Vascular Dementia

Contents

Introduction

- Dementia - disease process marked by progressive cognitive impairment in clear consciousness.
- Development of multiple cognitive deficits manifested by both memory impairment and impairment in at least one other cognitive domain including language, praxis, gnosis, and executive functioning.
- Types of dementia based on etiology:
  - Alzheimer's disease
  - Dementia with Lewy bodies
  - Vascular dementia
  - Frontotemporal dementia
- Dementia can also be caused by other medical and neurological conditions or can be caused by various substances.

Definition

- Vascular dementia (VaD) - cognitive decline caused by ischemic, hemorrhagic, or oligemic injury to the brain due to cerebrovascular or cardiovascular disease.
- Part of a spectrum of vascular disease causing cognitive impairment, which includes
  - Mild cognitive impairment of vascular origin
  - Mixed Alzheimer's disease plus cerebrovascular disease.
- Presentation of VaD is variable and the clinical spectrum is wide

History

- Kraepelin (1896.) - “arteriosclerotic dementia” - direct result of arteriosclerotic disease in brain.
- Hachinski - “multi-infarct dementia” - dementia related to series of multiple cerebral infarcts – 1975 - Hachinski Ischemic Score
- Scope of vascular dementia was expanded to include a heterogeneous group of conditions including large vessel disease, small vessel disease, cerebrovascular disease related to cardiac embolic events or hemodynamic mechanisms.

History

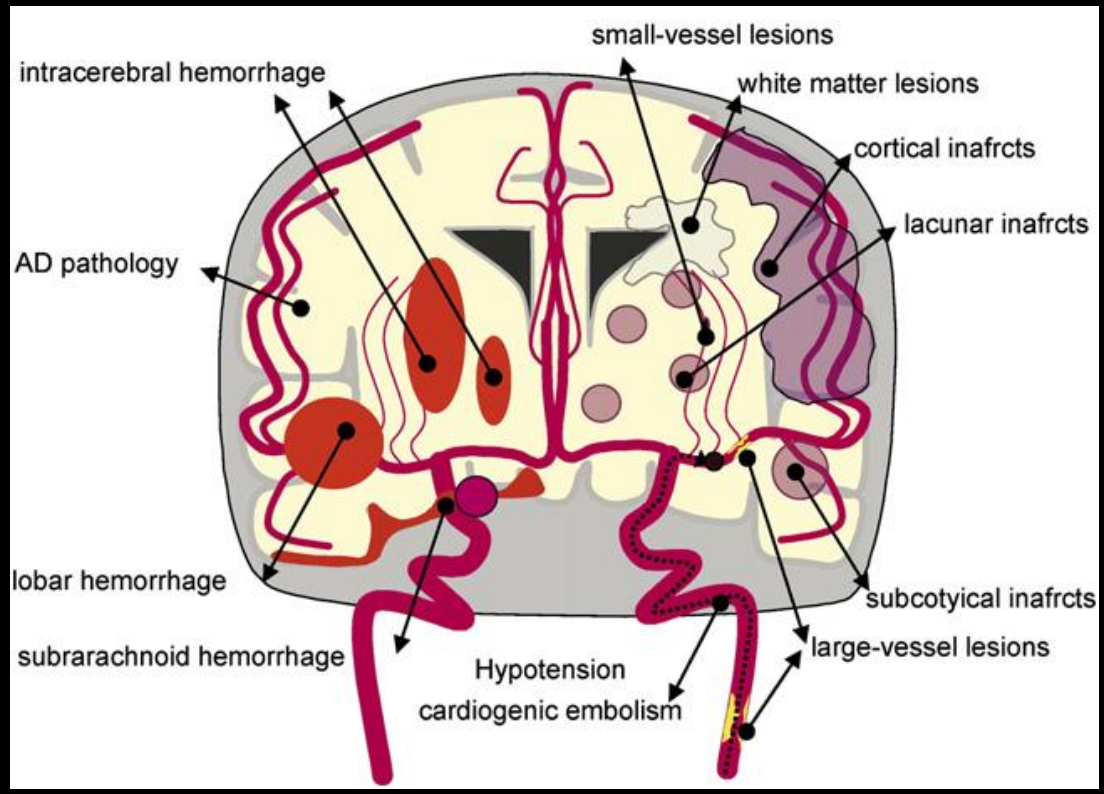
- New criteria - published in 1992 by the State of California Alzheimer's Disease Diagnostic and Treatment Centers - more inclusive and included more mixed cases of Alzheimer's disease with cerebrovascular disease
- In 1993, the **NINDS-AIREN** criteria were published - most widely accepted and used today in research studies.

