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Podcast Issue

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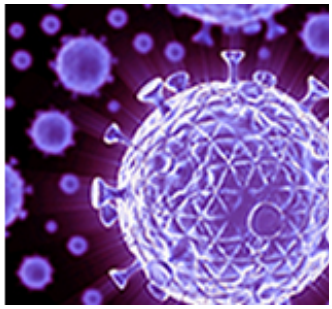

VOLUME 1 — ISSUE 8: TRANSCRIPT

Featured Cases: HIV-Associated Neurocognitive Disorder (HAND)

Our guest authors are Justin McArthur, MBBS, MPH, FAAN, Professor of Medicine, Neurology, Medicine, Epidemiology and Pathology, and Bryan Smith, MD, Department of Neurology Fellow at the Johns Hopkins University School of Medicine in Baltimore.

After participating in this activity, the participant will demonstrate the ability to:

- Describe the clinical presentation, diagnosis, and appropriate management of HIV-associated neurocognitive disorder,
- Explain the differential diagnosis of cognitive symptoms for HIV-positive patients at different ages,
- Discuss the more complicated aspects of HAND and how treatments can be individualized depending on the varied mechanisms of HAND development, including IRIS

This discussion, offered as a downloadable audio file and companion transcript, covers the important issues related to HIV-Associated Neurocognitive Disorder (HAND), in the format of case-study scenarios, for the clinical practice. This program is a follow up to the Volume 1, Issue 7 eHIV Review newsletter — HIV-Associated Neurocognitive Disorder (HAND).

Unlabeled/Unapproved Uses
The presentation today will include discussion of the off-label use of memantine for the treatment of HAND.

MEET THE AUTHORS

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Faculty Disclosure
The authors have indicated that they have no financial interests or relationships with a commercial entity whose products or services are relevant to the content of this presentation.

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Next Issue
HIV/HCV Co-Infection

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STATEMENT OF NEED
Three central ideas emerged from our needs assessment. In order to provide optimal treatment to patients with HIV.

- Clinicians caring for patients with HIV need current information about: appropriate treatment and maintenance of care…guidance for treating comorbidities…and information about emerging findings for treating HIV-associated neurocognitive disorders (HAND)
- The need for more information on HIV topics including updated guidelines for HIV, treating older patients with HIV, managing patients with comorbidities and coinfections, treatment and sequencing strategies for maximizing future therapeutic options, and new and emerging agents for HIV
- Treating comorbidities in patients with HIV, especially among people older than age 50

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MR. BOB BUSKER: Welcome to this *e*HIV Review Podcast.

*e*HIV Review is presented by The Johns Hopkins University School of Medicine. This program is supported by educational grants from Abbott Laboratories, Boehringer Ingelheim Pharmaceuticals, Inc., and Bristol-Myers Squibb.

Today's program is the companion piece to our Volume 1, Issue 7 newsletter topic: *HIV-Associate Neurocognitive Disorder, or HAND*.

Our guests today are that issue's authors: Dr. Justin McArthur and Dr. Bryan Smith from the Johns Hopkins University School of Medicine.

This activity has been developed for infectious disease specialists, primary care physicians, nurse practitioners, and other health care practitioners whose practice includes treating HIV patients.

There are no fees or prerequisites for this activity.

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Learning objectives for this program are, that after participating this activity, the participant will demonstrate the ability to:

- Describe the clinical presentation, diagnosis, and appropriate management of HIV-associated neurocognitive disorder;
- Explain the differential diagnosis of cognitive symptoms for HIV-positive patients at different ages; and
- Discuss the more complicated aspects of HAND and how treatments can be individualized depending on the varied mechanisms of HAND development, including IRIS.

I'm Bob Busker, managing editor of eHIV review. Our guests today are Dr. Justin McArthur, professor of neurology, medicine, epidemiology and pathology at The Johns Hopkins University School of Medicine; and Dr. Bryan Smith, a Department of Neurology fellow, also at Johns Hopkins.

