# DEMENTIA TOUR

Dr Aisling Denihan

Consultant Old Age Psychiatrist

Growing old, it's not nice, but it's interesting.

*August Strindberg (1849–1912)*

# What is dementia

- A 34-year old man with a history of TBI following a RTA presents with severe memory, attention, language and executive deficits
- Significant difficulties carrying out IADL's and needs assistance for ADL's
- Unable to return to work
- Is he demented?

# Defining Dementia

Laypeople may confuse dementia with one particular condition, such as Alzheimer's disease

Tendency to label dementing conditions as "hardening of the arteries", "senility", "old-timers' disease", reflecting a perception that the problem is inevitable in ageing.

Dementia refers to a cluster of behavioural syndrome, and not one disease or cause.

# Classification of Dementias

- Treatable vs. non-treatable
- Progressive vs. static vs. reversible
  - Degenerative/worsening disease process vs. toxic exposure or injury resulting in a behavioural decline that plateaus vs. potentially reversible medical condition (e.g. severe anemia)
- Primary site of damage
  - Cortical (grey matter) vs. subcortical (white matter) vs. mixed
- There are well over 50 causes of dementia

# Classification of Dementia

- **Static Dementias**
  - **Toxic Conditions**
    - Alcoholic dementia
    - Heavy metal poisoning (e.g. lead)
  - **Infectious Conditions**
    - Herpes Encephalitis
  - **Miscellaneous**
    - Tumor
    - Normal pressure hydrocephalus
    - Trauma
- Progressive Dementias
  - Cortical Dementias
    - Alzheimer's Disease
    - Motor Neuron Disease
    - Frontotemporal Dementia
    - Progressive Aphasia
    - Wilson's disease
    - Vascular Dementia
  - Subcortical Dementias
    - Huntington's Disease
    - Parkinson's Disease
    - Progressive Supranuclear Palsy
    - AIDS dementia
    - Vascular Dementia
    - Creutzfeldt-Jakob disease
- **Potentially Reversible Dementias**
  - **Systemic Illness**
    - Severe Anemia
    - Uremia
  - **Deficiency States**
    - $B_{12}$ Deficiency
  - **Endocrine Disorders**
    - Addison's disease
    - Thyroid Disorders
  - **Drug Toxicity**
    - Anticholinergics
    - Antipsychotics
    - Sedatives/hypnotics

# Cortical vs. Subcortical



**Table 14.2 The Major Characteristics That Distinguish Cortical and Subcortical Dementias**

| | Type of dementia | |
|---|---|---|
| **Characteristic** | **Subcortical** | **Cortical** |
| *Mental status* | | |
| Language | No aphasia | Aphasia |
| Memory | Forgetful (difficulty retrieving learned material) | Amnesia (difficulty learning new material) |
| Cognition | Impaired (poor problem solving produced by slowness, forgetfulness, and impaired strategy and planning) | Severely disturbed (based on agnosia, aphasia, acalculia,and amnesia) |
| | Slow processing time | Response time relatively normal |
| Personality | Apathetic | Unconcerned or euphoric |
| Mood | Affective disorder common (depression or mania) | Normal |
| *Motor system* | | |
| Speech | Dysarthric | Normal[a] |
| Posture | Abnormal | Normal, upright[a] |
| Gait | Abnormal | Normal[a] |
| Motor speed | Slow | Normal[a] |
| Movement disorder | Common (chorea, tremor, rigidity, ataxia) | Absent |
| *Anatomy* | | |
| Cortex | Largely spared | Involved |
| Basal ganglia, thalamus, mesencephalon | Involved | Largely spared |
| *Metabolism* | | |
| Fluorodeoxyglucose scan | Subcortical hypometabolism (cortex largely normal) | Cortical hypometabolism (subcortical metabolism less involved) |
| Neurotransmitters preferentially involved | Huntington's disease: γ-aminobutyric acid | Alzheimer's disease: acetylcholine |
| | Parkinson's disease: dopamine | |

[a]Motor system involvement occurs late in the course of Alzheimer's disease and Pick's disease.
*Note.* Adapted from Cummings & Benson, 1984, p. 875.