History

- The Nun Study and the Cognitive Function in Ageing Study - highlighted the interaction b/w Alzheimer's disease pathology and CVD.
- Nun Study, in pts. with Alzheimer's disease, brain infarction was a better predictor of dementia severity than density of plaques and tangles.

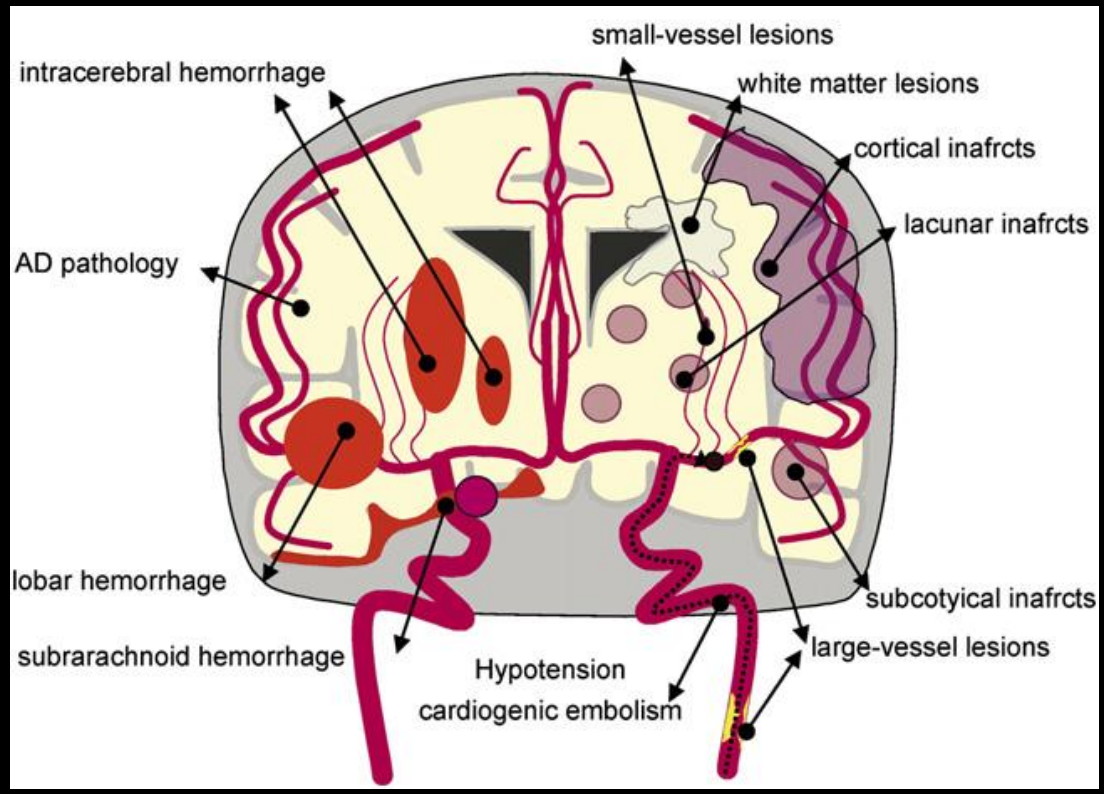
Etiology

- Heterogeneous
- Stroke - leading cause
- 3 subtypes (clinical, radiological, and neuropathological features):
    1. Cortical
    2. Subcortical
    3. Strategic infarct



Etiology

1. Cortical:
   - Multiple cortical infarcts aka “multi-infarct dementia”; multiple small infarcts throughout cortical regions; due to large vessel disease
2. Subcortical:
   - Affect basal ganglia, thalamus, deep or periventricular white matter; disrupt strategic cortical-subcortical circuits (disconnection syndromes); due to small vessel disease
3. Strategic:
   - Single strategically located infarct can also produce dementia.



Etiology

- Small vessel ischemic disease causing extensive white matter changes may disrupt subcortical-cortical pathways.
- Binswanger's disease (Subcortical Arteriosclerotic Encephalopathy): atherosclerotic changes of small vessels - subcortical dementia.
- Hemorrhage:
  - Hemorrhagic stroke
  - Subdural hematoma
  - Epidural hematoma
  - Intraparenchymal hemorrhage from aneurysm or trauma

Etiology

- Chronic hypoperfusion due to hypotension or other cardiopulmonary etiologies
- Cardiovascular factors
  - Congestive heart failure
  - Cardiac arrhythmias - atrial fibrillation
- CADASIL
  - **Inherited disorder caused by mutation in the NOTCH3 gene**
  - Osmiophilic deposits in the basal lamina of small intracerebral arteries and arterioles - lacunar infarcts and white matter changes - subcortical dementia

