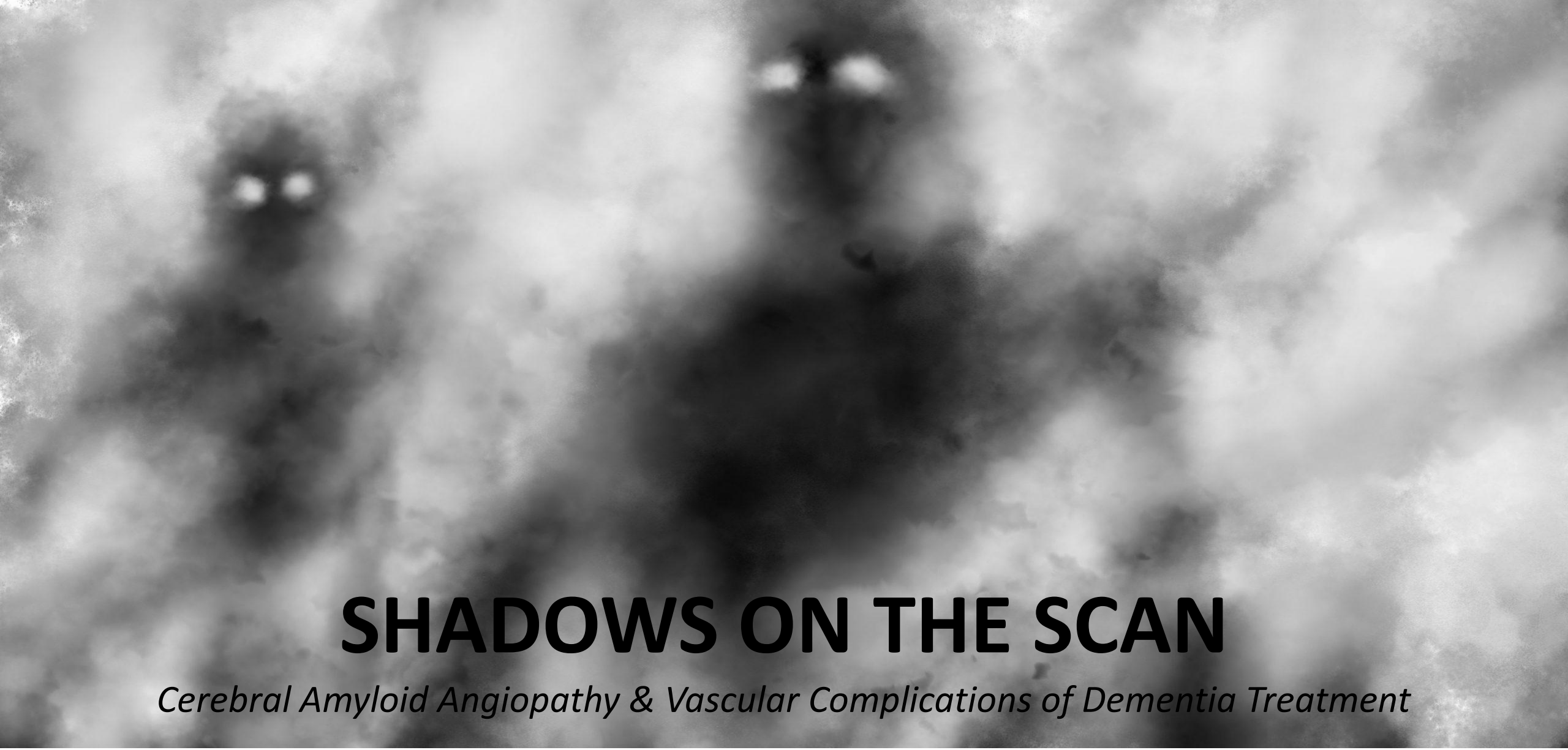


SHADOWS ON THE SCAN

Cerebral Amyloid Angiopathy & Vascular Complications of Dementia Treatment

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Objectives

At the end of the presentation, learners will understand:

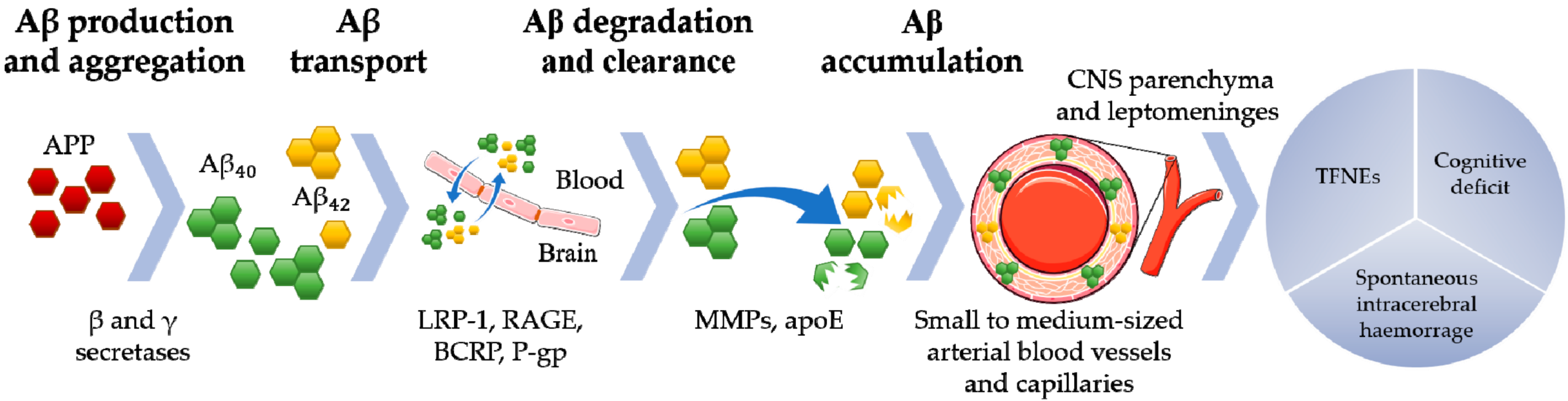
1. *the pathophysiology of CAA and how is contributes to Intracranial hemorrhages*
2. *the diagnostic criteria for CAA and it's challenges*
3. *the decision points for acute stroke treatment in patient with CAA*
4. *secondary stroke prevention for patients with CAA*
5. *potential complications of new Alzheimer's disease treatment to be aware of*