# Medications Affecting Cognition

**EXHIBIT 2**

**Commonly Used Medications That May Cause Cognitive or Affective Change in Elderly Patients**

*Beta-blockers*, especially propranolol (Inderal)

*Antihypertensive agents*

- Beta-blockers (see above)
- Methyldopa
- Reserpine
- Clonidine
- Diuretics

*Neuroleptics*

- Haloperidol (Haldol)
- Chlorpromazine (Thorazine)
- Thioridazine (Mellaril)
- Fluphenazine (Prolixin)
- Perphenazine (Trilafon)
- Loxapine (Loxitane)
- Molindone (Moban)
- Thiothixene (Navane)
- Trifluoperazine (Stelazine)

*Benzodiazepines*

- Diazepam (Valium)
- Flurazepam (Dalmane)
- Clorazepate (Tranxene)
- Chlordiazepoxide (Librium)
- Prazepam (Centrax)
- Alprazolam (Xanax)
- Halazepam (Paxipam)
- Triazolam (Halcion)
- Temazepam (Restoril)
- Oxazepam (Serax)
- Lorazepam (Ativan)

*Antiseizure medications*

- Barbiturates
- Carbamazepine (Tegretol)
- Phenytoin (Dilantin)
- Phenobarbital

*Antihistamines*

- Cimetidine (Tagamet)

*Anticholinergic agents*

- Atropine
- Benztropine
- Diphenhydramine
- Trihexyphenidyl

*Antiarrythmic agents*

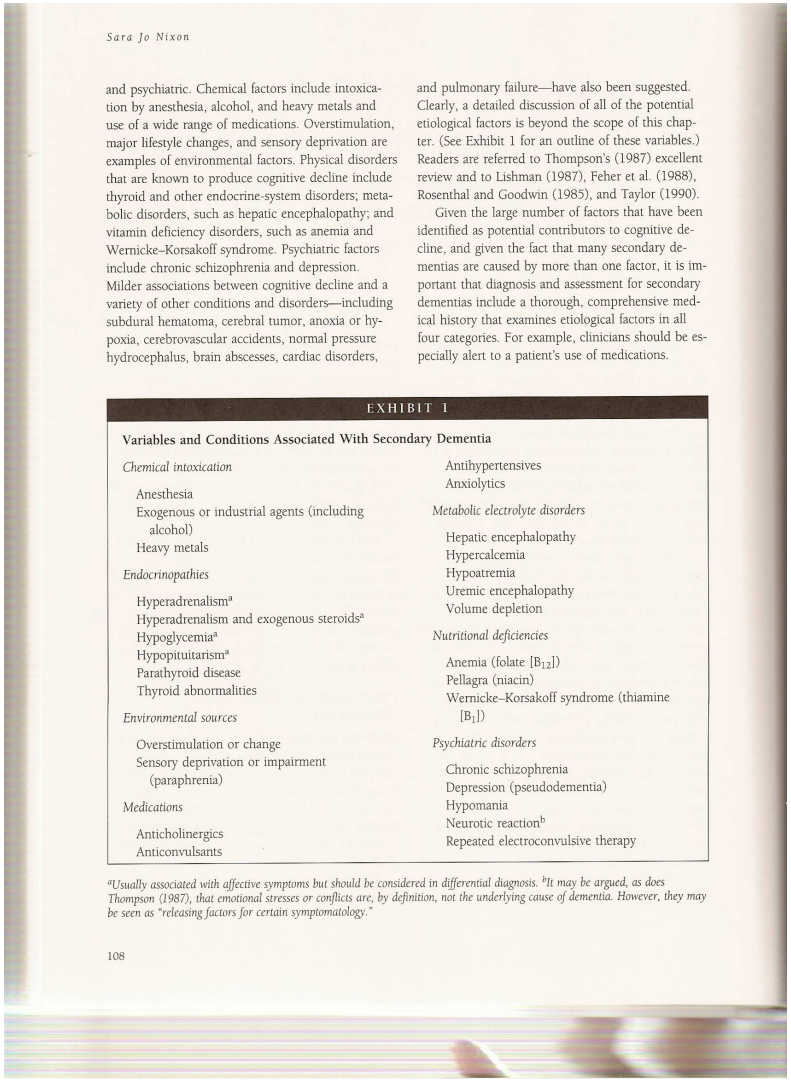
- Procainamide
- Disopyramide
- Quinidine