Etiology

- Cerebral amyloid angiopathy - causes cerebrovascular disease and vascular dementia.
- Cerebrovascular disease - causes a cholinergic deficit similar to that seen in Alzheimer's disease.
- Cholinergic pathways affected in vascular dementia - cortex, hippocampus & striatum show:
  - low levels of Ach in the CSF
  - reduced levels of AchE transferase

Risk Factors

Factors	Remarks	
Demographic factors	Older age, lower educational level, lower income	
Personal factors	Current smokers	
Genetic factors	Family history	
Vascular factors	HTN, AF, MI, CAD, DM, generalized atherosclerosis, lipid abnormalities	
Stroke-related factors	**Type**	Recurrent
	Location	Left-sided, “strategic strokes”
	Volume	>50-100mL of tissue destruction, large perilesional incomplete ischemic areas involving white matter
	Complications (Hypoxic & Ischemic)	Seizures, cardiac arrhythmias, hypotension, aspiration pneumonia
	Manifestations	Dysphagia, gait limitations, urinary impairments

Pathophysiology

Vascular changes in the brain - main cause of cognitive impairment - related to:

- Volume of brain infarcts (with a critical threshold)
- No. of infarcts
- Site of infarcts (B/l, strategic, cortical or subcortical, or affecting white matter)
- Ischemic factors (incomplete ischemic injury, delayed neuronal death, functional changes)
- Atrophic changes (origin, location, extent)
- Additive effects of other pathologies (Alzheimer's disease, LBD, FTD)

Pathophysiology

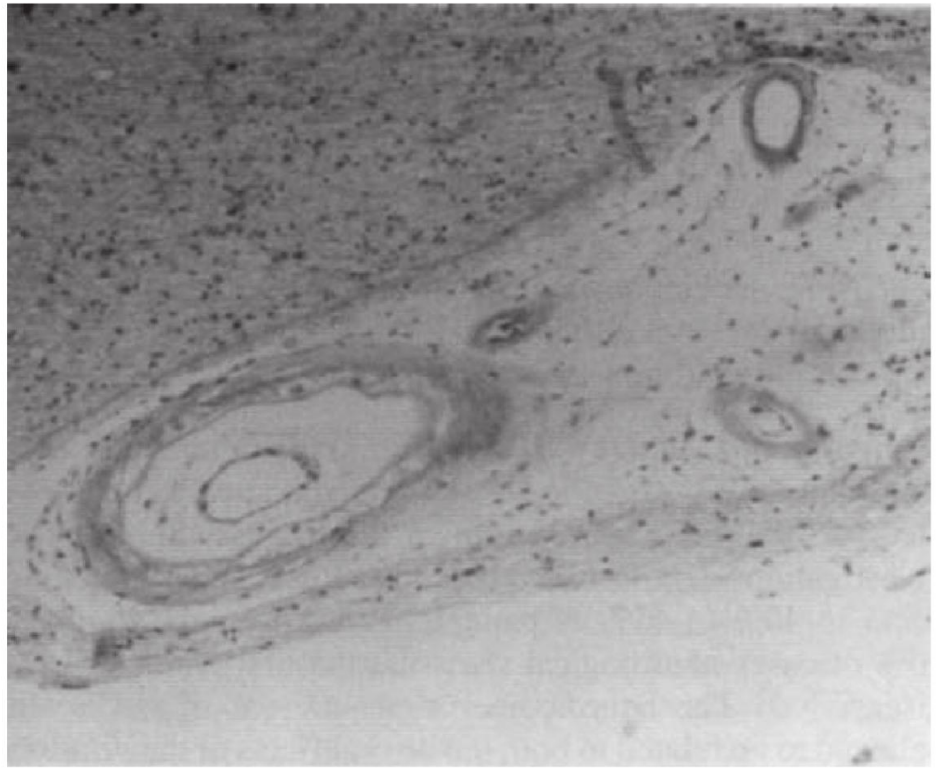


Figure 51–9 *Arteriosclerotic vessels in cerebral ischemia. (Courtesy of Joseph Parker, MD, Duke University Medical Center, Durham, NC.)*