Dr. McArthur and Dr. Smith have indicated that they have no financial interests or relationships with any commercial entity whose products or services are relevant to the content of this presentation. Our guests today have indicated that their presentation will include discussion of the off-label or unapproved use of memantine for the treatment of HAND.

Dr McArthur and Dr. Smith, welcome to this eHIV Review Podcast.

DR. JUSTIN MCARTHUR: Oh, it's my pleasure to be here.

DR. BRYAN SMITH: Thank you so much for inviting us.

MR. BUSKER: In your newsletter issue, you reviewed the current literature describing HAND from a variety of perspectives. What I'd like to do today is discuss how that information can be translated into clinical practice. So if you would, Dr. Smith, start us out by describing a patient.

DR. SMITH: Our first case is a patient who presented with a fairly typical case of HIV-associated neurocognitive disorder. It's a good illustration of the process involved in a relatively uncomplicated diagnosis and management of HAND.

He is a 46-year-old man with three years of cognitive impairment. His HIV was diagnosed in 2007, with a nadir CD4 count of 34 cells, and he was quickly started on antiretroviral therapy. He has maintained an undetectable viral load since then with mtricitabine, tenofovir, ritonavir, and darunavir. His CD4 count has now stabilized and is consistently greater than 300 cells.

This patient has a history of head trauma 20 years ago from which he was comatose for several weeks. He had subsequent cognitive impairments, though with rehabilitation he was able to fully regain his cognitive abilities and within months he was back to work without any deficits.

In 2009, however, he started to notice new cognitive impairments. He noticed the gradual decline in his abilities to work as a bank manager, and

unfortunately, he was fired from his job because of that. He's since worked part time at a counseling center. He continues to live independently, but he does rely on his family and friends for activities such as managing his finances. There is no family history of neurologic disorders.

On examination he has disinhibited behavior suggesting frontal lobe dysfunction. His eye movements are not smooth and are what we call saccadic or choppy eye movements, indicative of a disconnection in motor control outside of the classic corticospinal paramatal tracks. Other extrapyramidal signs include rigidity in the arms, significantly reduced speed with finger and toe taps, and postural instability.

On the HIV dementia scale he scores 9 of 16 possible points, indicating a positive screen that warrants further testing. An MRI brain without contrast shows mild T2 hyperintensities around the ventricles and into the deep white matter, as well as some mild volume loss that is in a diffuse pattern.

There is no encephalomalacia, which is softening of the brain, that would suggest permanent brain injury from his prior traumatic brain injury. CFS shows normal results including an undetectable viral load.

MR. BUSKER: What are the salient features of this case?

DR. SMITH: The salient features of this case are several. He has a low nadir CD4 count and we know that low nadir CD4 counts are a consistent risk factor for HAND development, despite no immunosuppression at the actual time of symptom onset.

One other thing that's important is that he has a prior head trauma; however, he fully recovered from this, and there is nothing structural on MRI that would suggest any permanent damage from this.

In talking about the diagnosis of HAND, we require that there are no confounding factors such as other sources for cognitive impairment, and I don't suspect that his traumatic brain injury confounds the diagnosis in this case.

Another important thing is that he lost his job as a manager. Being a bank manager requires performance with executive functions such as multitasking, mental flexibility, and loss of executive function is a common symptom that we see with new cases of HIV-associated neurocognitive disorder.

His examination is also important because it shows several signs of subcortical dysfunction, including frontal disinhibition and extrapyramidal signs that we classically see in cases of HIV-associated neurocognitive disorder.

MR. BUSKER: Based on his presentation, and on what you've just described, what's your differential on this patient?

DR. SMITH: The leading differential is HAND. The symptoms, the exam, and the MRI are all classic for HAND. The temporal course fits as well, with HAND being the sequela of prolonged immunosuppression. But we also need to consider reversible causes of cognitive impairment, and those include neurosyphilis, vitamin B-12 deficiency, hypothyroidism, or a potential psychiatric overlap.

