

## GUIDE NO. 5

# Evaluation of Chronic Memory Changes in Persons with HIV

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## ABOUT THIS HIV SYMPTOM EVALUATION GUIDE

The *HIV Symptom Evaluation Guide* addresses the initial diagnostic evaluation of common problems that occur in persons with HIV. The goal of this decision guide is to provide a practical approach to the initial evaluation and diagnosis of chronic memory changes in persons with HIV.

Clinical judgment should be used to determine whether hospitalization is required. If needed, clinicians should seek expert consultation for assistance with the diagnostic evaluation or management.

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## DEFINITIONS OF ACUTE VERSUS CHRONIC MEMORY CHANGES

Chronic memory changes are those lasting months or longer. Such changes must be distinguished from acute mental status changes or neurologic deficits, which should prompt emergent evaluation.

## KEY CLINICAL QUESTIONS

### What is the most recent CD4 cell count?

Persons not taking antiretroviral therapy (ART) and with a low CD4 cell count are at increased risk for central nervous system opportunistic infections. Certain opportunistic infections may present with chronic memory changes, such as progressive multifocal leukoencephalopathy (PML), which typically occurs when the CD4 count is less than 50 cells/mm<sup>3</sup> but may occur at higher levels.

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### Is the person taking a medication known to cause neurologic or cognitive side effects?

In general, antiretroviral medications are unlikely to cause memory impairment, though the non-nucleoside reverse transcriptase inhibitor (NNRTI) efavirenz can cause insomnia, depression, and other neuropsychiatric symptoms, which may contribute to or worsen cognitive complaints. Non-antiretroviral medications, such as benzodiazepines, opiates, and other central nervous depressants, especially in the setting of polypharmacy, can impact cognition.

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### Has syphilis testing been performed?

Although persons with neurosyphilis are more likely to present with acute or subacute neurological symptoms (including ocular, auditory, or vestibular changes), subtle neurologic symptoms can occur, including long-term cognitive changes.

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### Are there associated symptoms that suggest a metabolic, toxic, or psychiatric disorder?

Particular attention should be paid to symptoms of thyroid disease, liver disease, vitamin deficiencies, depression, anxiety, and substance use, including alcohol and marijuana.

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### Are there signs or symptoms that suggest obstructive sleep apnea?

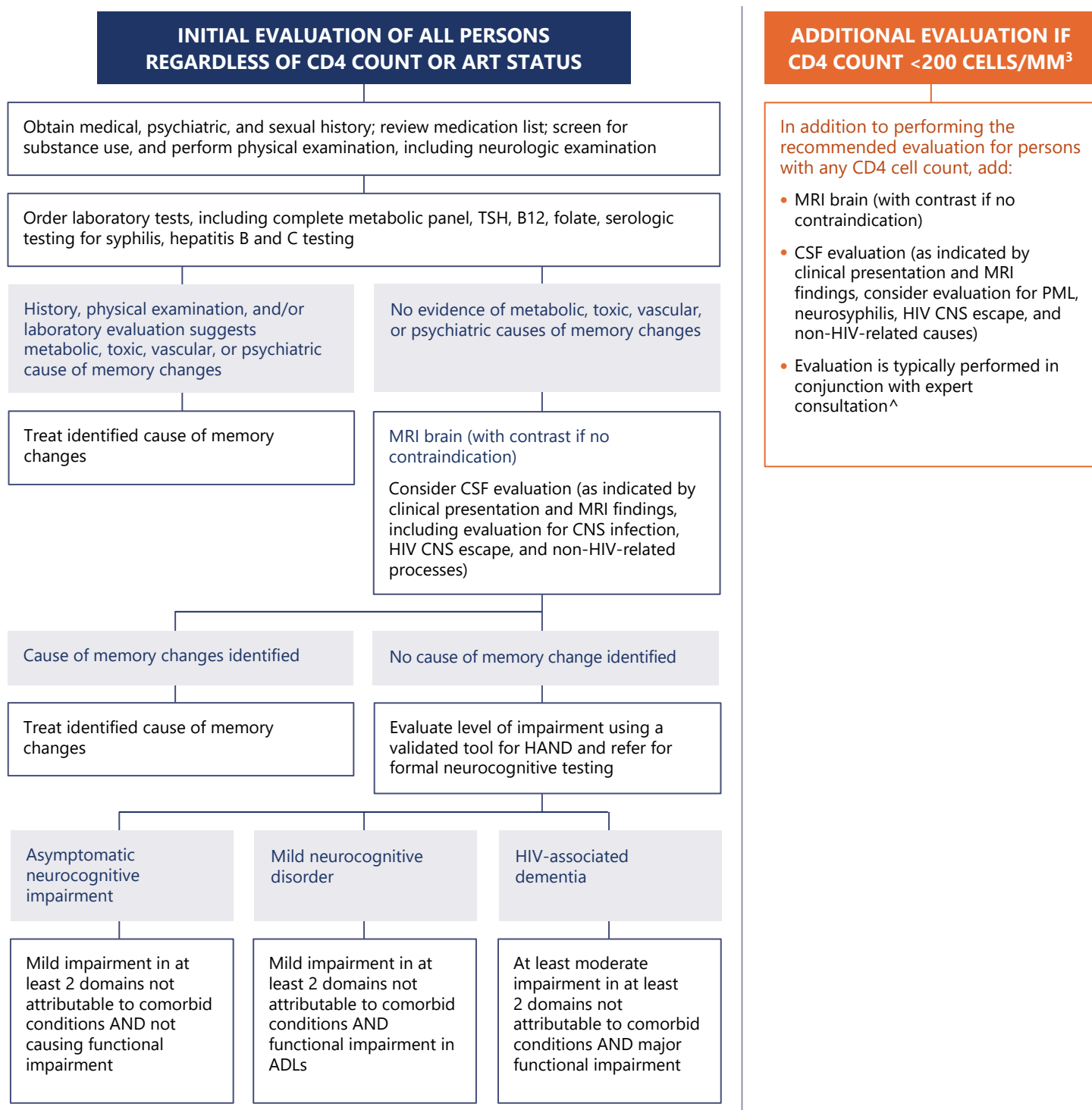
Obstructive sleep apnea is a common cause of memory impairment in persons with HIV, even with normal body mass index (BMI). Evaluation should be pursued, especially in the setting of concurrent fatigue, headaches, and/or hypertension.

