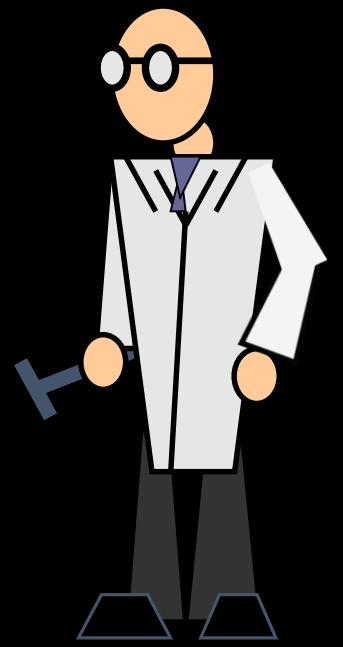
# Stroke and Dementia Update: Vascular Cognitive Impairment

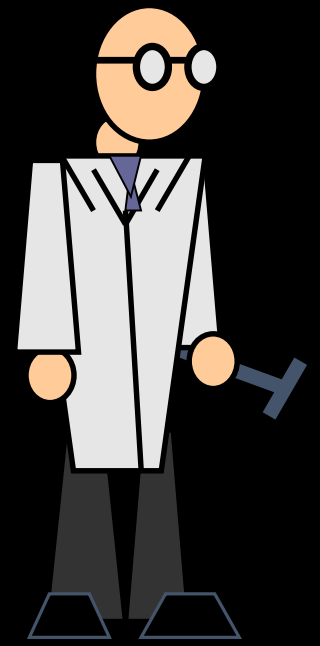
Sean J. Udow, MD FRCPC Neurology
Assistant Professor, Section of Neurology
Department of Internal Medicine
University of Manitoba



# Faculty/Presenter Disclosure

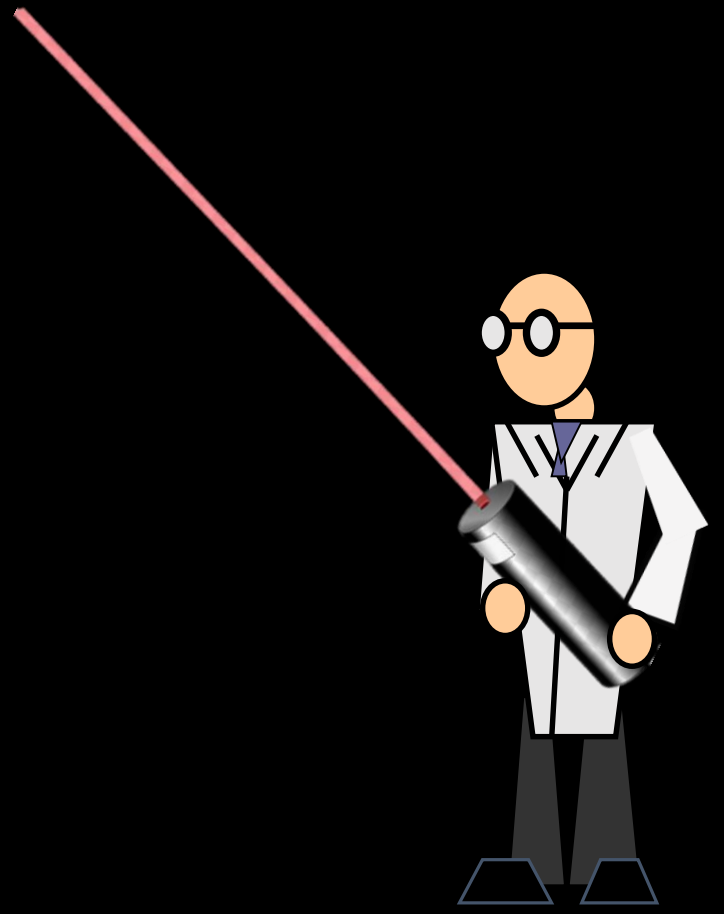
- **Faculty:** Sean J. Udow

- **Relationships with commercial interests:**
  - No conflict



# Objectives

- To review normal cognitive functions



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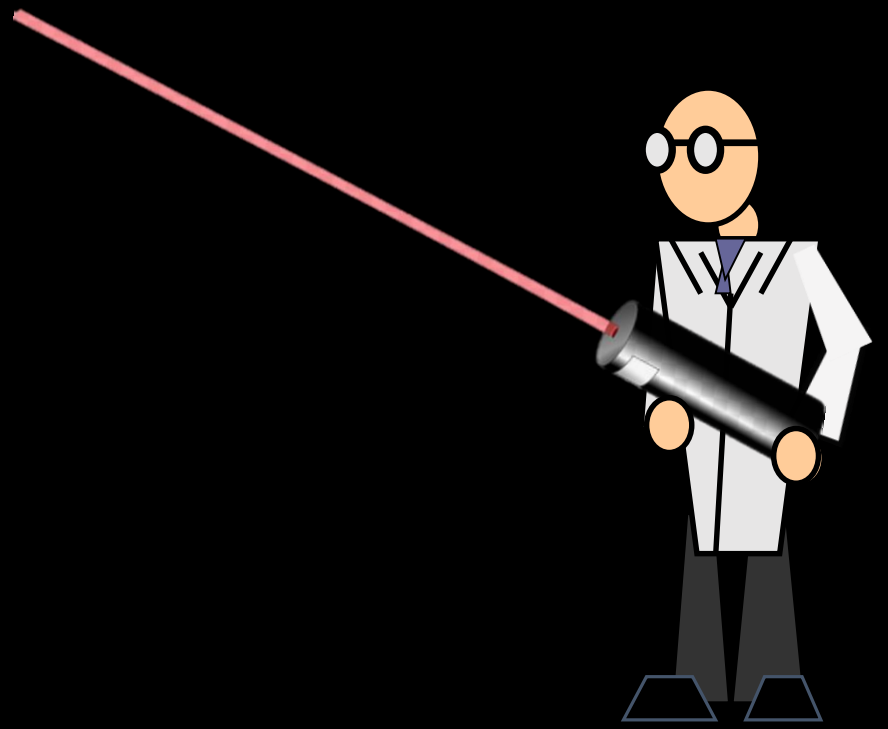

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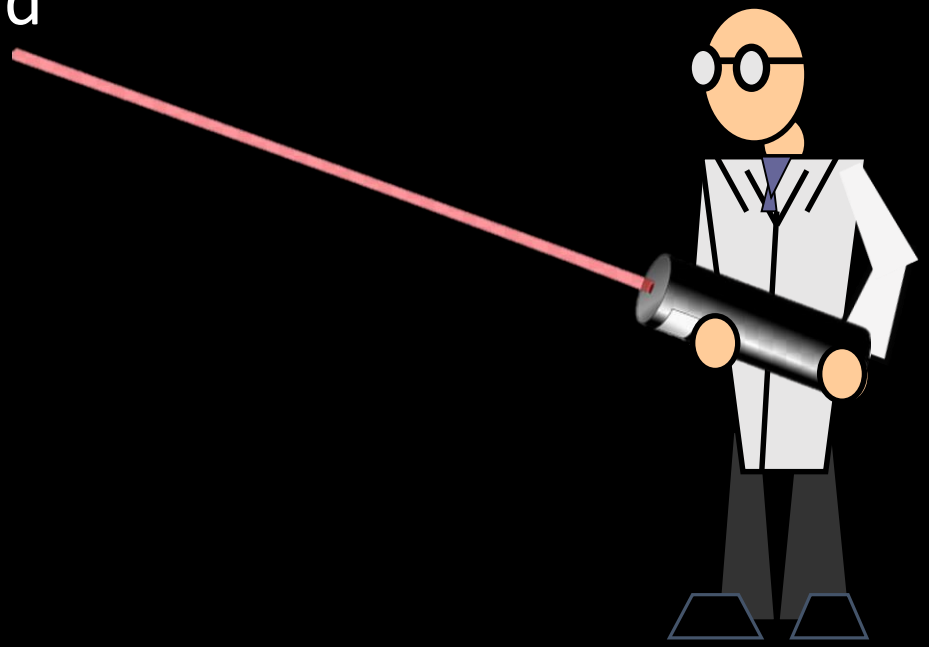