MR. BUSKER: So to make an actual diagnosis of HAND, what would be required?

DR. SMITH: One of the really important things that we struggle with in making a diagnosis of HAND is finding the appropriate patients from a screening test. A screening test is essential for primary providers to have to find patients who potentially could have HIV-associated neurocognitive disorder.

There is the HIV dementia scale, it was developed by Dr. McArthur, actually, and it has a diagnostic accuracy of over 80% percent. There is a current app for it available on the iTunes, under Hopkins HIV, and it's simple for non-neurologists to perform. It requires about two minutes.

When making a diagnosis of HAND, neuropsychological testing is required, according to the 2007 American Academy of Neurology guidelines. Our patient had a classic pattern of executive dysfunction, including problems with planning, organization, multitasking, and mental flexibility, as well as with psychomotor speed and less severe impairments in memory and inattention.

Typically for a diagnosis of HAND, CSF is not required. It was done in this case, however, and the CSF viral load was actually undetectable.

MR. BUSKER: Your management approach, Dr. Smith — are there therapies that specifically target HAND?

DR. SMITH: The mainstay of management of HAND is antiretroviral therapy, and this is especially important for patients who could potentially have resistance to their medicines or potentially low adherence rates.

Our patient is on a stable ARV regimen, and there is no detectable virus in CSF. So for our patient it seems that we would consider his ARVs unchanged. Unfortunately, there are no currently approved adjunctive therapies for HAND. There have been multiple treatment trials that have been unsuccessful, but research is still ongoing.

Our patient's history highlights the likely neurotoxicity associated with untreated HIV, that is CNS replication, that can lead to symptoms years later, and this is especially important in the brain, even when the CD4 count is normal and the viral load is suppressed.

Typically, for our patients we recommend nonpharmacologic therapies that are helpful for other forms of cognitive impairment. These include things like cognitive behavioral therapy, aerobic exercise, a Mediterranean diet, increased activity levels, and we're always careful to point out that the management of HAND involves a multidisciplinary team. We work not only with the patient, but also the patient's family, social workers and psychiatry for a multidisciplinary approach.

MR. BUSKER: Dr. McArthur, your thoughts on this case?

DR. MCARTHUR: I would like to bring up the issue of central nervous system penetration of antiretrovirals and perhaps, Bryan, you could give me your comments or thoughts about whether or not antiretrovirals should be adjusted on the theoretical basis that they may penetrate better with a particular composition of a regimen.

DR. SMITH: I think that's a good point, Justin. The CNS Penetration Effectiveness Index was recently developed to score how well antiretroviral therapies make it into the brain and how effective they are at treating infection in the brain. This is relatively new information, and we don't have a clear answer on that. We know that higher CPE scores are occasionally associated with better outcomes; however, we don't know whether changing someone's stable antiretroviral regimen to one with a higher CPE index score actually benefits the patient yet, and results so far are somewhat conflicting, but hopefully this question will be answered sometime in the near future.

MR. BUSKER: Thank you, doctors, for that case and discussion. Dr. McArthur, let me ask you to bring us another patient now, if you would please.

DR. SMITH: The second patient we'd like to discuss is especially relevant in the current era where patients with HIV are aging and are now susceptible to conditions like Alzheimer's disease, that we never thought possible in earlier decades.

She is a 58-year-old African-American woman with HIV diagnosed 15 years before presentation with a nadir CD4 of 140 cells. Her primary provider noted memory impairments and referred her to the neurology clinic. The patient is unsure why she was asked to see a neurologist and presents with her husband who describes a five-year history of slowly progressive, short-term memory troubles. She relies on her husband for activities that she had no difficulties with a few years ago, including paying the bills, following recipes, and planning activities. She was driving until recently, when she had an accident that was deemed her fault, although she strongly denies this. She currently takes abacavir, lamivudine, atazanavir, and ritonavir, although she doesn't remember the names of her ARVs well, and there is some concern that she is not fully adherent with these because of her memory troubles.