Cerebral Amyloid Angiopathy (CAA)

- Disease of age
- Characterized by progressive amyloid beta-peptide deposits within small to medium sized blood vessels of the brain and leptomeninges
- Important differential dx in:
  - lobar intracerebral hemorrhages (ICH)
  - Incidental microbleeds or hemosiderosis on MRI
  - Transient neurologic symptoms
  - Cognitive impairment age >50yo

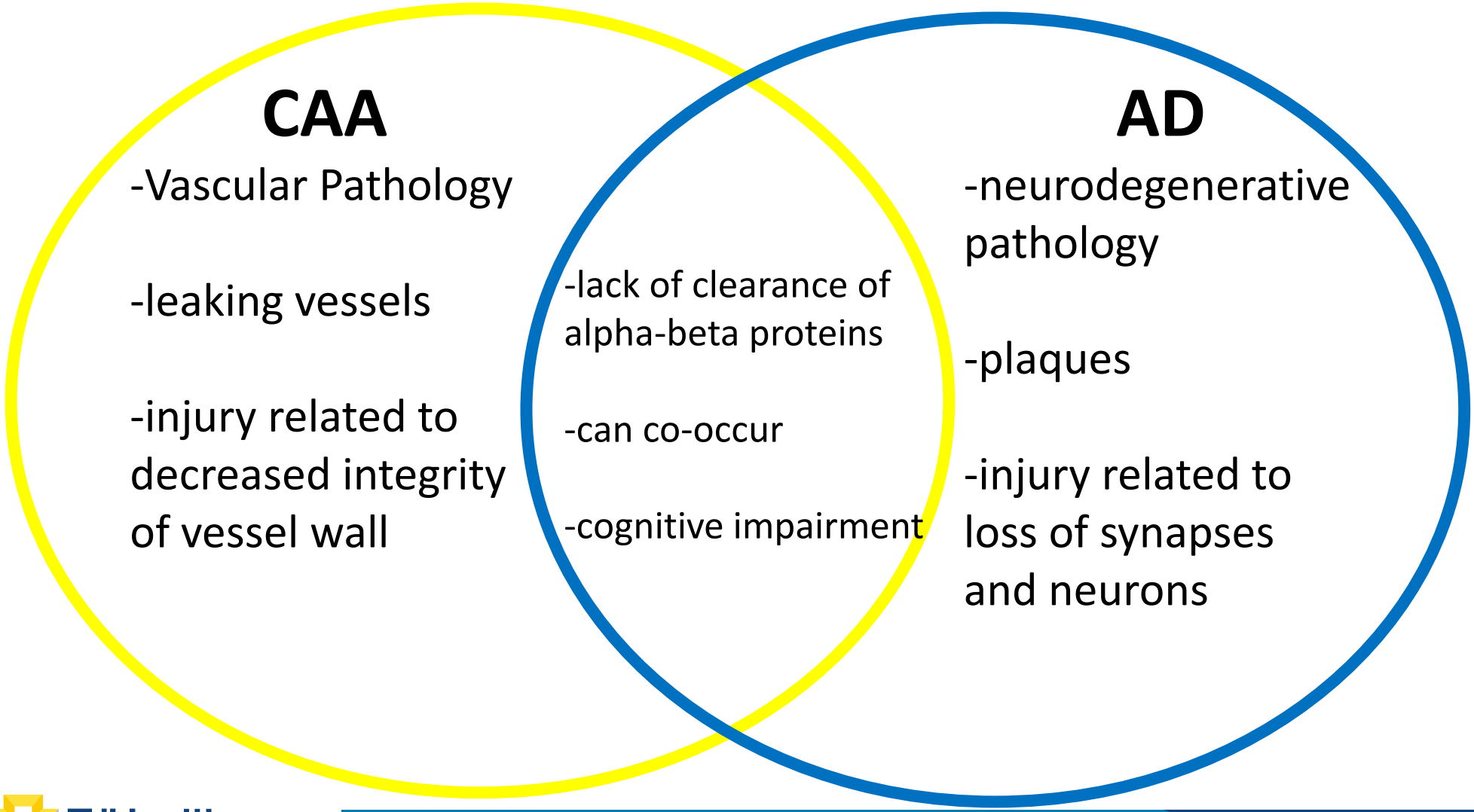
Development of CAA

Amyloid beta peptides



- Alzheimer's disease
  - The *AB* peptides that lead to CAA, are similar to the *AB* that produces plaques seen in some AD patients
- Development
  - A disease of age
  - Minority have genetic component