*Steroids*

*From "Depression and Other Psychiatric Disorders," by M. A. Jenike. In* Geriatric Neuropsychology *(p. 127), edited by M. S. Albert and M. Moss, 1988, New York: Guilford Press. Copyright 1988 by Guilford Press. Reprinted with permission.*

- **Anticonvulsants:** all anticonvulsants impair cognition.
- **Antidepressants:** risk highest in tricyclics. Withdrawal delirium also occurs.
- **Antipsychotics:** impairs cognition.
- **Anti-parkinsonian drugs:** risk highest with anticholinergics, but also can occur with any medication, COMT inhibitors or amantadine.
- **Cardiac drugs:** including Digoxin and calcium antagonists.
- **Corticosteroids:** risk is dose related.
- **Hypnotics/Sedatives:** more common with long-acting benzodiazepines.
- **Opioid analgesics:** all opioids cause problems. Risk highest with Pethidine.
- **Anticholinergics:** bladder relaxants, antihistamines, tricyclics.

# Secondary Dementias: Potentially Reversible





and psychiatric. Chemical factors include intoxication by anesthesia, alcohol, and heavy metals and use of a wide range of medications. Overstimulation, major lifestyle changes, and sensory deprivation are examples of environmental factors. Physical disorders that are known to produce cognitive decline include thyroid and other endocrine-system disorders; metabolic disorders, such as hepatic encephalopathy; and vitamin deficiency disorders, such as anemia and Wernicke–Korsakoff syndrome. Psychiatric factors include chronic schizophrenia and depression. Milder associations between cognitive decline and a variety of other conditions and disorders—including subdural hematoma, cerebral tumor, anoxia or hypoxia, cerebrovascular accidents, normal pressure hydrocephalus, brain abscesses, cardiac disorders, and pulmonary failure—have also been suggested. Clearly, a detailed discussion of all of the potential etiological factors is beyond the scope of this chapter. (See Exhibit 1 for an outline of these variables.) Readers are referred to Thompson's (1987) excellent review and to Lishman (1987), Feher et al. (1988), Rosenthal and Goodwin (1985), and Taylor (1990).

Given the large number of factors that have been identified as potential contributors to cognitive decline, and given the fact that many secondary dementias are caused by more than one factor, it is important that diagnosis and assessment for secondary dementias include a thorough, comprehensive medical history that examines etiological factors in all four categories. For example, clinicians should be especially alert to a patient's use of medications.

EXHIBIT 1

**Variables and Conditions Associated With Secondary Dementia**

*Chemical intoxication*

- Anesthesia
- Exogenous or industrial agents (including alcohol)
- Heavy metals

*Endocrinopathies*

- Hyperadrenalism[a]
- Hyperadrenalism and exogenous steroids[a]
- Hypoglycemia[a]
- Hypopituitarism[a]
- Parathyroid disease
- Thyroid abnormalities

*Environmental sources*

- Overstimulation or change
- Sensory deprivation or impairment (paraphrenia)

*Medications*

- Anticholinergics
- Anticonvulsants
- Antihypertensives
- Anxiolytics

*Metabolic electrolyte disorders*

- Hepatic encephalopathy
- Hypercalcemia
- Hypoatremia
- Uremic encephalopathy
- Volume depletion

*Nutritional deficiencies*

- Anemia (folate [$B_{12}$])
- Pellagra (niacin)
- Wernicke–Korsakoff syndrome (thiamine [$B_1$])