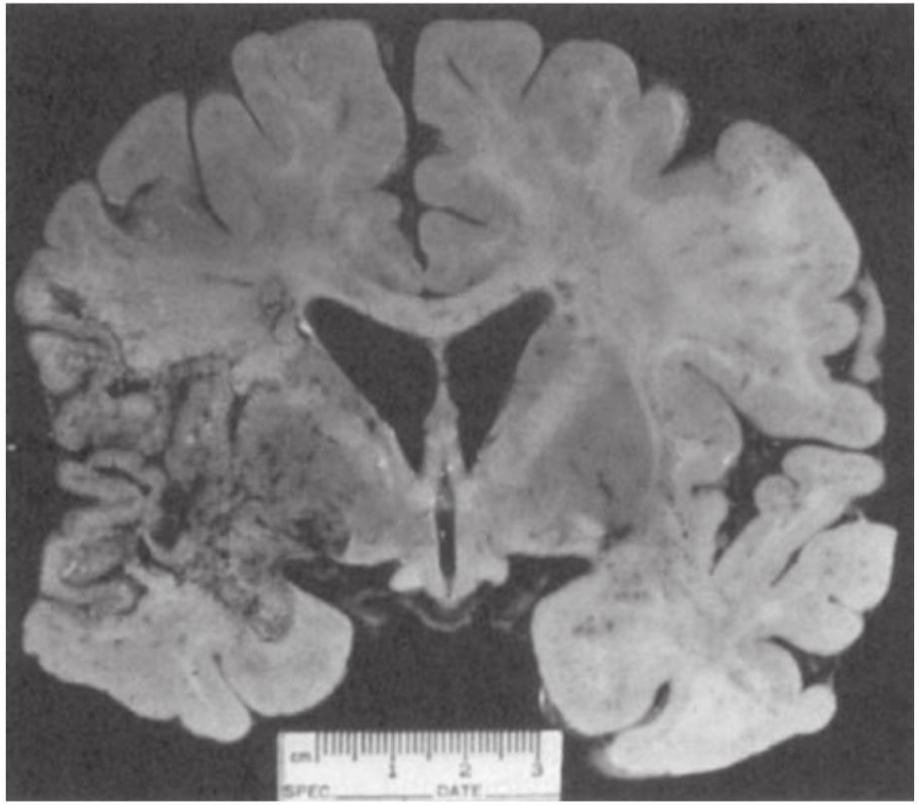
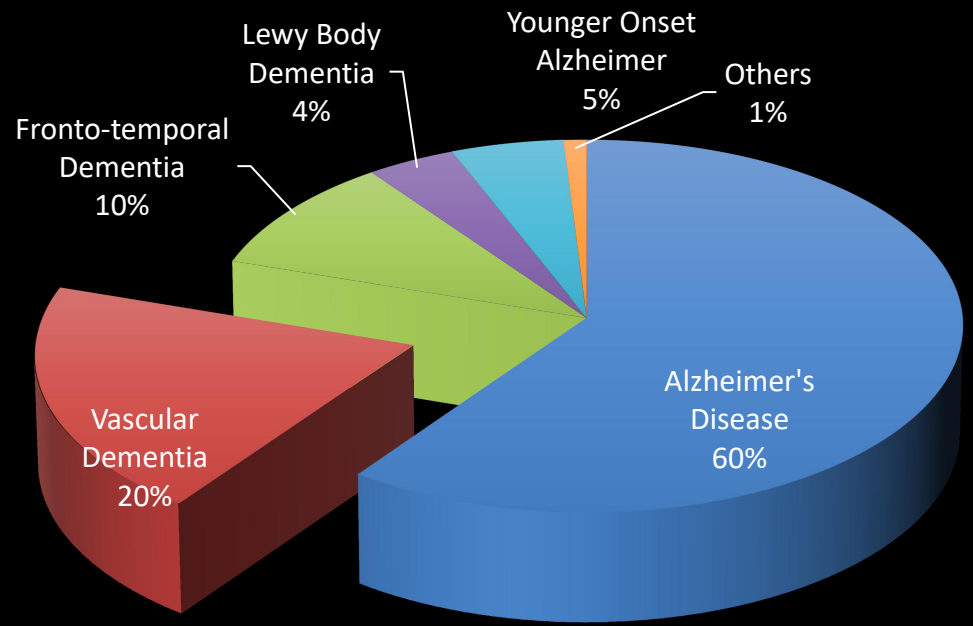


Figure 51–10 *Subacute left frontotemporal infarction. (Courtesy of Joseph Parker, MD, Duke University Medical Center, Durham, NC.)*

Epidemiology

- Accounts for about 10-20% of dementia (pure vascular etiology)
- Prevalence: 1.2 - 4.2 % of persons aged 65 years and older,
- Incidence: 6-12 cases per 1000 persons aged >70 yrs. per year
- Prevalence & incidence increases with increasing age
- Men > Women
- Affected by variations in definition, clinical criteria used, and clinical methods applied



Clinical Features

- Memory deficit
- Dysexecutive syndrome
- Slowed information processing
- Mood and personality changes - patients with subcortical lesions
- Personality and insight - relatively preserved in mild and moderate cases of vascular dementia

Clinical Features

Memory Deficit

- Less severe than in Alzheimer's disease
- Characterized by
  - Impaired recall
  - Relatively intact recognition, and more benefit from cues