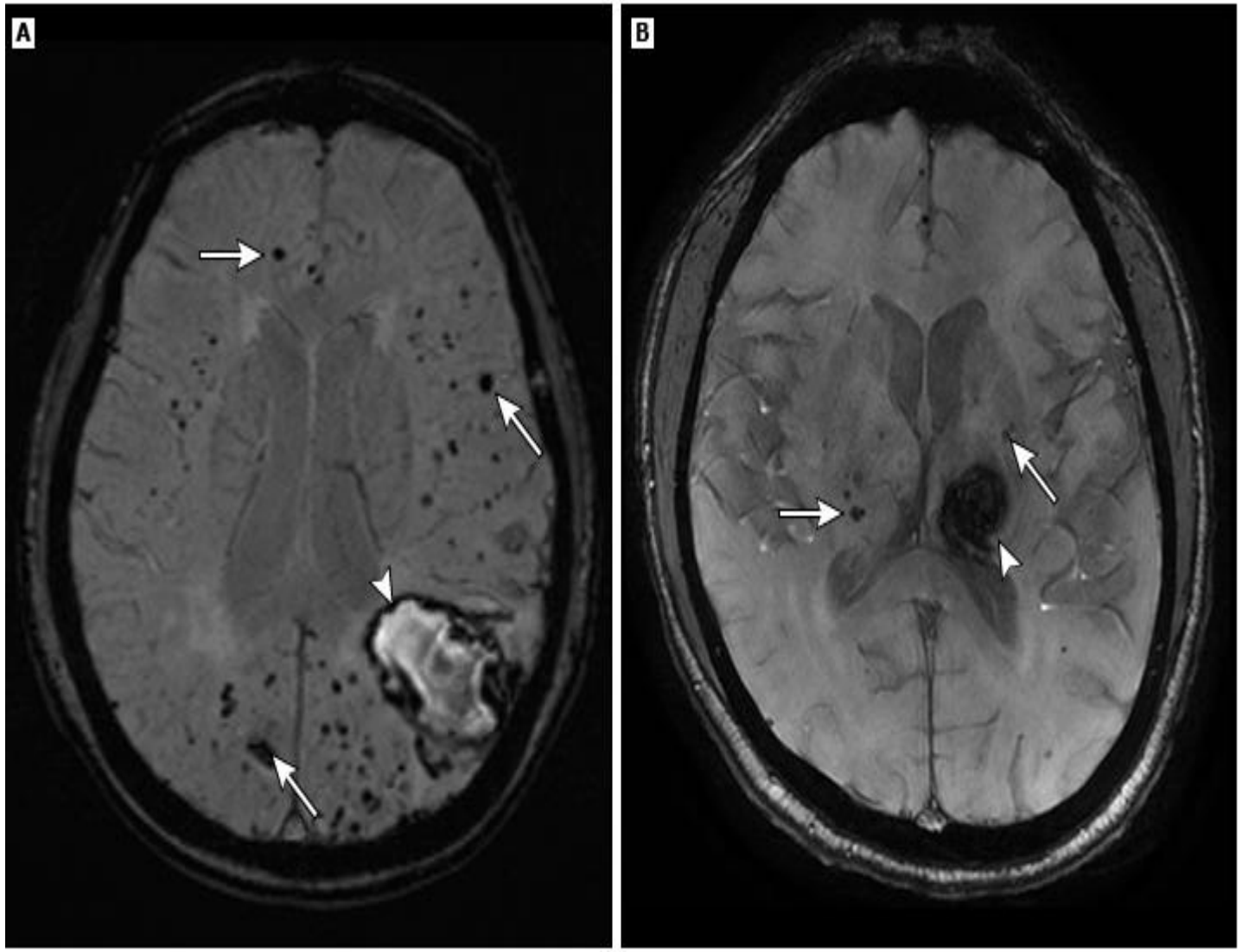
CAA vs AD


CAA
-Vascular Pathology
-leaking vessels
-injury related to decreased integrity of vessel wall
-lack of clearance of alpha-beta proteins
-can co-occur
-cognitive impairment
AD
-neurodegenerative pathology
-plaques
-injury related to loss of synapses and neurons