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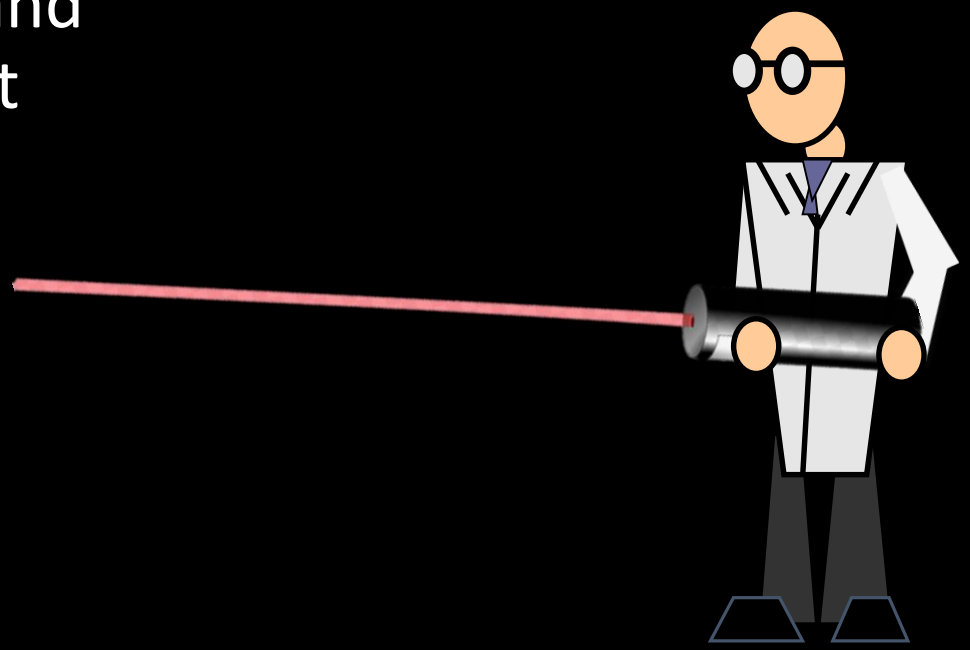

# Objectives

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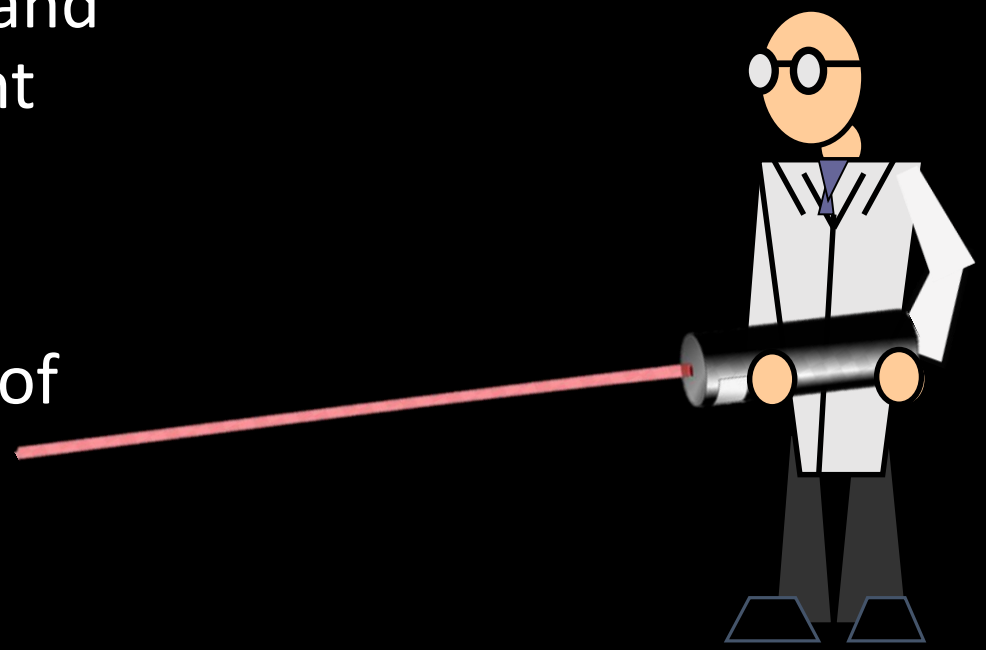
- To discuss the diagnosis, classification and causes of vascular cognitive impairment (VCI)
- To identify the clinical features of VCI
- To describe principles of management of VCI

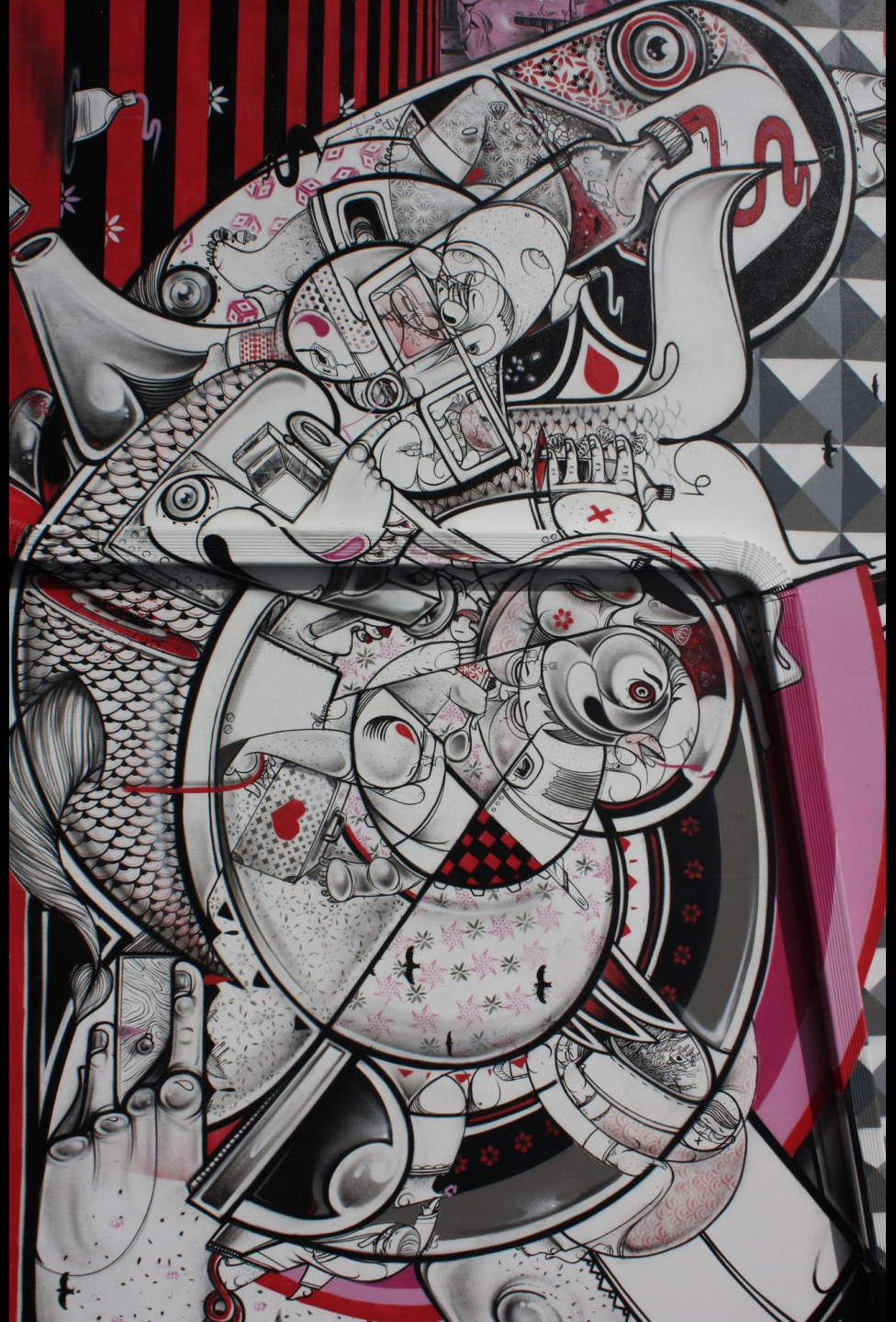


# What is Cognition?

- **Cognition** is the mental process of acquiring knowledge and understanding through thought, experience and the senses

