits may be mild improvement in memory function, mood, and alertness. If the patient has vascular disease or mixed dementia, they should receive management and education regarding modification of cardiovascular risk factors.

Managing HAND is sometimes difficult because side effects from medications, other HIV infections, nutritional imbalances, depression, and anxiety, as well as the effects of comorbid diseases (e.g. vascular disease and liver impairment) can all contribute to cognitive, behavioral, and mood disturbances.

Medications to Avoid

Medications with strong anticholinergic side effects, such as sedating antihistamines, barbiturates, narcotics, benzodiazepines, gastrointestinal and urinary antispasmodics, central nervous system (CNS) stimulants, muscle relaxants, and tricyclic antidepressants should be avoided. Antipsychotics should be used with caution. If used, carefully evaluate effectiveness of medication and consider discontinuing if there is no improvement in six weeks.\[^2,3,4\]

Non Pharmacologic Management

**Healthy Lifestyle**

There are lifestyle habits that promote health and well-being. Research suggests that the combination of good nutrition, physical activity, and mental and social engagement may provide benefit in promoting health although more research is needed to determine the actual mechanisms.\[^5,6\] A heart-healthy diet (lower in sugar and fat and higher in vegetables and fruit) is considered to be good for both the body and the brain. An example is the Mediterranean diet that promotes nutrition based on fruit, vegetables, nuts, and grains with limits on consumption of red meat and saturated fats. Physical exercise has been associated with improvement of mood and mobility, and a decrease in the risk for falls.\[^7,8\] Physical activities that are socially engaging (walking or swimming with a friend and participating in exercise groups) can be especially enjoyable. Engagement in activities that are mentally stimulating (crossword puzzles, Sudoku, computer games) is encouraged as long as the activity is enjoyable.

The Alzheimer’s Association has more information on tips for maintaining your health: [alz.org/we_can_help_brain_health维持_brain_health.asp](http://alz.org/we_can_help_brain_health维持_brain_health.asp)

**Sleep**

Disrupted sleep can negatively impact memory and thinking, though the mechanisms are not well understood.\[^9\]

Components of sleep hygiene include:

- Avoid napping during the day
- Avoid stimulants such as caffeine, nicotine, and alcohol too close to bedtime
- Get regular exercise
- Avoid eating right before sleep

- Ensure adequate exposure to natural light
- Establish a regular relaxing bedtime routine
- Associate your bed with sleep. It’s not a good idea to use your bed to watch TV, listen to the radio, or read.

For more details on sleep hygiene, you can refer to the National Sleep Foundation at [sleepfoundation.org/ask-the-expert/sleep-hygiene](http://sleepfoundation.org/ask-the-expert/sleep-hygiene).

**Other Considerations**

**Support Resources**

- Alzheimer’s Association: [alz.org](http://alz.org)
- Family Caregiver Alliance: [caregiver.org](http://caregiver.org)
- National Institute of Health/National Institute on Aging: [nia.nih.gov/alzheimers](http://nia.nih.gov/alzheimers)
- Alzheimer’s Australia Vic: [fightdementia.org.au/sites/default/files/20140723_-_NAT_-_Professional_resources_-_HAND_booklet_for_workers%5b1%5d.pdf](http://fightdementia.org.au/sites/default/files/20140723_-_NAT_-_Professional_resources_-_HAND_booklet_for_workers%5b1%5d.pdf)

**Research and Clinical Trials**

The National Institutes of Health maintains an extensive listing of clinical trials at [clinicaltrials.gov](http://clinicaltrials.gov). Academic medical centers may be engaged in research and clinical trials.
Safety

Patients with HAND don’t typically wander. However, if wandering or getting lost is a concern, refer the patient and family to the MedicAlert + Alzheimer’s Association Safe Return program (operated by the Alzheimer’s Association) alz.org/care/dementia-medic-alert-safe-return.asp.

Other strategies for ensuring safety concerns may include door alarms and increased supervision.

Driving

Depending on cognitive and motor findings, the patient may be requested to stop driving, complete test of driving abilities through the Department of Motor Vehicles (DMV), or be referred to a driver’s safety course that will assess driving ability. Reporting to the department of motor vehicles should be consistent with state laws. Some states have mandatory reporting requirements: the diagnosis is reported to local health departments who then report to the DMV. Individual state requirements can be found at: dmvusa.com.

Living Situation and Environment

It is important to determine if the patient’s residential setting best meets his or her functional and cognitive abilities. Areas of concern may include personal safety (ability to manage medications safely, ability to manage nutritional requirements, ability to manage personal hygiene) and quality of life (activities and engagement that match the person’s needs and abilities). Due to social isolation and stigma, many HIV-positive elders live alone and have minimal support. Thus, it is crucial to inquire about living situation, especially in cases of severe dementia where cART adherence may be compromised due to cognitive difficulties.

Types of living situations range from living at home alone or living at home with supervision, to board and care, assisted living, or memory care units.

Elder Abuse

Patients with dementia and their caregivers are vulnerable to abuse. Refer to Adult Protective Services (APS) if there is concern for the well-being of the patient or the caregiver.

To locate an APS office in your state, see: napsa-now.org/get-help/help-in-your-area/.

Legal Planning

Provide information about advance directives and durable power of attorney while the patient is in the early stages of disease and able to articulate his or her wishes. Make referrals for legal and financial advice, especially if there are concerns about the patient’s judgment, decision-making, or vulnerability. A formal evaluation for capacity may be warranted. The Alzheimer’s Association provides a brochure that covers legal planning: alz.org/national/documents/brochure_legalplans.pdf.

- **Advanced Directives**
  These documents allow individuals to state their preferences for medical treatments and to select an agent or person to make health care decisions in the event they are unable to do so or if they want someone else to make decisions for them.

- **Power of Attorney**
  A Power of Attorney (POA) is a legal document that gives someone of an individual’s choosing the power to act in his or her place. POAs can be for medical or financial matters.

- **Living Will**
  A living will is a written, legal document that spells out medical treatments that an individual would and would not want to be used to keep them alive, as well as other decisions such as pain management or organ donation.

References