*Psychiatric disorders*

- Chronic schizophrenia
- Depression (pseudodementia)
- Hypomania
- Neurotic reaction[b]
- Repeated electroconvulsive therapy

*[a]Usually associated with affective symptoms but should be considered in differential diagnosis. [b]It may be argued, as does Thompson (1987), that emotional stresses or conflicts are, by definition, not the underlying cause of dementia. However, they may be seen as "releasing factors for certain symptomatology."*

# Diagnostic Criteria for Dementia

- **There is not a universal set of criteria**
- No definitive agreement
- Varying diagnostic standards

- **DSM-5 vs. (NINCDS-ADRDA)** National Institute of Neurological and Communicative Disorders and Stroke-Alzheimer's Disease and Related Disorders Association

# Some Agreement on Major Features

1. **Dementia results in a loss of cognitive function** representing a marked change from previous level of cognitive functioning

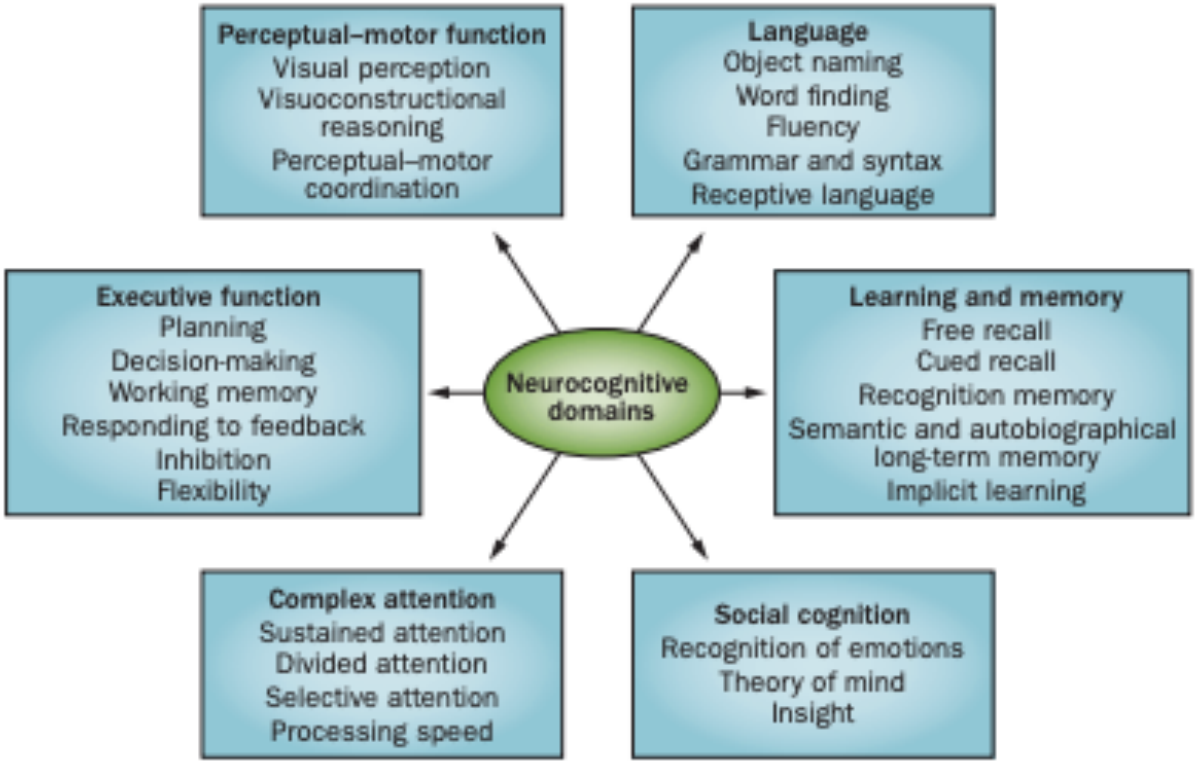
2. Greater than what would be expected with normal ageing