She has a history of diabetes mellitus that is well controlled with oral medications. Her family history is unremarkable for any history of neurologic disease or dementia. Her current CD4 count is 589, her plasma viral load is undetectable, and vitamin B-12, RPR, and TSH are negative or normal. An MRI without contrast of the brain shows moderate loss, primarily in the bilateral parietal and medial temporal lobes.

On the HIV dementia scale she scores a low 5.5 points out of 16. She has no memory of hearing words that she was asked to recall after a short delay and she is unable to copy a cube figure. Her neurological examination is also notable for difficulties following

complex commands and with word finding, and she has diffuse 3+ hyperrefelxia with extensive plantar responses bilaterally.

MR. BUSKER: What do you consider the most relevant factors in this case?

DR. MCARTHUR: First, the age of the patient: she's 58. Now HAND can present at this age, and when it does we commonly see memory-predominant symptoms, particularly with short-term memory. Alzheimer's disease and other neurodegenerative conditions typically present at a later age than this unless there's a rare genetic mutation either in presenilin or amyloid precursor protein.

One exception to this is for patients with HIV. We now think that patients in their fifties with chronic HIV infection can present with symptoms very similar to Alzheimer's disease and imaging, even without a genetic mutation. Interestingly, pathological studies have shown diffuse amyloid plaques in the brains of patients with HIV that are identical to those seen in uninfected patients many years older, suggesting that HIV might lead to premature aging and amyloid deposition, and thus to a greater susceptibility to age related conditions like Alzheimer's disease at a much younger age.

The second facet of this case that is important to comment on is the symptoms. This patient had difficulties with memory, visual spatial capacity, such as cube-drawing, and language naming; these are all cortical symptoms that are unusual or atypical for HAND, certainly in the initial phases of HAND where the deficits are typically subcortical. This strongly suggests a neurodegenerative process like Alzheimer's disease.

The patient also denies or seems indifferent to the symptoms that she's displaying; she forgets that she forgets. In HAND, by contrast, patients often present themselves with complaints indicating a relatively preserved memory. That means they're aware of their deficits.

The third element is her MRI scan, which shows moderate volume loss in a focal pattern consistent with Alzheimer's disease. Alzheimer's disease typically causes volume loss or atrophy in the parietal and medial temporal lobes, then followed by global loss as the symptoms advance. HAND, by contrast, usually the symptoms are out of proportion to any volume loss and white matter hyperintensities are seen on the MRI scan.

MR. BUSKER: Considering Alzheimer's disease in a patient with HIV — what other tests would you recommend as being helpful?

DR. MCARTHUR: Neuropsychological testing is important. First, it delineates which cognitive domains are most affected. It's especially useful when the patient cannot describe, or as in this case, denies their symptoms. It establishes a baseline for cognitive function, and it can also help determine the disease course and the prognosis.

The second diagnostic test is lumbar puncture, or LP. And in the case of Alzheimer's disease, there are, in fact, CSF biomarkers that are very helpful. So a low beta amyloid, A-beta-42, as we call it, or a high tau level, has a diagnostic accuracy of about 90 percent. We don't yet know whether this is true for patients with HIV and comorbid Alzheimer's disease.

HAND can be associated with low A-beta-42 but normal tau levels, in contrast to AD. We don't know what pattern we will see in patients who have both HIV infection and Alzheimer's disease.

The third type of diagnostic test is PET scanning, or positron emission tomography. This can be useful for the diagnosis of Alzheimer's disease in HIV negative patients, and typically we expect temporoparietal hypometabolism.

Recently, PET imaging with an amyloid marker – florbetapir – this is an amyloid tracer that has just recently been FDA approved to rule out Alzheimer's disease.

Research is ongoing with older patients with HIV using these amyloid tracers to see if we can potentially distinguish HAND or HIV-associated Alzheimer's disease from conditions where amyloid would not be expected to accumulate. This could potentially distinguish HAND from HIV-associated AD, although we don't know this for a fact yet.