# Cognitive Domains

- Memory
- Language
- Visual-Perceptual-Spatial
- Executive Function
- Social cognition

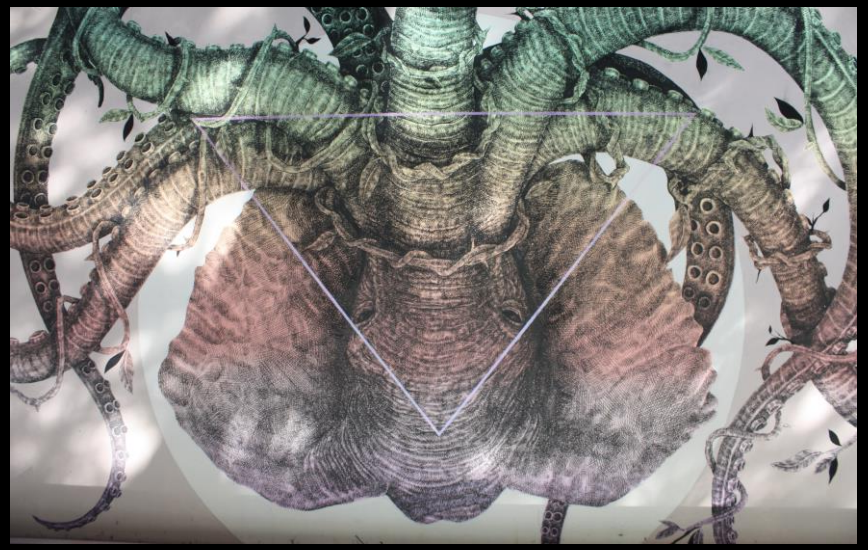


# Cognitive Domains

- **Memory** is the ability to learn and recall new experiences
- **Language** is the ability to express thoughts through speech, and understand the speech of others
- **Visuospatial ability** involves navigation and recognizing faces and objects
- **Executive function** includes the ability to pay attention, organize, plan, solve problems and multitask
- **Social cognition refers to the regulation of behavior, personality and social comportment**

# Functional Networks

- Cognitive domains are not easily localized to a single anatomic structure
- Rather, they rely on large-scale neural networks
- Roughly - grey matter nodes brain connected by white matter tracts
- A lesion in one or more parts of these networks can impair cognition

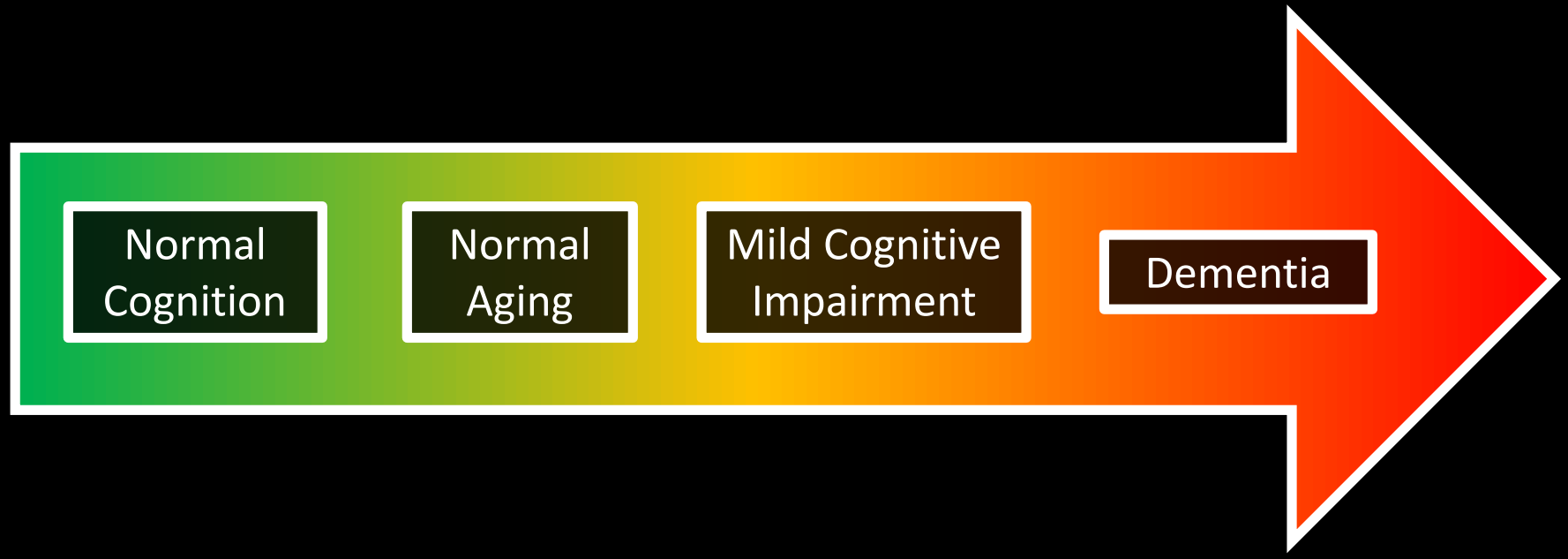


# Cognitive Impairment

- Because a lesion in one or more of the components of a neural network can cause cognitive impairment, the differential diagnosis of cognitive impairment is broad
- Anything that can damage brain tissue can impair cognition
- Roughly, these causes are divided into neurodegenerative and non-degenerative classifications
- Cognitive impairment comes in two varieties:
  - Mild cognitive impairment
  - Dementia

# Mild Cognitive Impairment

- The state between normal cognition and dementia
- A syndrome, not a diagnosis
  - Has an underlying cause, which is the diagnosis
- The prevalence among older adults (> 70 years) is roughly ~15%



# Mild Cognitive Impairment – Diagnostic Criteria

- 1. A patient presents with a complaint about cognitive function
  - Complaint can arise from the patient, a caregiver or physician
- 2. There is an **objective** deficit in cognition
  - May or may not involve memory impairment: amnestic or non-amnestic types
  - May involve one or more cognitive domain (single or multi)
  - Deficit in cognition is NOT NORMAL FOR AGE
- 3. Decline from previous state – a change in performance
- 4. **‘Essentially normal’ functional activities**
  - Can live independently in the community (independent with IADLs)

# Dementia- Diagnostic Criteria

- 1. A patient presents with a **complaint** about cognitive function
- 2. There is an **objective** deficit in cognition
- 3. **Decline** from previous state – a change in performance
- 4. **The cognitive deficits interfere with independence in every day activities**

# Neurodegenerative Dementias

- Alzheimer Disease
- Frontotemporal Dementia
- Parkinsonian Dementias
  - Dementia with Lewy bodies
  - Parkinson disease dementia
  - Atypical parkinsonian syndromes
- Less common:
  - Huntington disease

# Nondegenerative Cognitive Impairment

- Vascular
  - Vascular Dementia
  - CADASIL*
- Infectious
  - Eg. HIV, syphilis
- Toxic
  - Alcoholic Dementia
  - Heavy metals
  - Posttraumatic Dementia
- Autoimmune / Inflammatory
  - Multiple Sclerosis
  - Collagen disorders and vasculitis
  - Paraneoplastic Limbic Encephalitis
- Metabolic / Endocrine
  - Eg. Hypothyroidism, B12 deficiency
- Neoplastic
  - Brain tumors
  - Metastases
  - CNS lymphoma
- Depression
- Chronic traumatic encephalopathy
- Normal-Pressure Hydrocephalus
- Rapidly Progressive Dementias

*CADASIL = cerebral autodomal dominant arteriopathy with subcortical infacts and leukoencephalopathy

CONTINUUM **Review Article**

# Vascular Cognitive Impairment

Eric Smith, MD, MPH

Address correspondence to Dr Eric Smith, University of Calgary, Room C1261, Foothills Medical Centre, 1403 29 St NW, Calgary, AB, Canada, *Eesmith@ucalgary.ca*.

