Thursday, July 24, 2014 | 1:30 – 2:30 pm (EDT)

**Facilitator**
Todd S. Will, MD
University of South Florida

**Didactic Presenter**
Patrick Marsh, MD
University of South Florida

**Case Discussant(s)**
Maribel Gonzalez, RN, ARNP
University of South Florida

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**HIV Case Conference:**
Cognitive Dysfunction and Hepatitis C/HIV
Patrick Marsh, MD
Faculty, Florida/Caribbean AIDS Education and Training Center
Assistant Professor, College Of Medicine, Psychiatry And Behavioral Neurosciences, USF Health Morsani College of Medicine

www.FCAETC.org/ECHO
At the conclusion of this session participants will be able to discuss the following:

• cognitive deficits in patients with Hepatitis C and HIV/Hepatitis C coinfection
• potential etiologies of cognitive impairment in Hepatitis C/HIV coinfection
• prevalence of cognitive impairment in Hepatitis C/HIV

HIV Associated Neurocognitive Disorder (HAND)

• HIV dementia
  – Pre-HAART prevalence 20%
  – Post-HAART prevalence <5%

• Asymptomatic neurocognitive impairment
• Mild neurocognitive disorder
  – Post HAART 20-50% prevalence

Bruce 2014
HAND Symptoms

Early
• Inattention
• Slowed thinking
• Gait unsteadiness
• Impaired handwriting
• Social withdrawal
• Irritability

Late
• Parkinsonian symptoms
• Cortical features
  – Language
  – Memory
  – Executive function

Bruce 2014

HAND Impact

• Poor adherence to HAART
  – Disease progression
  – Increased resistance
  – Increased transmission
• Reduced Quality of Life
• Impaired activities of daily living (ADL)/instrumental activities of daily living (IADL)
  – Loss of independence

Bruce 2014
**Subcortical Circuits**

![Brain circuit diagram](image)

**Hepatitis C and the CNS**

- Peripheral Blood Mononuclear Cells
  - “Trojan Horse”
- Microvascular Endothelial Cells
  - Disruption of Blood Brain Barrier
- Primary Human Astrocytes
  - Inflammatory cascade
- HIV co-infection

Fletcher 2012
Neuropsychiatric Symptoms of Hepatitis C

- Hepatic Encephalopathy (HE)
- Minimal Hepatic encephalopathy (MHE)
- Cognitive Impairment
- Dementia

Cordoba 2003

Hepatic Encephalopathy (HE)

- Waxing and waning alteration of attention, concentration and level of consciousness
- Reversible, associated with decompensated liver failure
  - Elevated ammonia
  - Unfiltered toxins and metabolites

Dihman 2009
**Minimal Hepatic Encephalopathy**

- No recognizable clinical symptoms of HE
  - Normal labs
- Mild cognitive and psychomotor deficits
  - Exam and history
- 30-85% of cirrhotic patients
- Impaired health-related quality of life
- Predicts the development of overt HE
- Associated with poor survival

Dihman 2009

**Cognitive Impairment**

- 33% of non-cirrhotic patients with Hep C
- Associated with “Fatigue”
- “Subcortical”
  - Attention/Working Memory
  - Processing Speed
  - Executive Function
  - Motor Function
  - Verbal Learning

Chiu 2013
Weissenborn 2004
Dementia

- Hazard Ratio 1.36 for dementia diagnosis in HCV patients compared to Non-HCV over 10 years
- Currently no HCV-associated dementia entity
- HIV Dementia Scale or International HIV Dementia Screen

Chiu 2013
HIV Dementia Scale

**HIV Dementia Scale**

- **Memory registration**: Give the patient four words to recall (dog, hat, green, peach)—one second to say each. Then ask the patient to recall all four after you have said them.

- **Attention**: Ask the patient to move their arms: 10 commands. If three errors = 1, four errors = 2, five errors = 3, six errors = 4. Ask the patient to look at your nose. Move the index finger of one hand, and instruct the patient to look at the finger that moves, then look back to your nose. Practice until the patient is familiar with the task. Then, instruct the patient to look at the finger that is NOT moving. Practice until the patient understands the test. Perform 20 trials. An error is recorded when the patient looks toward the finger that is moving.

- **Psychomotor speed**: Ask patient to write the alphabet in uppercase letters horizontally across the page and record time: seconds. If 21 seconds = 0, 21.1 to 24 seconds = 1, 24.1 to 27 seconds = 2, 27.1 to 30 seconds = 3, 30.1 to 33 seconds = 4, 33.1 to 36 seconds = 5, 36.1 to 40 seconds = 6.

- **Memory recall**: Ask for the four words from memory registration (above). Give one point for each correct recall. For words not recalled, penalized with a semantic clue, as follows: animal (dog) name of clothing (hat), color (green), fruit (peach). One half point for each correct recall after prompting.

- **Construction**: Copy the shape below; record time: seconds. If 25 seconds = 0, 25.1 to 29 seconds = 1, 30 seconds = 2.

**Total score**

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Cognitive Impairment/ Dementia Impact

- **Poor Adherence to Therapy**
  - Disease progression
  - Increased resistance
  - Increased transmission
- **Reduced Quality of Life**
- **Impaired ADL/IADL**
  - Loss of independence

Chiu 2013
Possible Etiologies

- Premorbid characteristics and lifestyle
- Psychiatric disease
- Direct of effect of virus
- Secondary effects of inflammation
- HIV coinfection
- Antiviral therapy effects

Perry 2006

Treatment

- Removal of HCV
- Symptomatic treatment
  - Antidepressants
  - Cholinesterase inhibitors
  - Antipsychotics
  - Stimulants
References

• Dhiman RK, Chawla YK. Minimal hepatic encephalopathy. Indian J Gastroenterol. 2009 Jan-Feb;28(1):5-16.
• Bruce J. Brew & Phillip Chan Update on HIV Dementia and HIV-Associated Neurocognitive Disorders Curr Neurol Neurosci Rep (2014) 14:468
• N. F. Fletcher and J. A. McKeating Hepatitis C virus and the brain Journal of Viral Hepatitis, 2012, 19, 301–306
• Cordoba J et al, Quality of life and cognitive function in hepatitis C at different stages of liver disease. J. Hepatology 39 (2003) 231-238

Question & Answer Session