As the HIV population ages, we expect to see quite a bit more HIV-associated Alzheimer's disease.

MR. BUSKER: Talk to us, if you would, Dr. McArthur, about managing an individual with HIV and Alzheimer's disease.

DR. MCARTHUR: Managing Alzheimer's disease in a patient with chronic HIV infection is really no different from what we would do for a patient without HIV. I think referral to a cognitive subspecialty practice is important. The field is rapidly evolving, and we have new diagnostics and new treatments that are under development and in trial right now.

I think it is also important that a specialty practice such as a memory center can provide a holistic approach to the patient with social workers, case managers, etc.

In terms of specific treatments, disease modification for AD is still not a reality, even through there have been tremendous advances in clinical trials in recent years. We do have symptomatic treatment, for example, the cholinesterase inhibitors can be useful in mild to moderate AD. They can slow the progression of symptoms, but generally they don't typically improve the overall situation and they are not disease-modifying. There is a risk of seizures in patients with severe Alzheimer's disease.

Another agent, memantine, is also an adjunctive agent for moderate to severe AD.

In terms of lifestyle changes, aerobic exercise, cognitively stimulating activities, such as participation in a book club, playing chess, sudoku, crosswords, and a heart-healthy diet, there is some evidence that these modifications at least improve the quality of life.

MR. BUSKER: Dr. Smith, your comments on this patient?

DR. SMITH: Justin, I know this is a rather complicated matter, but what do you think could be the source for Alzheimer's disease and other aging related phenomena in patients with HIV?

DR. MCARTHUR: Thanks, Bryan. I think we simply don't fully understand the pathogenesis at this point. It is clear that amyloid is deposited, but it is not exactly in the same pattern that we see in AD, and there is very little information at this point that points to deposition of the other pathogenic protein, tau. Investigators have been looking recently at whether energy failure in the form of mitochondrial dysfunction could play a role in some of the cognitive dysfunction that we see in patients with HIV and AD. In fact, mitochondrial mutations do occur with age, and they seem to recur at an accelerated rate in patients who have chronic HIV infection. This is a developing field, we've got to watch it carefully to see where the investigations lead us.

MR. BUSKER: And we'll return to our discussion of HAND in just a moment.

DR. MICHAEL MELIA: Hello. I'm Michael Melia, Associate Professor of Medicine in the Division of Infectious Diseases and Associate Fellowship Program Director at The Johns Hopkins University School of Medicine. I'm one of the Program Directors of *e*HIV Review.

*e*HIV Review is a combination newsletter and podcast program delivered by email to subscribers. Newsletters are published every other month. Each issue reviews the current literature in areas of importance to infectious disease specialists, primary care physicians, nurse practitioners, and other health care practitioners whose work or practice includes treating HIV patients

Bimonthly podcasts are also available as downloadable transcripts, providing case-based scenarios to help bring that new clinical information into practice in the exam room and at the bedside.

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MR. BUSKER: Welcome back to this eHIV Review podcast. I'm Bob Busker, managing editor of the program. Our guests are Dr. Justin McArthur and Dr. Bryan Smith from the Johns Hopkins University School of Medicine. And our topic is HIV-Associated Neurocognitive Disorder, or HAND.

We've been looking at how some of the information Drs. McArthur and Smith discussed in their newsletter issue can be translated into clinical practice. So if you would, Dr. Smith, bring us another patient, please.

DR. SMITH: The next case I'd like to discuss involves IRIS, or immune reconstitution inflammatory syndrome. It's a frequently encountered but also feared complication of HIV because it is associated with initiation of antiretroviral therapy.

Our patient is 56, she's a woman with HIV and a nadir CD4 count of 7. In July 2004, her antiretroviral regimen was changed from nelfinavir and lamivudine with zidovudine to nelfinavir with tenofovir and mtricitabine because she had incomplete viral control.