**Relationship Disclosure:**
Dr Smith serves as a board member of the Quality Oversight Committee of the American Heart Association and as an assistant editor for *Stroke*. Dr Smith receives grant support from the Alzheimer Society of Canada, the Canadian Institutes of Health Research, the Canadian Partnership Against Cancer, and the Heart and Stroke Foundation of Canada and receives research support from McMaster University.

**Unlabeled Use of Product/Investigational Use Disclosure:**
Dr Smith discusses the unlabeled/investigational use of cholinesterase inhibitors for the treatment of vascular dementia.



## ABSTRACT

**Purpose of Review:** This article provides a diagnostic framework for vascular cognitive impairment, discusses prevalence and relationships to other neurodegenerative pathologies, and provides advice on diagnostic workup and management.

**Recent Findings:** Vascular cognitive impairment is the second most common cause of cognitive impairment and frequently coexists with other neurodegenerative neuropathologies. Three new diagnostic criteria have been published recently; common diagnostic elements include the need to classify cognitive impairment as mild cognitive impairment or dementia and to link the cognitive impairment to evidence of clinically significant cerebrovascular disease. Vascular cognitive impairment may be further subclassified into poststroke vascular cognitive impairment and nonstroke vascular cognitive impairment, most commonly caused by cerebral small vessel disease, which may only be recognized on neuroimaging.

**Summary:** Vascular cognitive impairment is a potentially treatable common cause of cognitive impairment, progression of which may be slowed or halted by secondary prevention of vascular disease.

Continuum (Minneap Minn) 2016;22(2):490–509.

# Vascular Cognitive Impairment

- ‘VCI’
- Cognitive impairment caused by or associated with vascular factors

# Vascular Cognitive Impairment

- 2nd most common cause of dementia after Alzheimer disease (AD)
- May be the most preventable and treatable cause
- VCI contributes to mixed dementia
  - Can accompany other neuropathologies like AD

- Two forms
  - Post-stroke – immediate and direct consequence of symptomatic stroke
  - Chronic small vessel ischemic change – detected with neuroimaging

# Single Infarcts

‘Strategic locations'

- Left hemispheric language areas
- Thalamus
- Midbrain
- Medial temporal lobe
- Medial frontal lobe

- Affect networks sustaining language, attention or memory

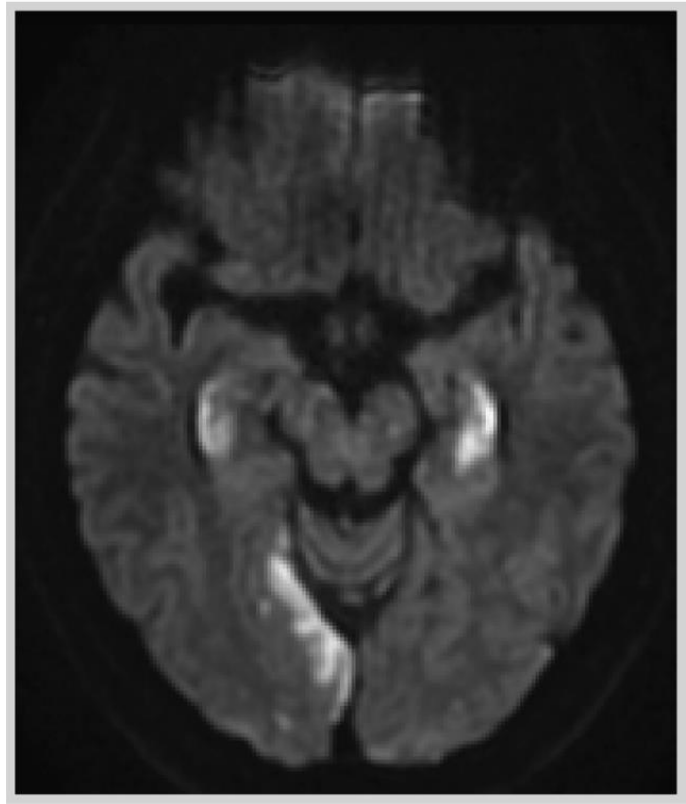


**FIGURE 6-2** Axial diffusion-weighted MRI of the patient in **Case 6-1** shows acute infarction (bright signal) in the right occipital and bilateral medial temporal lobes.

# Small Vessel Disease

- Chronic cerebral SVD stronger association with cognitive impairment
- Blood-brain barrier compromise
  - Leakage of fluid and macromolecules
  - Chronic white matter disease
- Cortical and subcortical microinfarcts
- Lacunar strokes
- Chronic cerebral hypoperfusion
- Hippocampal atrophy

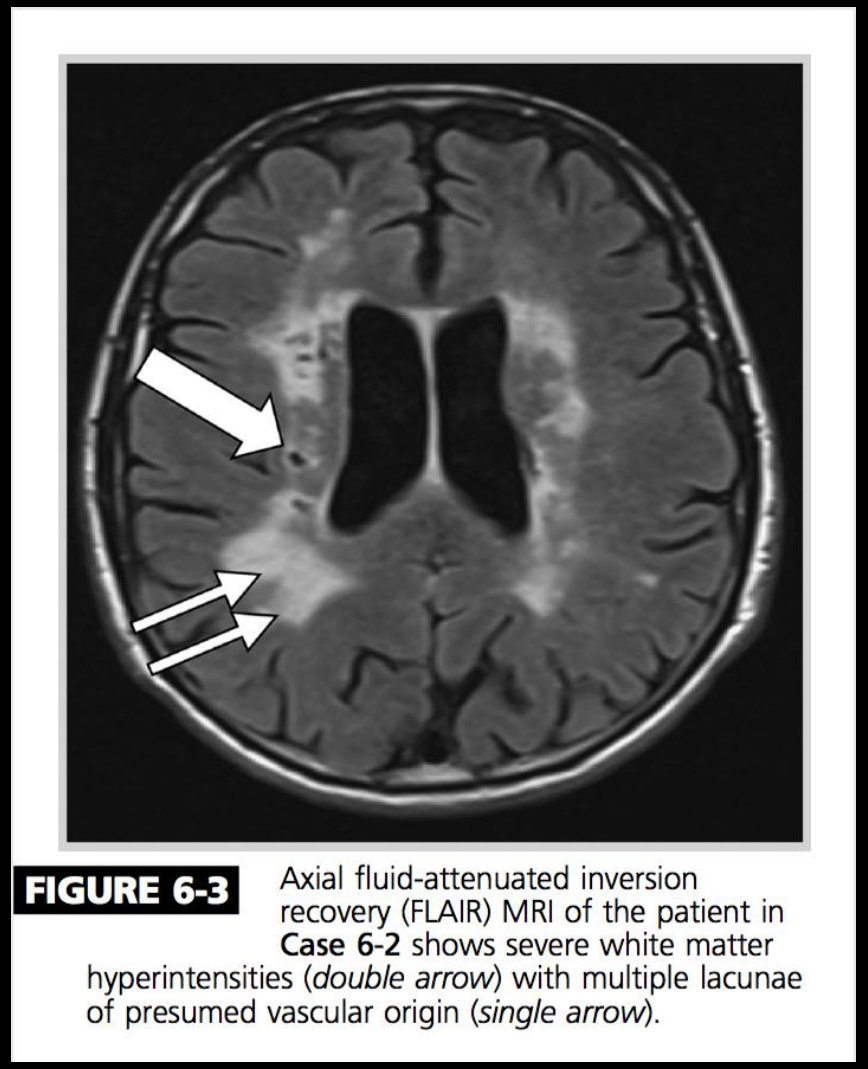


**FIGURE 6-3** Axial fluid-attenuated inversion recovery (FLAIR) MRI of the patient in **Case 6-2** shows severe white matter hyperintensities (*double arrow*) with multiple lacunae of presumed vascular origin (*single arrow*).