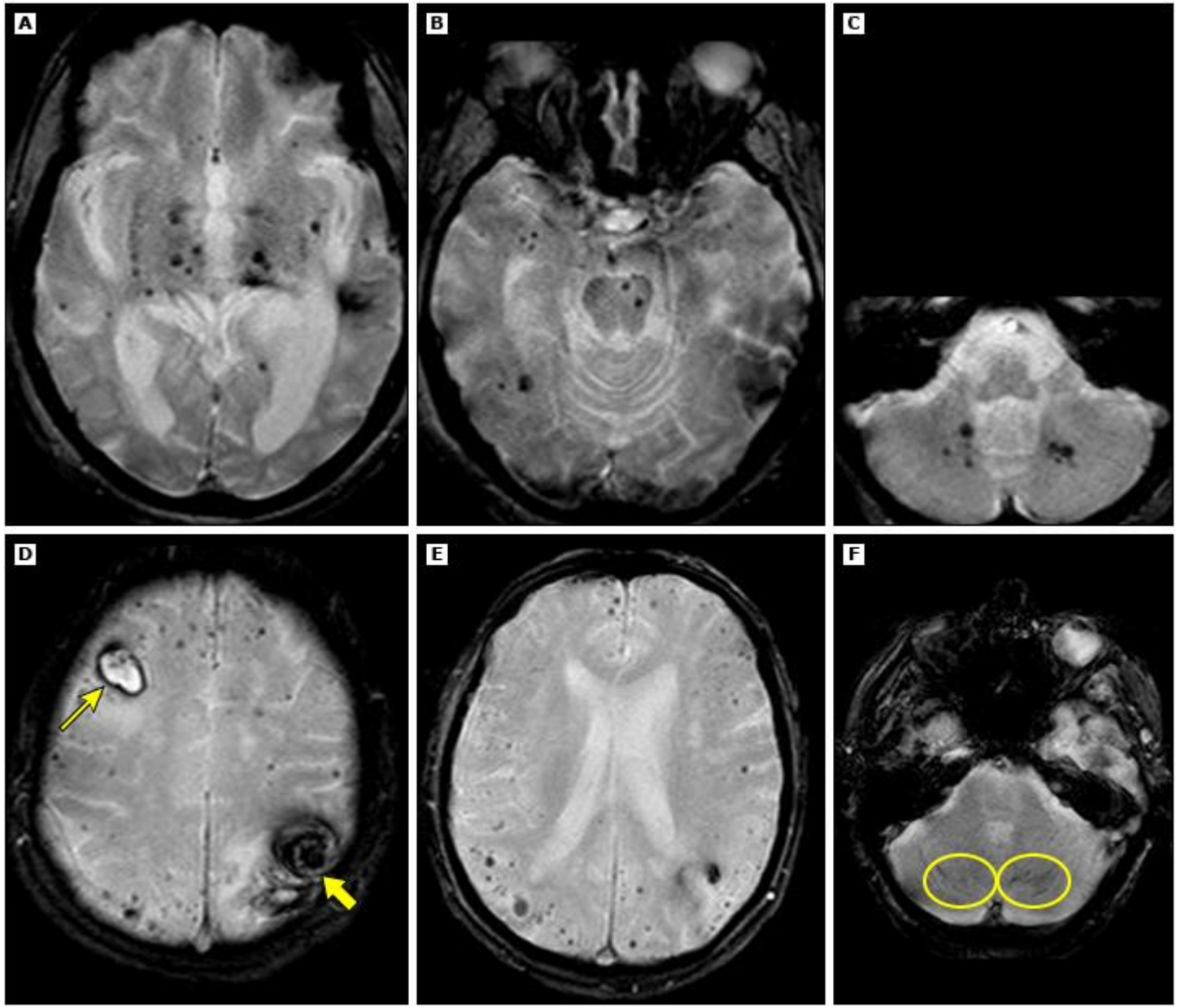
CAA-Pathophysiology

- Lobar Intracerebral Hemorrhage (ICH)
  - "lobar" refers to a location in the cortex and subcortical white matter of a hemispheric lobe of the brain.
  - Alternatively, deeper brain structures like thalamus, pons, putamen are characteristics of HTN related ICHs
  - Many patients with a CAA lobar ICH, typically are normotensive however there are some who can be HTN and the relationship is not clearly understood
- Subarachnoid and Subdural hematomas
  - Less likely, but can be seen depending where lesions are