Clinical Features

Dyexecutive syndrome - impairment in:

- goal formulation
- initiation
- planning
- organizing
- sequencing
- executing
- set-shifting and set-maintenance
- abstracting

Clinical Features

Behavioral & Psychological Symptoms

- Depression, abulia, anxiety, emotional lability and incontinence, psychomotor retardation and other psychiatric symptoms
- Frequently seen in subcortical vascular dementia disease

Clinical Features

Neurological findings:

- Mild motor or sensory deficits
- Decreased co-ordination
- Brisk tendon reflexes
- Babinski's sign, visual field loss
- Bulbar signs
- Disordered gait (hemiplegic, apraxic–ataxic, or small-stepped)
- Unsteadiness
- Unprovoked falls
- Urinary frequency and urgency

Clinical Features

Features that make the diagnosis of vascular dementia disease unlikely include:

- Early and progressive worsening of memory
- Absence of focal neurological signs
- Other cognitive cortical deficits in the absence of corresponding focal lesions on brain imaging

Cortical v/s Subcortical Dementia

Cortical vascular dementia:

- Lateralized sensorimotor changes
- Abrupt onset of cognitive impairment
- Aphasia

Subcortical vascular dementia:

- Pure motor hemiparesis
- Bulbar signs
- Dysarthria
- Depression
- Emotional lability
- Deficits in executive functioning

Hachinski Ischemia 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/Presence of HTN	1
History of Strokes	2
Evidence of artherosclerosis	1
Focal neurological symptoms	2
Focal Neurological signs	2

A score of >7 indicates a vascular etiology

Comparative Nosology - ICD

ICD 8 (1965)	ICD 9 (1975)	ICD 10 (1990)
Organic psychosis 293.0 Psychosis associated with cerebral arteriosclerosis 293.1 Psychosis associated with other cerebrovascular disturbances	290.4 Arteriosclerotic dementia	**F01 Vascular dementia** F01.0 Vascular dementia of acute onset F01.1 Multi-infarct dementia F01.2 Subcortical vascular dementia F01.3 Mixed cortical and subcortical vascular dementia F01.8 Other vascular dementia F01.9 Vascular dementia, unspecified

Comparative Nosology - DSM

DSM - I	DSM - II	DSM - III R	DSM - IV	DSM-5
`Organic Brain Syndrome' (OBS), chronic and ‘more or less’ irreversible in contrast to ‘Acute brain injury’.	Psychoses associated with organic brain syndromes with cerebral arteriosclerosis (293.0)	Multi-Infarct Dementia	Vascular Dementia - course quite variable and not always stepwise, dropped the requirement of patchy distribution of deficits, and allowed evidence to be either laboratorial or physical.	Major or Mild Vascular Neurocognitive Disorder

Clinical Criteria

- Most widely used: DSM-5, ICD-10 and NINDS-AIREN
- Cardinal elements of any clinical criteria for vascular dementia are:
  - Definition of the cognitive syndrome
  - Definition of the cause.
- Criteria based on the concept of ischaemic infarcts.
- Designed to have high specificity, but have been poorly validated
- Different diagnostic criteria identify different populations

- Evidence of significant cognitive decline from a previous level of performance in one or more cognitive domains (complex attention, executive function, learning and memory, language, perceptual-motor, or social cognition) based on:
- 1. Concern of the individual, a knowledgeable informant, or the clinician that there has been a significant decline in cognitive function; and
- 2. A substantial impairment in cognitive performance, preferably documented by standardized neuropsychological testing or, in its absence, another quantified clinical assessment.
- B. The cognitive deficits interfere with independence in everyday activities (i.e., at a minimum, requiring assistance with complex instrumental activities of daily living such as paying bills or managing medications).

DS

Major or Mild Vascular Neurocognitive Disorder

Diagnostic Criteria

A. The criteria are met for major or mild neurocognitive disorder.

B. The clinical features are consistent with a vascular etiology, as suggested by either of the following:

   1. Onset of the cognitive deficits is temporally related to one or more cerebrovascular events.
   2. Evidence for decline is prominent in complex attention (including processing speed) and frontal-executive function.

C. There is evidence of the presence of cerebrovascular disease from history, physical examination, and/or neuroimaging considered sufficient to account for the neurocognitive deficits.

D. The symptoms are not better explained by another brain disease or systemic disorder.

Probable vascular neurocognitive disorder is diagnosed if one of the following is present; otherwise **possible vascular neurocognitive disorder** should be diagnosed:

1. Clinical criteria are supported by neuroimaging evidence of significant parenchymal injury attributed to cerebrovascular disease (neuroimaging-supported).
2. The neurocognitive syndrome is temporally related to one or more documented cerebrovascular events.
3. Both clinical and genetic (e.g., cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy) evidence of cerebrovascular disease is present.