3. **Involves multiple areas of cognitive impairment including memory….however…multiple neuropsychological profiles**

4. **Decline in social or occupational function**

# Changing Terminology

- **DSM-5 (2015):** Replaced the term 'dementia' with major neurocognitive disorder and minor neurocognitive disorder
- Major neurocognitive disorder is mostly synonymous with dementia
- Criteria to delineate specific aetiological subtypes of major and minor neurocognitive disorder
- Incorporates criteria from various Expert Groups, includes clinical features and biomarkers
- Qualifies cases as probable or possible




# Diagnostic Framework

***Table 3: DSM-5 Dementia Diagnostic Criteria***

- Evidence from the history and a clinical assessment that indicates significant cognitive impairment in at least one of the following cognitive domains:

    1. Learning and memory
    2. Language
    3. Complex attention
    4. Perceptual-motor function
    5. Social cognition

- The impairment must be acquired and represent a significant decline from a previous level of functioning.
- The cognitive deficits must interfere with independence in everyday activities.
- In the case of neurodegenerative dementia such as Alzheimer's disease, the disturbances are of insidious onset and are progressive, based on evidence from the history or serial mental status examinations.
- The disturbances are not occurring exclusively during the course of delirium.

# Prevalence

- Incidence rises dramatically with age (Jorm & Jolley, 1998), and that its prevalence doubles every 5 years (Rocca et al., 1991).
- About 5% of people over 64 yrs and 30-50% of 84+ in western countries suffer from dementia (Ritchie, 1995)
- In Ireland, prevalence rates are generally in line with these figures (Keogh & Roche, 1996).
- Over 66,000 people in Ireland have dementia

# Alzheimer's Disease

Most common cause of dementia > 65 years

Prototypical cortical dementia

5% incidence 65-74 age range; 50% incidence over 95 years

'Probable' diagnosis during life-time(definitive diagnosis only on histopathological examination of brain tissue following death)