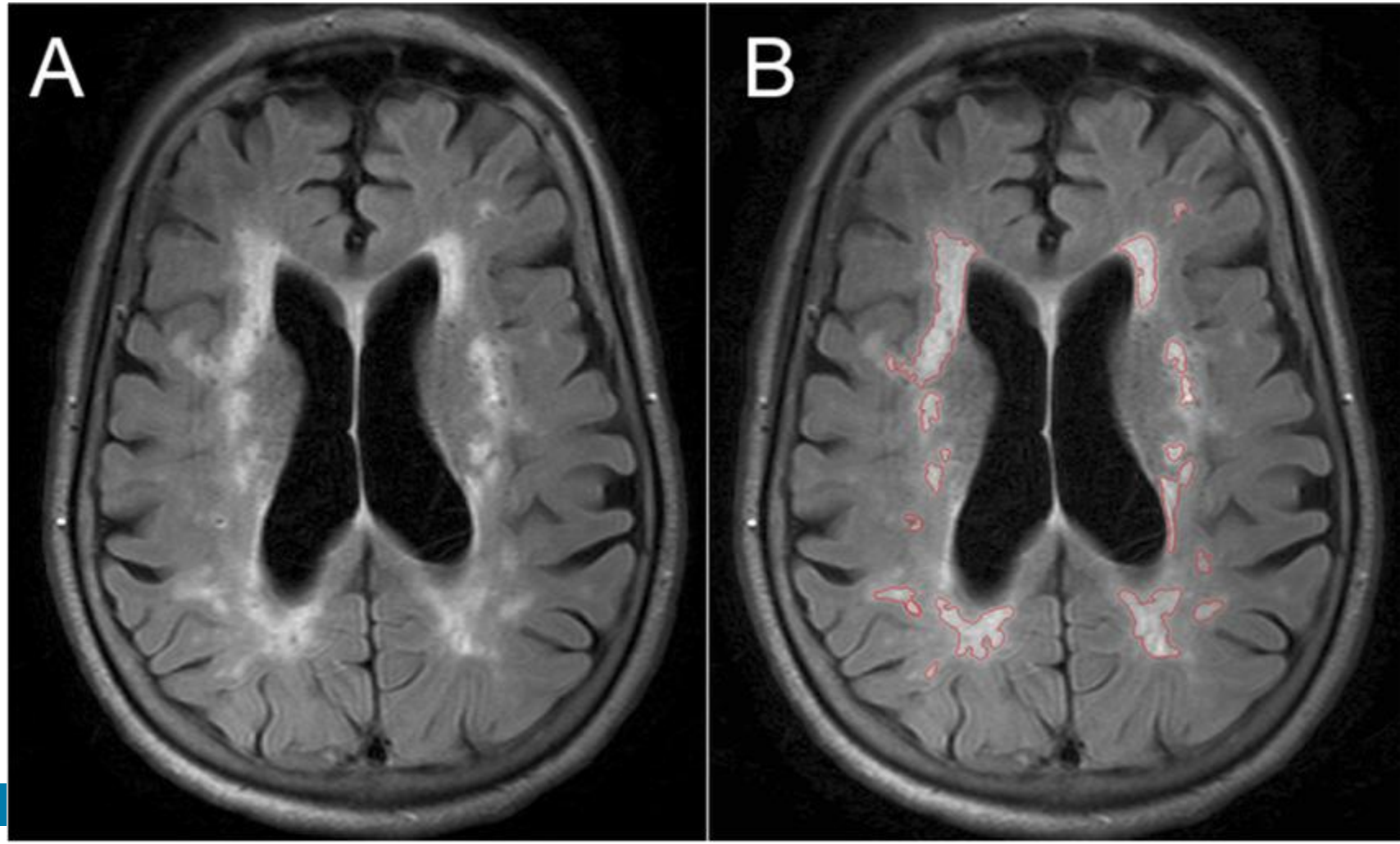
Lobar vs Non-Lobar Hemorrhages



Cerebral Microbleeds (CMB): CAA v HTN



White Mater Hyperintensities



Diagnosis of CAA- Definite

Boston criteria for sporadic CAA version 2.0, 2022[1]
Definite CAA
Full postmortem examination demonstrating: ▪ Spontaneous ICH, TFNE, cSAH, cognitive impairment ▪ Severe CAA with vasculopathy ▪ Absence of other diagnostic lesion

Diagnosis of CAA

Boston criteria for sporadic CAA version 2.0, 2022[1]

Probable CAA

Clinical data and MRI demonstrating:

- Age ≥50 years
- **Plus either:**
  - Presentation with spontaneous ICH, TFNE, or cognitive impairment
  - Two or more lobar hemorrhagic lesions on T2*-weighted imaging (eg, ICH, CMB, cSS, cSAH)¶
  - Absence of other cause of hemorrhage△

  or

  - One lobar hemorrhagic lesion on T2*-weighted imaging (eg, ICH, CMB, cSS, cSAH)◇
  - One white matter feature (eg, >20 perivascular spaces in centrum semiovale or WMH in a multispot pattern)
  - Absence of any deep hemorrhagic lesions on T2*-weighted imaging (eg, ICH, CMB)¶
  - Absence of other cause of hemorrhagic lesions△

Probable CAA with supporting pathology

Clinical data and pathologic tissue (evacuated hematoma or cortical biopsy):

- Presentation with spontaneous ICH, TFNE, cSAH, or cognitive impairment
- Some degree of CAA in specimen
- Absence of other diagnostic lesion

Possible CAA

Clinical data and MRI demonstrating:

- Age ≥50 years
- **Plus either:**
  - Presentation with spontaneous ICH, TFNE, cSAH, or cognitive impairment
  - One lobar hemorrhagic lesion on T2*-weighted imaging (eg, ICH, CMB, cSS, cSAH)¶
  - Absence of other cause of hemorrhage△

  or

  - One white matter feature (eg, >20 perivascular spaces in centrum semiovale or WMH in a multispot pattern)
  - Absence of any deep hemorrhagic lesions on T2*-weighted imaging (eg, ICH, CMB)¶
  - Absence of other cause of hemorrhagic lesions△