Possible vascular neurocognitive disorder is diagnosed if the clinical criteria are met but neuroimaging is not available and the temporal relationship of the neurocognitive syndrome with one or more cerebrovascular events is not established.

ICD-10

Diagnostic guidelines

The diagnosis presupposes the presence of a dementia as described above. Impairment of cognitive function is commonly uneven, so that there may be memory loss, intellectual impairment, and focal neurological signs. Insight and judgement may be relatively well preserved. An abrupt onset or a stepwise deterioration, as well as the presence of focal neurological signs and symptoms, increases the probability of the diagnosis; in some cases, confirmation can be provided only by computerized axial tomography or, ultimately, neuropathological examination.

Associated features are: hypertension, carotid bruit, emotional lability with transient depressive mood, weeping or explosive laughter, and transient episodes of clouded consciousness or delirium, often provoked by further infarction. Personality is believed to be relatively well preserved, but personality changes may be evident in a proportion of cases with apathy, disinhibition, or accentuation of previous traits such as egocentricity, paranoid attitudes, or irritability.

Includes: arteriosclerotic dementia

ICD-10

F01.0 Vascular dementia of acute onset

Usually develops rapidly after a succession of strokes from cerebrovascular thrombosis, embolism, or haemorrhage, In rare cases, a single large infarction may be the cause.

F01.1 Multi-infarct dementia

This is more gradual in onset than the acute form, following a number of minor ischaemic episodes which produce an accumulation of infarcts in the cerebral parenchyma.

Includes: predominantly cortical dementia

F01.2 Subcortical vascular dementia

There may be a history of hypertension and foci of ischaemic destruction in the deep white matter of the cerebral hemispheres, which can be suspected on clinical grounds and demonstrated on computerized axial tomography scans. The cerebral cortex is usually preserved and this contrasts with the clinical picture, which may closely resemble that of dementia in Alzheimer's disease. (Where diffuse demyelination of white matter can be demonstrated, the term "'Binswanger's encephalopathy" may be used.)

F01.3 Mixed cortical and subcortical vascular dementia

Mixed cortical and subcortical components of the vascular dementia may be suspected from the clinical features, the results of investigations (including autopsy), or both.

F01.8 Other vascular dementia

F01.9 Vascular dementia, unspecified

NINDS-AIREN

I. Criteria for diagnosis of probable vascular dementia

A. Dementia
B. Cerebrovascular disease
C. A relationship between the above two disorders
   i. Onset of dementia within 3 months of a recognized stroke
   ii. Abrupt deterioration in cognitive functions or fluctuating, stepwise progression of cognitive deficits

II. Clinical features consistent with the diagnosis of probable vascular dementia

A. Early presence of gait disturbances
B. History of unsteadiness and provoked falls
C. Early urinary frequency, urgency, and other urinary symptoms not explained by urologic disease
D. Pseudobulbar palsy
E. Personality and mood changes

III. Features that make the diagnosis of vascular dementia uncertain or unlikely

A. Early onset of memory deficit and progressive worsening of memory and other cognitive functions in the absence of corresponding focal brain lesions on imaging
B. Absence of focal neurological consequences other than cognitive disturbances
C. Absence of cerebrovascular damage on brain imaging

NINDS-AIREN

III. **Clinical diagnosis of possible vascular dementia** may be made in the presence of dementia with focal neurologic signs in patients in whom brain imaging studies to confirm definite CVD are missing; or in the absence of clear temporal relationship between dementia and stroke; or in patients with subtle onset and variable course (plateau or improvement) of cognitive deficits and evidence of relevant CVD.

IV. **Criteria for diagnosis of definite vascular dementia**

A. Clinical criteria for probable vascular dementia

B. Histopathologic evidence of CVD obtained from biopsy or autopsy

C. Absence of neurofibrillary tangles and neuritic plaques exceeding those expected for age

D. Absence of other clinical or pathological disorder capable of producing dementia.

V. **Classification of vascular dementia for research purposes** may be made on the basis of clinical, radiologic, and neuropathologic features, for subcategories or defined conditions such as cortical vascular dementia, subcortical vascular dementia, BD, and thalamic dementia.