In October 2004, about three months after this new regimen started, she suffered a generalized tonic-clonic seizure. An evaluation showed a mild CSF pleocytosis with nine cells and slightly elevated CSF protein at 70mg/dL.

Such mild CSF abnormalities are common after seizures; however, her mental status never returned to normal. She continued to decline despite antiepileptic therapy, and she was comatose within two days. Repeat CSF now showed a large elevation in her CSF HIV viral load. It was previously 866 copies/mL and it's now 9,500 cells/mL. Pleocytosis increased to 17 cells and high protein to 183mg/Dl.

On MRI she had extensive white matter lesions throughout the subcortical and juxtacortical white matter. They were had a patchy appearance, and she had gadolinium enhancement throughout many of these lesions. A brain biopsy showed extensive CD8 infiltration within the brain parenchyma, and in perivascular regions, along with macrophages, B cells, and rare multinucleated giant cells, suggestive of HIV encephalitis.

She responded promptly to IV methyprednisolone at 1 gm/day for 5 days to the point that she was awake and interactive. She was then transitioned to an oral steroid taper and her cognition continued to improve.

She now has persistent mild cognitive deficits including slowing, to the point that she's unable to return to work as a college dean, but she does live independently and is independent in most of her daily activities.

MR. BUSKER: Summarize for us, if you would: what are the important points from her history and from your diagnostic workup of this patient?

DR. SMITH: Our patient was neurologically normal until just after the change in her antiretrovirals. This is classic for IRIS. Typically within weeks to in our case three months, someone can have no problems after starting the antiretrovirals and then things suddenly change, and in our patient's case she had a seizure and then a decline in arousal with rapid deterioration.

She had extensive MRI progression with rather diffuse enhancement, which is also typical for IRIS. And the brain biopsy showed a classic pattern for severe HIV dementia and she had a classic good response to steroids that is commonly seen in IRIS.

MR. BUSKER: There are specific distinctions between HAND, HIV encephalopathy, and HIV encephalitis. Clarify those for us, if you would, doctor.

DR. SMITH: HAND is a definition that was described in 2007 with the American Academy of Neurology guidelines, and it encompasses the entire spectrum of HIV cognitive impairment syndromes. Of course, we always have to exclude other possibilities that could account for cognitive impairments in those with HIV, but essentially HAND is an idiopathic form of cognitive impairment in those with HIV.

HIV encephalopathy, however, is an older term, and it refers to clinical disease that is usually severe, typically without neuropsychological testing, and it's also known as HIV dementia.

HIV encephalitis is a pathological diagnosis, as in this case the patient had a brain biopsy. It's associated with severe HIV infection in perivascular regions and brain parenchyma that leads to an abundance of CNS inflammation.

MR. BUSKER: Now IRIS — How significant a concern is it among HIV subspecialists, and how commonly is IRIS associated with HAND?

DR. SMITH: IRIS is rarely described in association with HAND and there are rare case reports in the literature. However, we caution that it's a strong possibility that milder forms of HAND-associated IRIS are unrecognized in patients who have HAND in whom cognitive symptoms persist or intensify despite good peripheral viral control.

We always have a low threshold for repeating MRI or LP to look for any evidence of an inflammatory component that might have developed. This inflammatory component is potentially treatable with steroids, and we really can't afford to miss it.

MR. BUSKER: What other considerations should clinicians be aware of in patients such as this?

DR. SMITH: Our patient had a meaningful recovery but it was incomplete. She was a college dean and she wasn't able to work anymore. She was independent, and that's important, but getting someone back to their baseline level is really our aim here, and unfortunately it didn't happen in this case.

I would strongly consider monitoring her CSF serially to specifically follow the viral load to make sure that the steroids are helping improve the inflammation and that her antiretroviral regimen is suppressing the CSF viral load.

If it does become elevated, I would consider a change in her antiretroviral regimen to increase CNS penetrance, that is one with a higher CPE index; however, those recommendations are currently unknown whether we should be doing this.