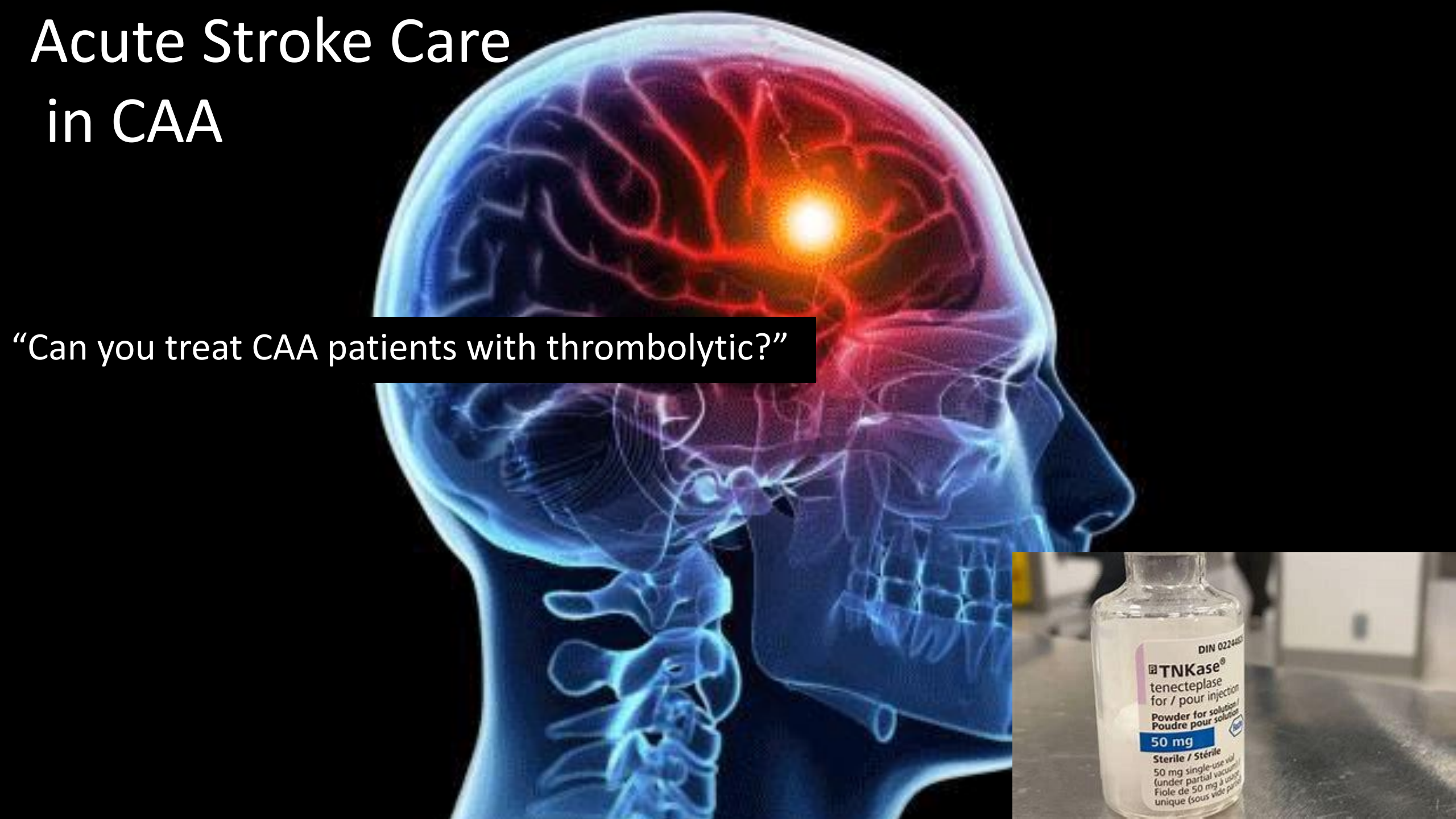
Other Available testing

- Repeat MRIs
- PET scan
- Brain biopsy
- CSF
- Genetic testing

Symptoms of CAA

- Silent
- BEFAST
- Decreased consciousness
  - Either directly or mass effect
- Rarely Headache
- Seizures
  - Typically, SAH

Acute Stroke Care in CAA



"Can you treat CAA patients with thrombolytic?"

Secondary Stroke Prevention in CAA

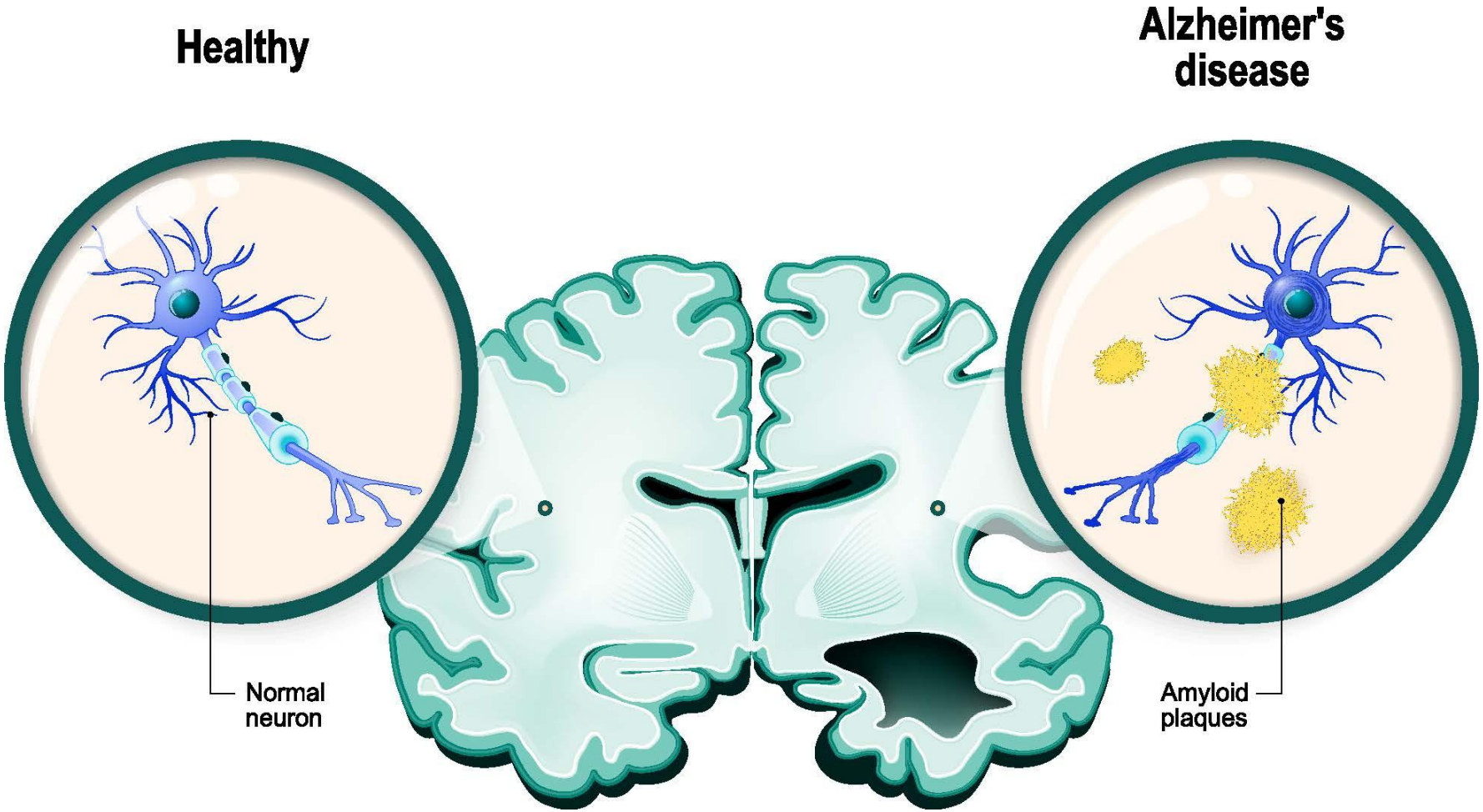
- Antiplatelet/anticoagulation
  - Afib
  - Atherosclerotic disease
- BP control
- Statin