# Diagnosis of VCI

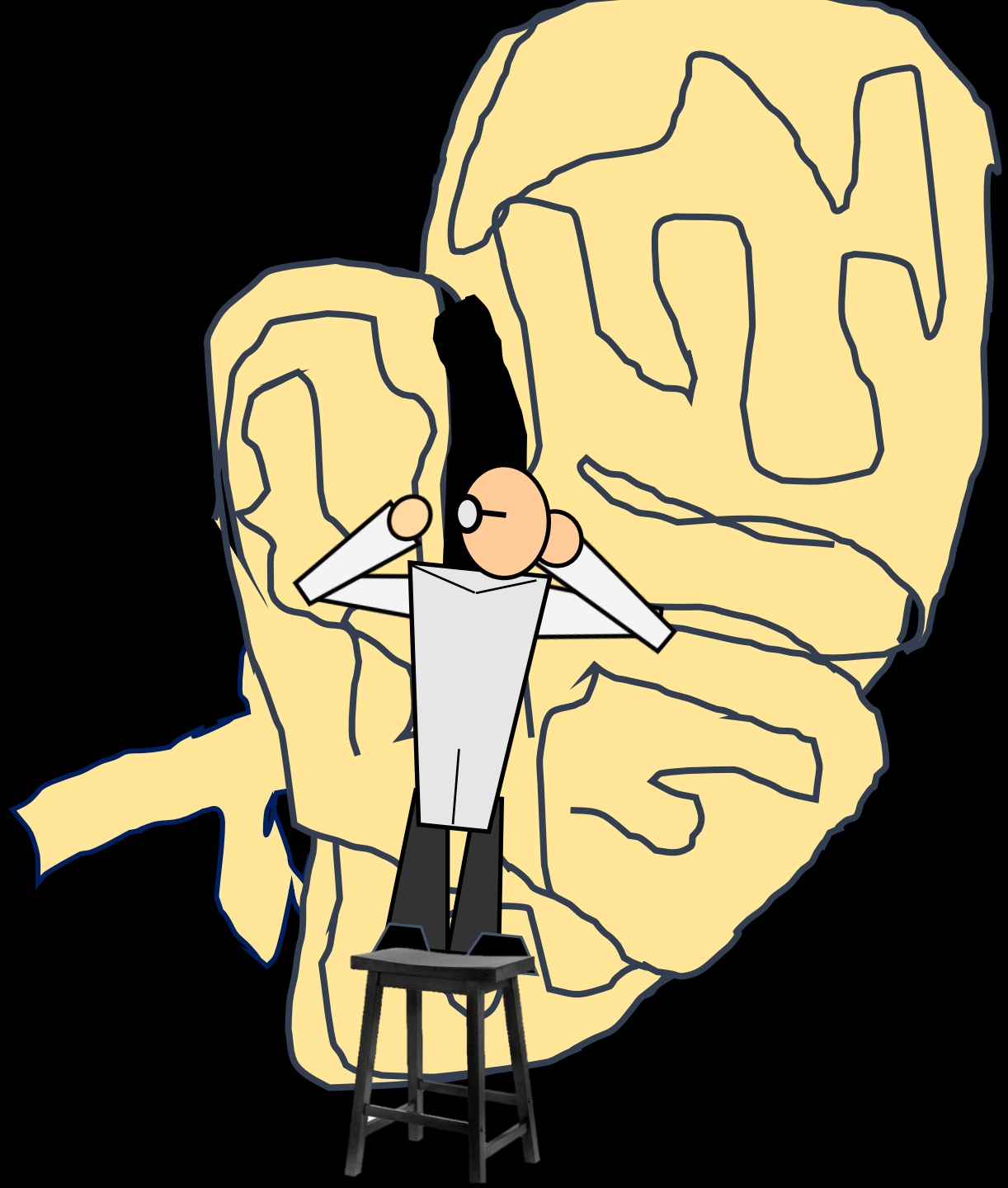


**TABLE 6-1 Recent Classification Criteria for Vascular Cognitive Impairment**

| | AHA/ASA[4] | Vas-Cog Society[5] | *DSM-5*[7] |
|---|---|---|---|
| **Cognitive criteria** | Discriminates between vascular mild cognitive impairment and vascular dementia | Discriminates between mild and major vascular cognitive disorder (dementia) | Discriminates between mild and major vascular neurocognitive disorder |
| **Criteria for probable vascular cognitive impairment** | There is imaging evidence of cerebrovascular disease and either:<br>There is a clear temporal relationship between a vascular event (eg, clinical stroke) and onset of cognitive deficits.<br>*OR*<br>There is a clear relationship in the severity and pattern of cognitive impairment and the presence of diffuse, subcortical cerebrovascular disease pathology.<br>There should be no history of gradually progressive cognitive deficits before or after stroke that suggest the presence of a nonvascular cognitive disorder (eg, Alzheimer disease). | Either:<br>The onset of cognitive deficits follows one or more strokes or there are physical signs consistent with stroke.<br>*OR*<br>If history of stroke or transient ischemic attack is absent, then there is evidence of cognitive decline in speed of information processing, complex attention or frontal executive functions, accompanied by one or more of: gait disturbances, urinary symptoms, or personality and mood changes.<br>There should be neuroimaging evidence of either large vessel infarct, strategically placed single infarct(s) or intracerebral hemorrhages(s), multiple (more than two) lacunar infarcts outside the brainstem, or extensive and confluent white matter lesions.<br>There should not be evidence of other nonvascular cognitive, medical, psychiatric, or neurologic disorders sufficient to explain the cognitive impairment (including Alzheimer disease). | The criteria are met for major or mild neurocognitive disorder.<br>The clinical features are consistent with a vascular etiology, as suggested by either of the following:<br>Onset of the cognitive deficits is temporally related to one or more cerebrovascular events.<br>*OR*<br>Evidence for decline is prominent in complex attention (including processing speed) and frontal-executive function.<br>There is evidence of the presence of cerebrovascular disease from history, physical examination, and/or neuroimaging considered sufficient to account for the neurocognitive deficits.<br>The symptoms are not better explained by another brain disease or systemic disorder. |

Smith, Continuum April 2016

Commonalities among diagnostic criteria:

- 1. Clinical or imaging evidence of cerebrovascular disease
- 2. Relationship between vascular disease cognitive problems
  - Temporally
  - Associated with burden subcortical vascular pathology
  - Associated with clinical evidence of subcortical pathology
    - Gait, urinary, personality, mood changes
- 3. No evidence of another cause
  - Eg AD, other conditions

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# VCI Etiologies

**TABLE 6-2 Vascular Pathology of Vascular Cognitive Impairment[a]**

▶ **Parenchymal Lesions of Vascular Etiology**

- Large vessel atherothromboembolic disease
  - Multiple infarcts
  - Single strategically placed infarct
- Small vessel disease
  - Multiple lacunar infarcts
  - Ischemic white matter damage
  - Dilated perivascular spaces
  - Microinfarcts
  - Microhemorrhages
- Hemorrhage
  - Intracerebral hemorrhage
  - Multiple microbleeds
  - Subarachnoid hemorrhage
- Hypoperfusion
  - Hippocampal sclerosis
  - Laminar cortical necrosis