Comparison

	Supportive Features	Neuroimaging	Remarks
DSM-5	Not specified	Not required but laboratory evidence may include neuroimaging	2 subtypes: mild and major vascular NCD
ICD-10	Not specified	Not required	6 subtypes are included
NINDS-AIREN	Early presence of gait, urinary, personality changes or unprovoked falls	CT or MRI Multiple large-vessel/ Strategic/ Multiple lacunes Diffuse/ extensive white matter changes.	Multiinfarct, strategic infarct, and subcortical (Binswanger's disease, lacunar state) types list of features that make the diagnosis uncertain

Differential Diagnosis

1. Alzheimer Disease with Cerebrovascular Disease
   - Patients meet both the NINCDS-ADRDA criteria for Alzheimer's disease and the NINDS-AIREN criteria for vascular dementia, they are diagnosed with both
   - If they meet the criteria for Alzheimer's disease but not for vascular dementia, then they are given a diagnosis of Alzheimer's disease with cerebrovascular disease
2. Frontotemporal Dementia
   - Similar presentation as subcortical vascular dementia
   - Slow insidious onset
   - Frontal lobe executive deficits
   - Relatively preserved memory early in the course
   - Neuropsychiatric manifestations such as personality change

Differential Diagnosis

3. Normal Pressure Hydrocephalus
4. White-matter lesions and dementia
5. Frontal lobe tumours and other intracranial masses
6. Lewy body dementia
7. Parkinsons's disease and dementia
8. Progressive Supranuclear Palsy
9. Multi System Atrophy

Vascular Dementia v/s Alzheimer's Disease

	Vascular Dementia	Alzheimer's Disease
History of atherosclerotic diseases	Present	Less common
Onset	Sudden/Gradual	Gradual
Progression	Slow, stepwise	Slow, progressive decline
Neurological deficits	Present	Absent
Memory	Mild impairment in early phase	Prominent impairment in early phase
Executive functions	Early, marked impairment	Impaired later
Gait	Disturbed early	Normal
Type of dementia	Subcortical	Cortical
Hachinski ischemic score	≥ 7	≤ 4
Neuroimaging	Infarction/White matter lesions	Normal/Hippocampal atrophy

Pathology and Laboratory Examination

- Structural neuroimaging - vascular damage (ischemic or hemorrhagic lesions)
- Strategically placed large vessel lesion to multiple scattered lesions to extensive small vessel ischemic changes in the white matter regions.
- Vascular damage evident will vary depending on the etiology but must correspond to the cognitive deficits observed
- No clear pathological changes diagnostic for vascular dementia.

Pathology and Laboratory Examination

- Evidence of stroke is required, and some schemes have suggested quantification of total volume of infarction, though these approaches have not reached the level of standardized criteria.
- Evidence of amyloidopathy may be present but is not required.
- The presence of neuropathological changes characteristic of Alzheimer's disease does not exclude vascular dementia, as the two processes are commonly comorbid and may both be diagnosed.

Treatment

Treatment of vascular dementia can be divided into:

1. Primary prevention
2. Secondary prevention
3. Symptomatic treatment

Primary Prevention

- Ameliorating vascular risk factors to prevent vascular damage from occurring in the brain.
- Treatment of HTN, D.M., Hyperlipidemia, TIA (Antiplatelet), AF (Anticoagulants), Carotid stenosis (Angioplasty)
- Healthy lifestyle changes such as diet, exercise, weight loss, stress reduction, decreased salt intake, and cessation of smoking.
- Patients with sleep apnea should also be adequately treated with positive airway pressure to optimize cardiopulmonary functioning.

Secondary Prevention

- Aim to modify vascular risk factors after vascular dementia has developed
- No evidence to support that it prevents further deterioration in cognitive functioning
- Intensive rehabilitation after stroke may help restore impaired cognitive function
- No FDA-approved treatments for vascular dementia.
- Cholinesterase inhibitors were also evaluated

Symptomatic Treatment

- Donepezil
  - Patients experienced statistically significant, dose-related improvement in cognitive function and global functioning
  - Functional deterioration was slowed compared to placebo
- Galantamine
  - Improvement noted in cognition, functioning and behavior
- Rivastigmine
  - Studied in patients with subcortical vascular dementia compared to aspirin.
- Memantine
  - May be useful in more severe disease.

Course and Prognosis

- Dependent on the nature and course of the vascular disease that causes it.
- Onset is often sudden if the cognitive impairment is associated with a particular large or strategic vascular event.
- Onset will be more insidious when associated with smaller subcortical or small vessel or microvascular changes.

Course and Prognosis

- Course may be static if there are no further vascular events, or remitting or progressive often with a fluctuating stepwise decline coinciding with further vascular events.
- There may also be continued decline even in the absence of clearly defined vascular events.
- Small vessel subcortical disease typically presents with insidious onset and slower gradual progression.

Summary

2. Vascular Dementia

VD is a type of dementia that develops when brain cells die due to the lack of oxygen supply.