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### Could HIV infection be the cause?

Cognitive impairment secondary to HIV itself includes a spectrum of disorders known as HIV-associated neurocognitive disorders (HAND), the most severe of which is called HIV-associated dementia (HAD). These are more likely if a person has longstanding HIV, is not taking ART, and/or has a low CD4 cell count nadir. Rarely, a person taking antiretroviral therapy (ART) may have continued HIV replication in the central nervous system (CNS) despite suppressed plasma HIV RNA levels; this condition is known as “CNS escape syndrome” and may contribute to cognitive impairment.

## DIAGNOSTIC APPROACH TO CHRONIC MEMORY CHANGES IN PERSONS WITH HIV



<sup>^</sup> If local expert consultation is not available, consultation can be obtained through the National Clinician Consultation Center (<http://nccc.ucsf.edu/> or 800-933-3413).

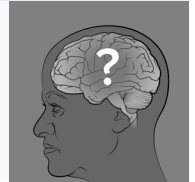
ABBREVIATIONS: ART = antiretroviral therapy; ADL = activities of daily living; CNS = central nervous system; CSF = cerebrospinal fluid; CT = computed tomography; HAND = HIV-associated neurocognitive disorder; MRI = magnetic resonance imaging; PML = progressive multifocal leukoencephalopathy; TSH = thyroid stimulating hormone