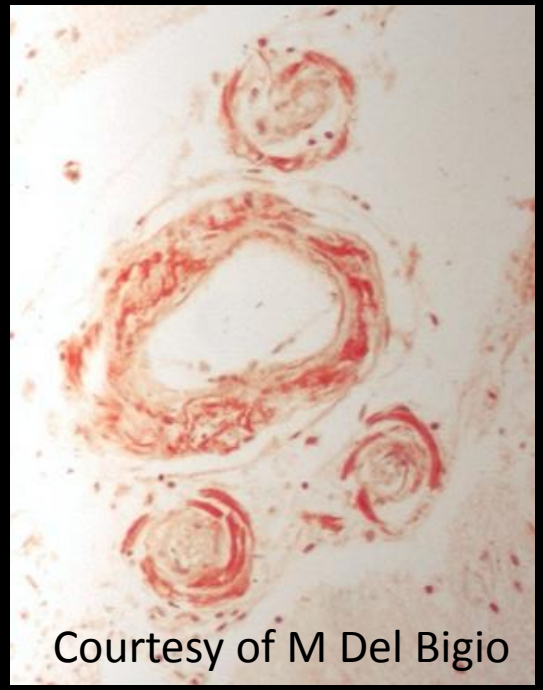
▶ **Types of Vascular Pathologies**

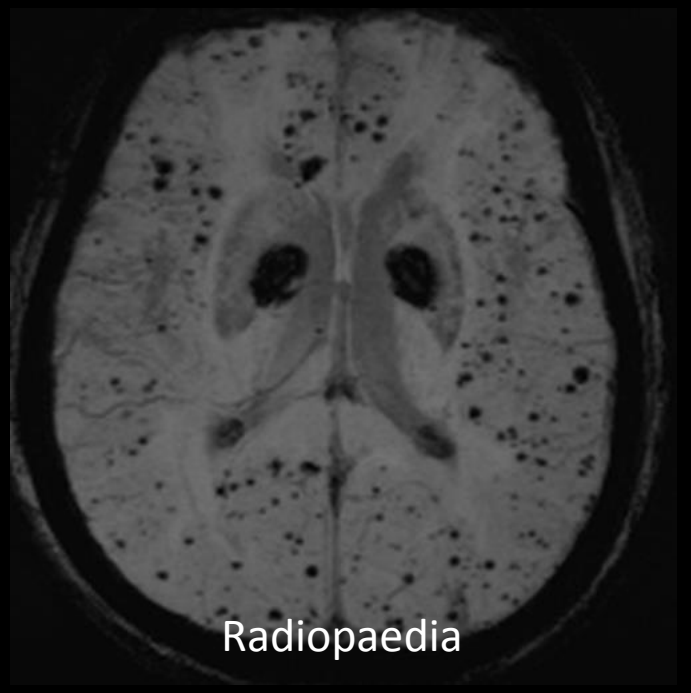
- Atherosclerosis
- Cardiac, atherosclerotic, and systemic emboli
- Arteriolosclerosis
- Lipohyalinosis
- Cerebral amyloid angiopathy
- Vasculitis
- Venous collagenosis
- Arteriovenous fistulae
- Hereditary angiopathies (eg, cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy [CADASIL])
- Berry aneurysms
- Miscellaneous vasculopathies (eg, moyamoya disease)
- Cerebral venous thrombosis

[a] Modified with permission from Sachdev P, et al, Alzheimer Dis Assoc Disord.[5] *journals.lww.com/alzheimerjournal/Abstract/2014/07000/Diagnostic_Criteria_for_Vascular_Cognitive.2.aspx*. 

# Cerebral Amyloid Angiopathy

- Amyloid beta – a protein that accumulates in neurons in Alzheimer disease
- accumulates in the walls of cerebral blood vessels
  - This narrows cerebral blood vessels
- Causes small strokes and cerebral hemorrhages
- Contributes to dementia


Courtesy of M Del Bigio

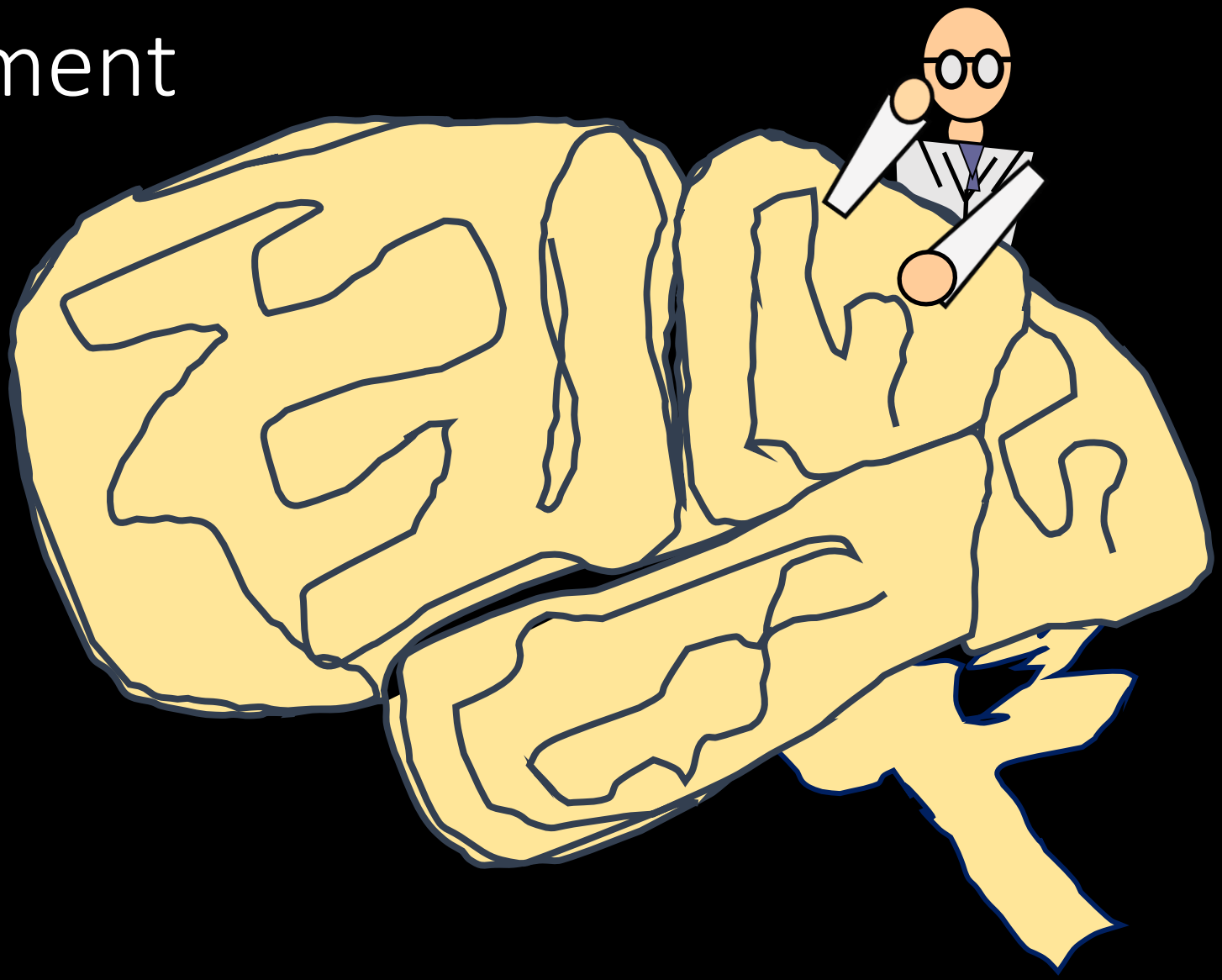

Radiopaedia

# CADASIL

- Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy

- Autosomal dominant *NOTCH3* gene mutation
- Migraine
- Lacunar strokes
- Vascular cognitive impairment due to multiple lacunar infarcts and white matter hyperintensities
- No disease modifying treatment