Alzheimer’s Disease (AD)

Overview of AD

- Pathology
  - Extracellular plaque deposits of the amyloid beta peptide
  - Protein tau
- Clinical significance
  - Now seen on imaging
  - CSF

Amyloid plaques in AD



New Treatment Emerges for Early AD

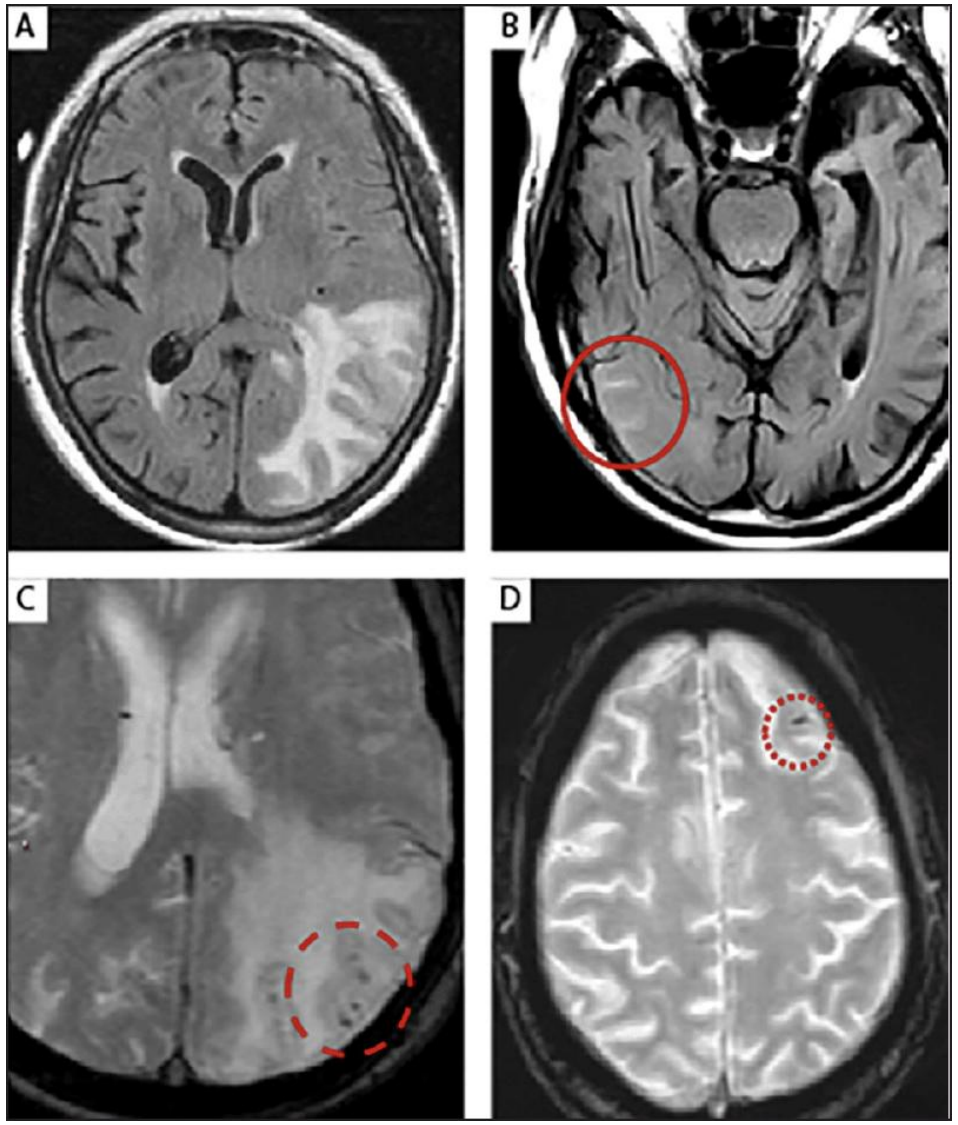
- IgG1 Monoclonal antibodies: anti-amyloid drugs
  - lacanemab (Leqembi)- 2023
  - donanemab (Kisunla)- 2024
- “Time is Brain”

Risk of Treatment?