## COMMON CAUSES AND INITIAL DIAGNOSTIC EVALUATION FOR CHRONIC MEMORY CHANGES IN PERSONS WITH HIV

CAUSE (in alphabetical order)	RISK FACTORS AND CHARACTERISTICS	TYPICAL CD4 CELL COUNT	INITIAL DIAGNOSTIC EVALUATION
Brain tumor or brain metastases	May be associated with mood or personality change	Any	Brain imaging with CT or MRI, with contrast if no contraindication
HIV-associated neurocognitive disorder (HAND)/HIV-associated dementia (HAD)	Uncontrolled or longstanding controlled HIV  Slowly progressive symptoms	Any; more prevalent with CD4 nadir <200 cells/mm <sup>3</sup>	International HIV Dementia Scale (IHDS) <a href="https://www.hiv.uw.edu/page/mental-health-screening/ihds">https://www.hiv.uw.edu/page/mental-health-screening/ihds</a>
HIV CNS escape syndrome	Good adherence to ART  Cognitive symptoms not attributable to other causes	Any	CSF evaluation  Detectable HIV RNA in CSF while undetectable in plasma
Major depression with cognitive dysfunction (pseudodementia)	Often accompanied by psychomotor slowing	Any	Validated depression screening tools and complete psychiatric evaluation
Metabolic disorder (thyroid disorders, vitamin B12 deficiency, etc.)	Poor nutrition  History of thyroid disorders  Concomitant physical examination signs	Any	CBC, CMP, thyroid studies, B12 level, and other tests as indicated
Neurosyphilis	Condomless sex  History of untreated or incompletely treated syphilis	Any	Syphilis screening per local laboratory protocols  CSF evaluation (cell counts, total protein, VDRL, and FTA-ABS)
Obstructive sleep apnea	Daily fatigue, chronic headaches, and/or HTN	Any	Overnight polysomnography
Progressive dementias (e.g., Alzheimer's, Lewy body, vascular, and others)	Gradual cognitive decline similar to course in person without HIV	Any	Evaluation similar to person without HIV  Referral to neurologist for evaluation
Progressive multifocal leukoencephalopathy (PML)	Immunomodulatory humanized antibodies  Uncontrolled HIV infection; receipt of immunomodulatory humanized antibodies	Usually <200 cells/mm <sup>3</sup>	MRI brain with contrast (if no contraindication); MRI typically demonstrates multifocal white matter changes crossing the midline  CSF evaluation (including JC virus PCR)
Substance use	May have waxing and waning quality	Any	Detailed history of current and prior drug use  Drug screen as appropriate

ABBREVIATIONS: ART = antiretroviral therapy; CBC = complete blood counts; CMP = complete metabolic panel; CNS = central nervous system; CSF = cerebrospinal fluid; CT = computed tomography; FTA-ABS = fluorescent treponemal antibody absorption; HTN = hypertension; MRI = magnetic resonance imaging; PCR = polymerase chain reaction; RNA = ribonucleic acid; VDRL = venereal disease research laboratory

## KEY SUMMARY POINTS



- In general, there is a 2-step approach to evaluating chronic memory changes in persons with HIV: (1) evaluate for an infectious, toxic, metabolic, or psychiatric process, and (2) if none are present, perform cognitive testing to confirm cognitive deficits, identify domains with limitations, and document extent of difficulties.
- Many factors that contribute to chronic memory impairment in persons with HIV are not directly related to HIV or ART. These include depression, anxiety, substance use, polypharmacy, insulin resistance, and obstructive sleep apnea.
- All persons with memory impairment or dementia symptoms should be screened for syphilis. Isolated memory or cognitive changes are rare manifestations of neurosyphilis.
- Consider performing MRI and CSF evaluation, particularly if the current or recent CD4 count is less than 200 cells/mm<sup>3</sup>, other neurologic symptoms are present, or symptoms are progressive. The MRI is ideally performed with contrast and can evaluate for certain opportunistic infections (including PML) as well as non-HIV-related causes, such as primary brain tumor or metastases to the brain.
- Evaluation of the CSF may help identify opportunistic infections or other coinfections, such as neurosyphilis. In addition, HIV CNS escape syndrome (detection of HIV RNA in the CSF of a person on ART with an undetectable plasma HIV RNA) should be considered if other causes have been ruled out.
- Progressive dementias, such as Alzheimer's, Lewy body, and vascular, can occur at any CD4 cell count and should be considered when clinical signs and symptoms are compatible with no other cause of cognitive impairment identified.
- If deficits remain after toxic, metabolic, and infectious causes have been treated or excluded, a diagnosis of HAND should be considered. There are three HAND sub-types: asymptomatic neurocognitive impairment (ANI), which does not interfere with everyday functioning; mild neurocognitive disorder (MND), which leads to some interference with daily activities; and HIV-associated dementia (HAD), which causes marked impairment of function. Validated tools for assessing the likelihood of HAND exist (e.g., International HIV Dementia Scale).
- Formal neuropsychological testing by an experienced provider is useful for establishing the diagnosis of HAND and identifying areas of deficit. A person with HIV not yet taking ART should start soon; otherwise, currently, there is no specific medication to treat HAND. Cardiovascular exercise has been shown to help reduce symptoms. Identifying areas of deficit aids in designing personalized interventions to support adherence and activities of daily living.

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## DISCLOSURES

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