# Clinical Features of Vascular Cognitive Impairment



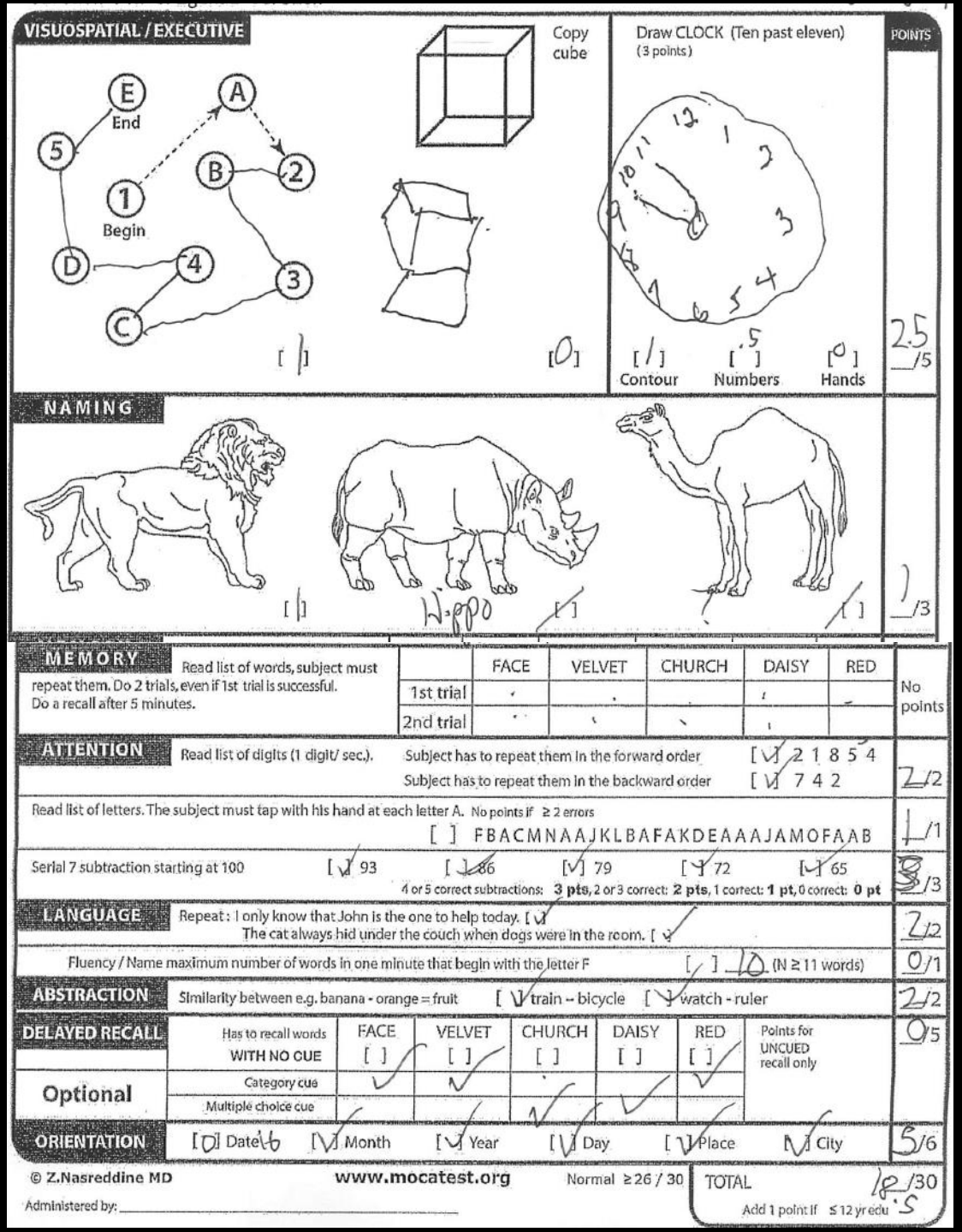
# Vascular Dementia – Clinical Features

- ‘Frontal subcortical’ cognitive profile
  - executive dysfunction and slow processing speed
- Frontal release signs
- Frontal gait disorder
- Urinary incontinence
- Apathy, depression, emotional incontinence
- Focal neurological signs
  - Asymmetric spasticity / hyperreflexia / Babinski sign
- Stepwise progression of dementia with intervening static periods
- Presence of vascular risk factors:
  - Diabetes mellitus, hypertension, smoking  - should increase suspicion

| Hachinski Ischemic Scale | |
|---|---|
| **Feature** | **Value** |
| Abrupt onset | 2 |
| Stepwise deterioration | 1 |
| Fluctuating course | 2 |
| Nocturnal confusion | 1 |
| Relative preservation of personality | 1 |
| Depression | 1 |
| Somatic complaints | 1 |
| Emotional incontinence | 1 |
| History or presence of hypertension | 1 |
| History of strokes | 2 |
| Evidence of atherosclerosis | 1 |
| Focal neurological symptoms | 2 |
| Focal neurological signs | 2 |

- Helps distinguish VCI from AD
- Score of >7 indicates vascular involvement

# 90 year old man
# 3 y worsening cognition & ambulation



VISUOSPATIAL / EXECUTIVE

Copy cube

Draw CLOCK (Ten past eleven) (3 points)

POINTS

E End, A, 5, B, 2, 1 Begin, D, 4, 3, C

[ 1 ] [ 0 ]

[ 1 ] Contour [ .5 ] Numbers [ 0 ] Hands

2.5 /5

NAMING

[ 1 ] Hippo [ ] [ ]

1 /3

MEMORY — Read list of words, subject must repeat them. Do 2 trials, even if 1st trial is successful. Do a recall after 5 minutes.

| | FACE | VELVET | CHURCH | DAISY | RED |
|---|---|---|---|---|---|
| 1st trial | ✓ | ✓ | ✓ | ✓ | ✓ |
| 2nd trial | ✓ | ✓ | ✓ | ✓ | ✓ |

No points

ATTENTION — Read list of digits (1 digit/ sec.).

Subject has to repeat them in the forward order [✓ 2 1 8 5 4]

Subject has to repeat them in the backward order [✓ 7 4 2]

2/2

Read list of letters. The subject must tap with his hand at each letter A. No points if ≥ 2 errors

[ ] F B A C M N A A J K L B A F A K D E A A A J A M O F A A B

1/1

Serial 7 subtraction starting at 100 [✓ 93] [✗ 86] [✓ 79] [✓ 72] [✓ 65]

4 or 5 correct subtractions: **3 pts**, 2 or 3 correct: **2 pts**, 1 correct: **1 pt**, 0 correct: **0 pt**

3/3

LANGUAGE — Repeat: I only know that John is the one to help today. [✓] The cat always hid under the couch when dogs were in the room. [✓]

2/2

Fluency / Name maximum number of words in one minute that begin with the letter F [ ] 10 (N ≥ 11 words)

0/1

ABSTRACTION — Similarity between e.g. banana - orange = fruit [✓ train – bicycle] [✓ watch - ruler]

2/2

DELAYED RECALL

| | Has to recall words WITH NO CUE | FACE | VELVET | CHURCH | DAISY | RED | Points for UNCUED recall only |
|---|---|---|---|---|---|---|---|
| | | [ ] | [ ] | [ ] | [ ] | [ ] | |
| Optional | Category cue | ✓ | ✓ | | | ✓ | |
| | Multiple choice cue | | | ✓ | ✓ | | |