- 12.6% amyloid related imaging abnormalities (ARIA) and edema
  - Genetics
- ICH
- Infusion related reactions
- Studies-no deaths directly related to tx

Parenchymal Edema

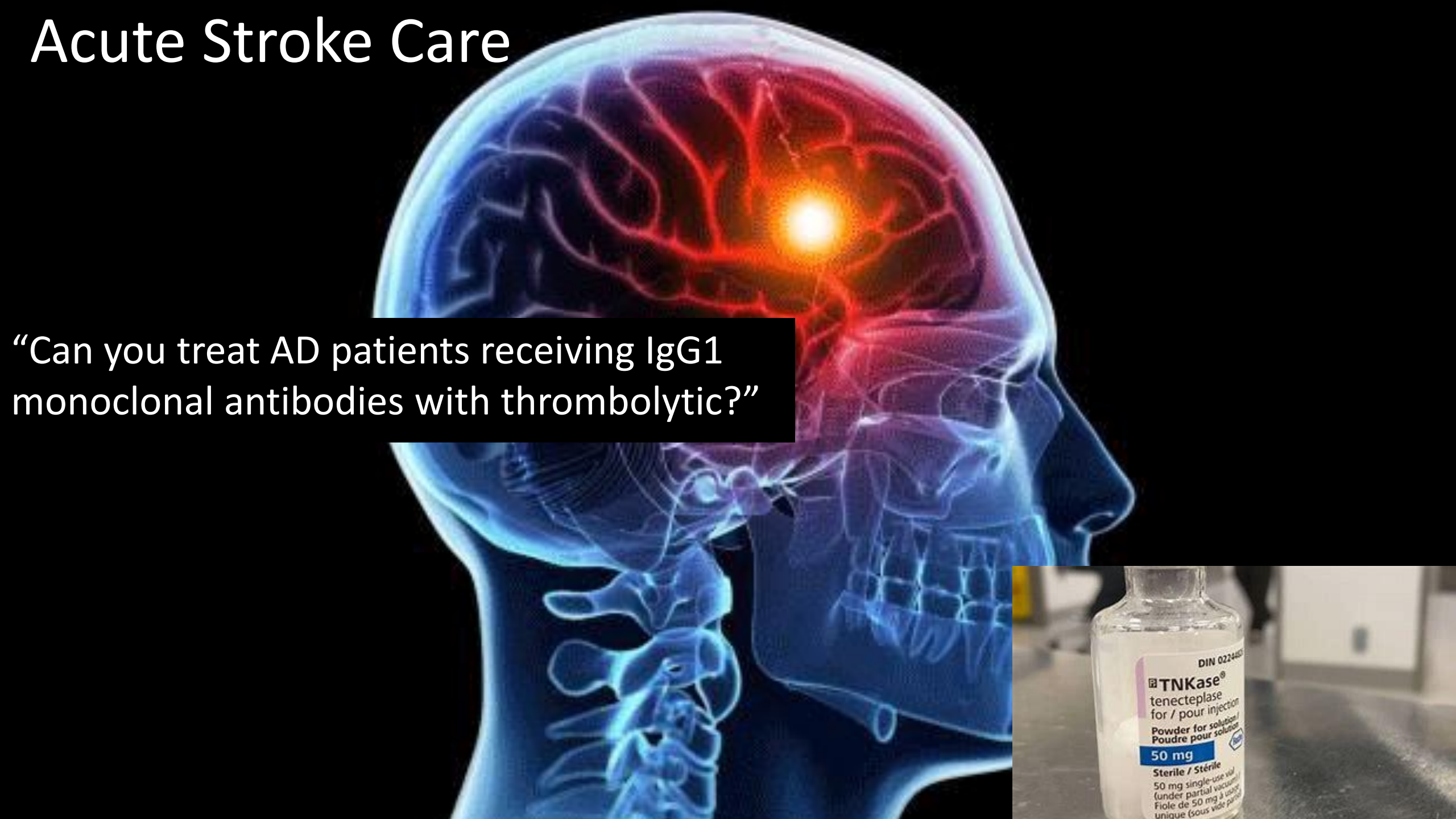
Microhemorrhages



Leptomeningeal Effusion

Leptomeningeal hemosiderin

Acute Stroke Care



"Can you treat AD patients receiving IgG1 monoclonal antibodies with thrombolytic?"

Wrap it up

- Amyloid Beta (A*B*) is a normal part of the brain
- Retention of excessive A*B* can lead to CAA and AD
- CAA is an important differential with cognitive impairment, spontaneous ICH, and TNFE in pts >50yo
- Interventions to slow the process of AD is showing benefit
- More long-term research is needed on the anti-amyloid medications
- Pts with CAA and AD may still be candidates for acute thrombolytic therapy for acute CVA but risk/benefit to be strongly considered


ANY
QUESTIONS?

Summary:

- Deposition of beta-amyloid peptides in small blood vessels of the brain leading to vessel breakdown and bleeding
- Clinical manifestations: hemorrhagic strokes and small brain injuries leading to cognitive decline
- High specificity with MRI
- Risk/benefit with antithrombotic treatment
- CAA can trigger autoimmune inflammatory syndrome in AD immunotherapy
- The future: developing methods for earlier detection and candidate treatments for blocking the cascade of pathogenic events

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