If symptoms or CNS inflammation persist and the CSF viral load is still elevated, typically this is used as a last resort in that we change her antiretroviral regimen to one with a higher CPE index. She could also possibly benefit from cognitive behavioral therapy, as this has been shown in a preliminary way to improve executive functions, which could possibly help her get back to work.

MR. BUSKER: Dr. McArthur, your thoughts on this patient?

DR. MCARTHUR: This patient was treated with high-dose steroids, Bryan, and in a patient in whom high-dose steroids might not be tolerated well — for example, a brittle diabetic — do you have any thoughts for steroid-sparing regimens? Is there evidence for those types of treatment?

DR. SMITH: That's an important point, because steroids potentially could be used long-term for IRIS and potentially patients won't be able to tolerate steroids for very long. Several steroid-sparing agents could potentially be used in this case. For example, mycophenolate mofetil or azathioprine, potentially could replace the steroids.

The evidence on those regimens is available; however, there is no systematic evidence for use of the steroid sparing agents in patients with HIV and IRIS.

MR. BUSKER: I want to thank you both for that discussion. To wrap things up, let's review what we've talked about today as it applies to our learning objectives. To begin: the clinical presentation, diagnosis, and appropriate management of HAND. Dr. Smith?

DR. SMITH: For patients with HAND, the diagnosis is often challenging. It's important to remember to exclude potentially confounding conditions such as vitamin B-12 deficiency, neurosyphilis, and hypothyroidism, and it's important to get neuropsychological testing, because this really delineates the pattern of impairment that may be specific for HAND.

MR. BUSKER: And the differential diagnosis of the cognitive symptoms for HIV positive patients at different ages?

DR. SMITH: It's important to note that HAND can develop at any age for a patient with HIV. We've seen in younger patients that typically the HAND symptoms are more executive impairments and slowing, and in older patients it's more-memory predominant. And we always want to exclude potentially confounding conditions, which can include psychiatric diseases and in older patients neurodegenerative diseases, such as Alzheimer's disease, Lewy Body Dementia, frontotemporal dementia, and it's important to remember someone's age and delineate which other comorbid cognitive impairments could potentially contribute to their presentation.

MR. BUSKER: And finally: the more complicated aspects of HAND and individualizing treatments

depending on the mechanisms that have caused HAND development.

DR. SMITH: HAND can come from a variety of sources. It can be associated with a low nadir CD4 count and prolonged chronic HIV infection, or it can develop subacutely in the setting of CNS inflammation associated with change in antiretroviral regimen. And when it gets more complicated with things like IRIS or many comorbid conditions, treatment can essentially be individualized.

It is important to remember that treating potentially conflicting or contributing conditions associated with HAND can really make a difference in someone's cognitive outcome. And it's important to remember that in cases of IRIS or CNS inflammation associated with HAND, treatment of the specific inflammation with steroids or steroid sparing agents can really make all the difference.

MR. BUSKER: Dr. McArthur — take the final word on today's discussion, please.

DR. MCARTHUR: In my opinion, HAND will continue to be a significant clinical problem. As we have indicated, as the population of people living with HIV infection continues to increase, so comorbidities such as HIV-associated aging effects or Alzheimer's disease may become even more relevant.

I think it's important when screening for everyone with HIV infection their neurocognitive function be included as a baseline, and when and if symptoms develop, that screening be repeated.

MR. BUSKER: Dr. Justin McArthur and Dr. Bryan Smith from the Johns Hopkins University School of Medicine, thank you for participating in this eHIV Review Podcast.

DR. MCARTHUR: It's been my pleasure to be here.

DR. SMITH: Thank you so much for the opportunity.

MR. BUSKER: This podcast is presented in conjunction with the *e*HIV Review Newsletter, a peer-reviewed, CME certified literature review e-mailed monthly to clinicians whose work or practice includes treating HIV patients.

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