Symptoms of VD

- Poor memory
- Trouble speaking
- Changes in mood
- Confusion and agitation
- Trouble walking
- Impaired judgement
- Mild but progressive deterioration in cognitive functions, i.e., ability to think, organize, and plan

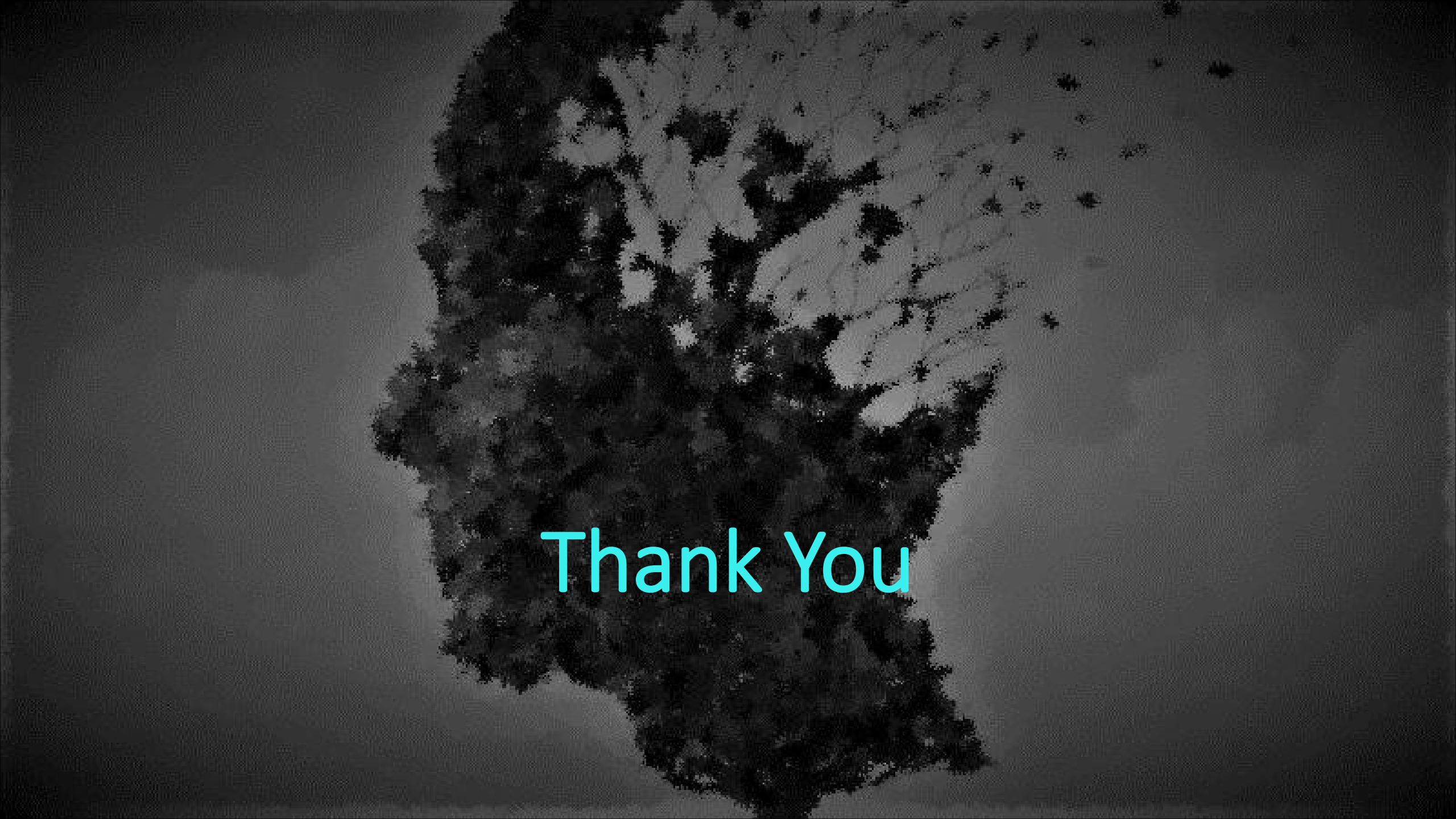
VD accounts for 10% cases of dementia.

Conclusion

- Vascular factors – one of the leading cause of cognitive impairment worldwide
- Concept of vascular dementia continues to evolve and undergone considerable revision in last 2 to 3 decades
- Variable presentation
- Wide clinical spectrum
- Variable diagnostic criteria
- New ways of treatment evolving apart from preventive measures

References

- Kaplan & Saddock's Comprehensive Textbook of Psychiatry, 9th ed. 2009
- Oxford Textbook Of Psychiatry 1st Edition
- Psychiatry 3rd ed [Vols 1 and 2] - A. Tasman, et al., (Wiley, 2008)
- DSM-5
- ICD-10
- Internet


Thank You