0/5

ORIENTATION — [0] Date [✓] Month [✓] Year [✓] Day [✓] Place [✓] City

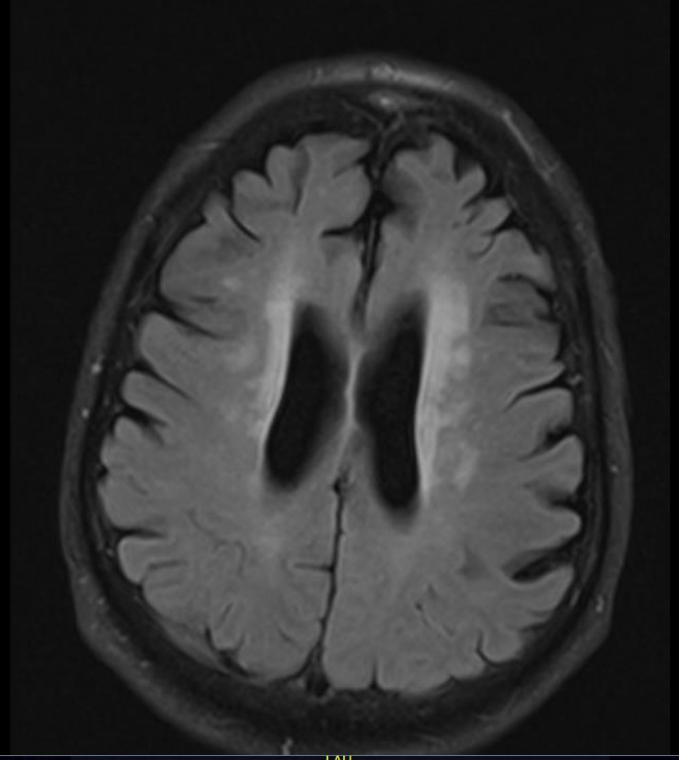
5/6

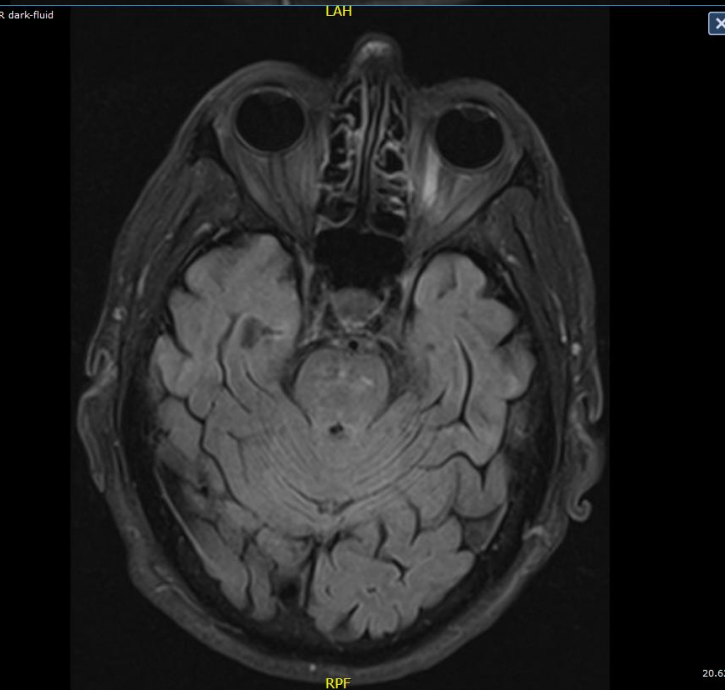
© Z.Nasreddine MD www.mocatest.org Normal ≥ 26 / 30

TOTAL 18 /30

Add 1 point if ≤ 12 yr edu .5

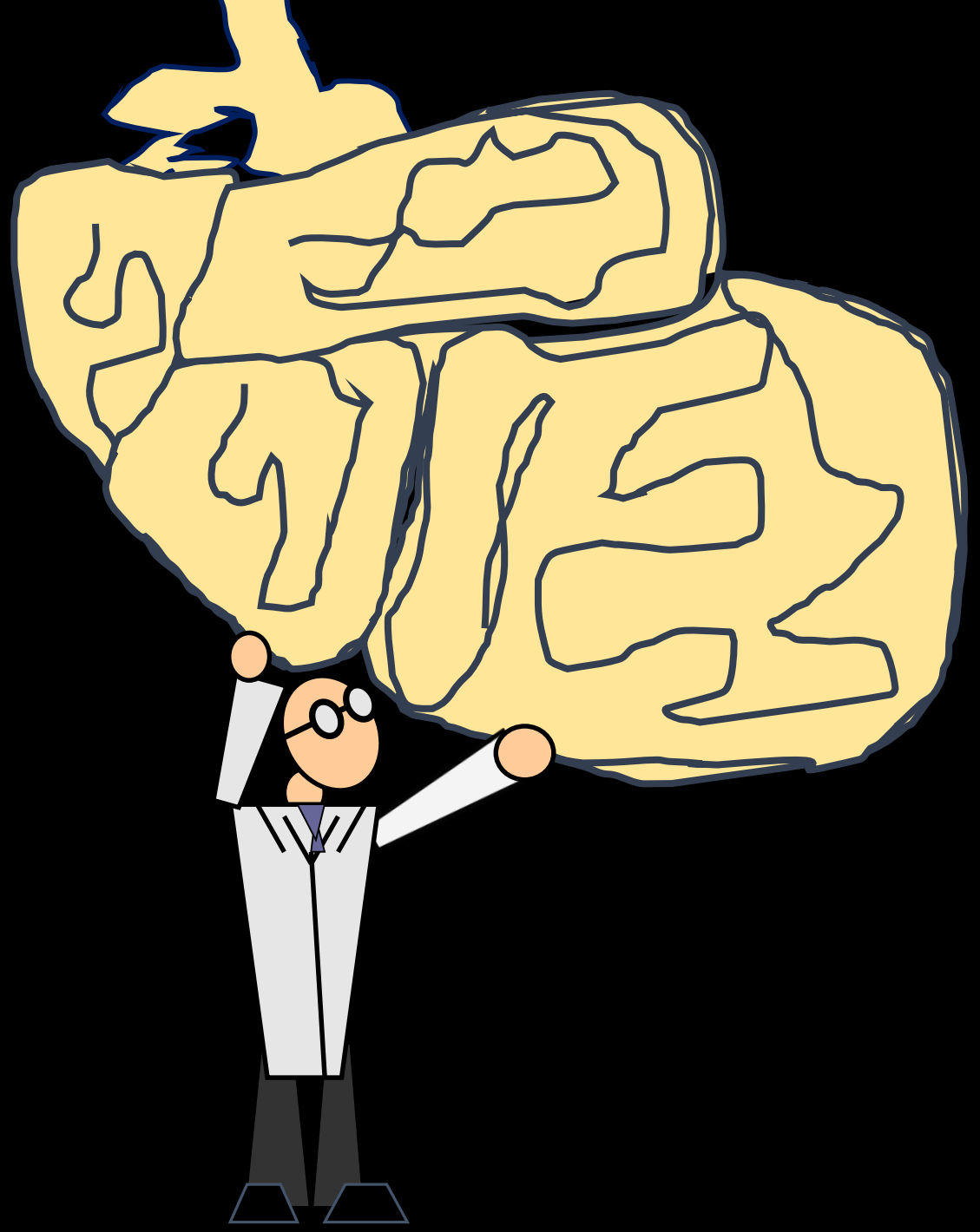
Administered by: _____





# Vascular Cognitive Impairment - Management

- Patient and caregiver support
- Cognitive rehabilitation (for post-stroke VCI)
- Cognitive enhancing medication
- Secondary stroke prevention



# Personal and Caregiver Support

- Assessment of driving safety
- Safety in the home
- Financial and medical advanced planning
- Management of neuropsychiatric complications
- Palliative care as appropriate

# Cognitive Enhancers

- = Cholinesterase inhibitors
  - Donepezil
  - Galantamine
  - Rivastigmine
- Modest benefit in VCI – including in mixed VCI & AD
- Canadian Best Practice Recommendations for Stroke Care:
  - Recommend cholinesterase inhibitor with intermediate level evidence

# Secondary Prevention

- “Mechanism Mechanism Mechanism” – Simerpreet Bal
  - Particularly in the ‘post-stroke’ VCI
- Control of risk factors may slow progression of small vessel disease
  - ASA reasonable
  - Statin – unclear evidence, use if hypercholesterolemia
  - Blood pressure control
- Lifestyle counselling
  - Healthy living – mediterranean diet, exercise, social / mental stimulation

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- To describe principles of management of VCI