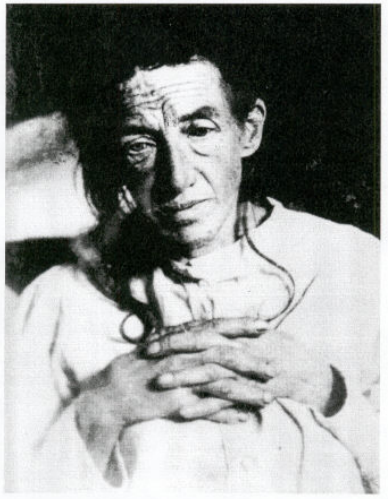
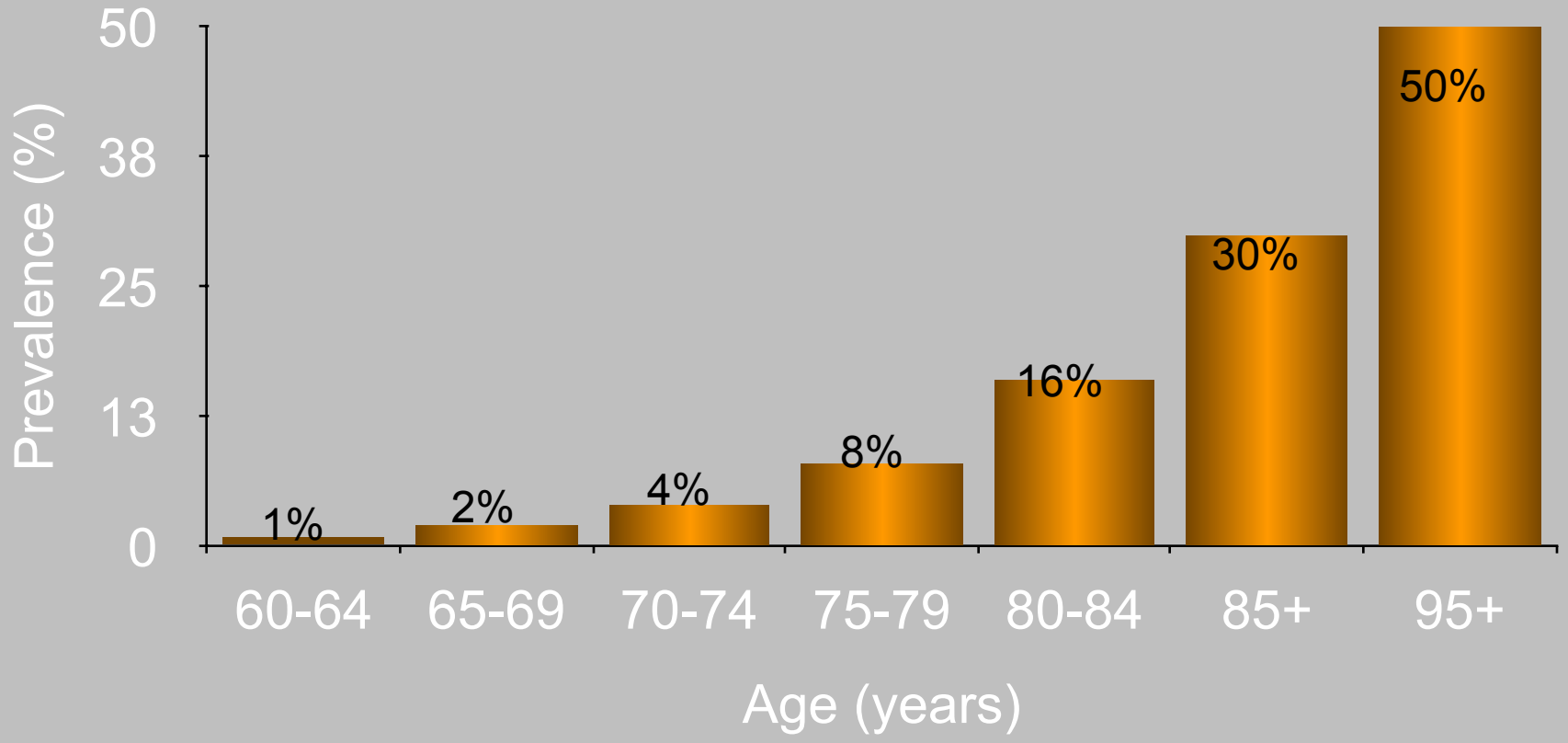


**FIG. 1.** Auguste D.: the original Alzheimer disease patient. (Courtesy of Professor Konrad Maurer.)

# Alzheimer's Disease

- **Primary Risk Factors**
  - Age
  - Family history
  - Genetic markers
  - Female gender after 80 years
  - Cardiovascular risks e.g. Hypertension, diabetes, obesity and hypercholesterolemia
  - Downs Syndrome
  - Severe head injury
  - Low level of education
  - Race

# Prevalence of Alzheimer's Disease




Kurz A. Eur J Neurol 1998; 5(Suppl 4): S1-8
Wimo A *et al*. Int J Geriatr Psychiatry 1997; 12: 841-56

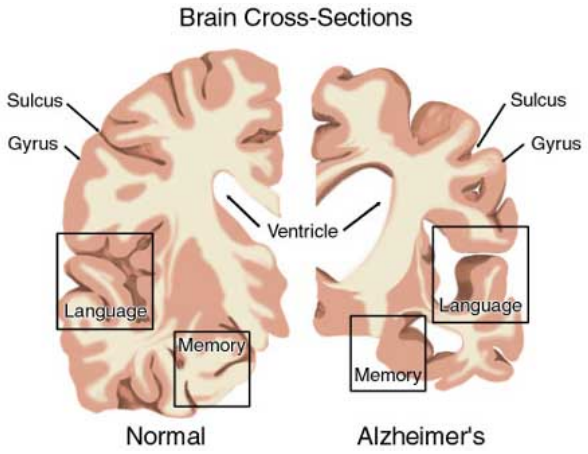
# Neuropathology of Alzheimer's Disease

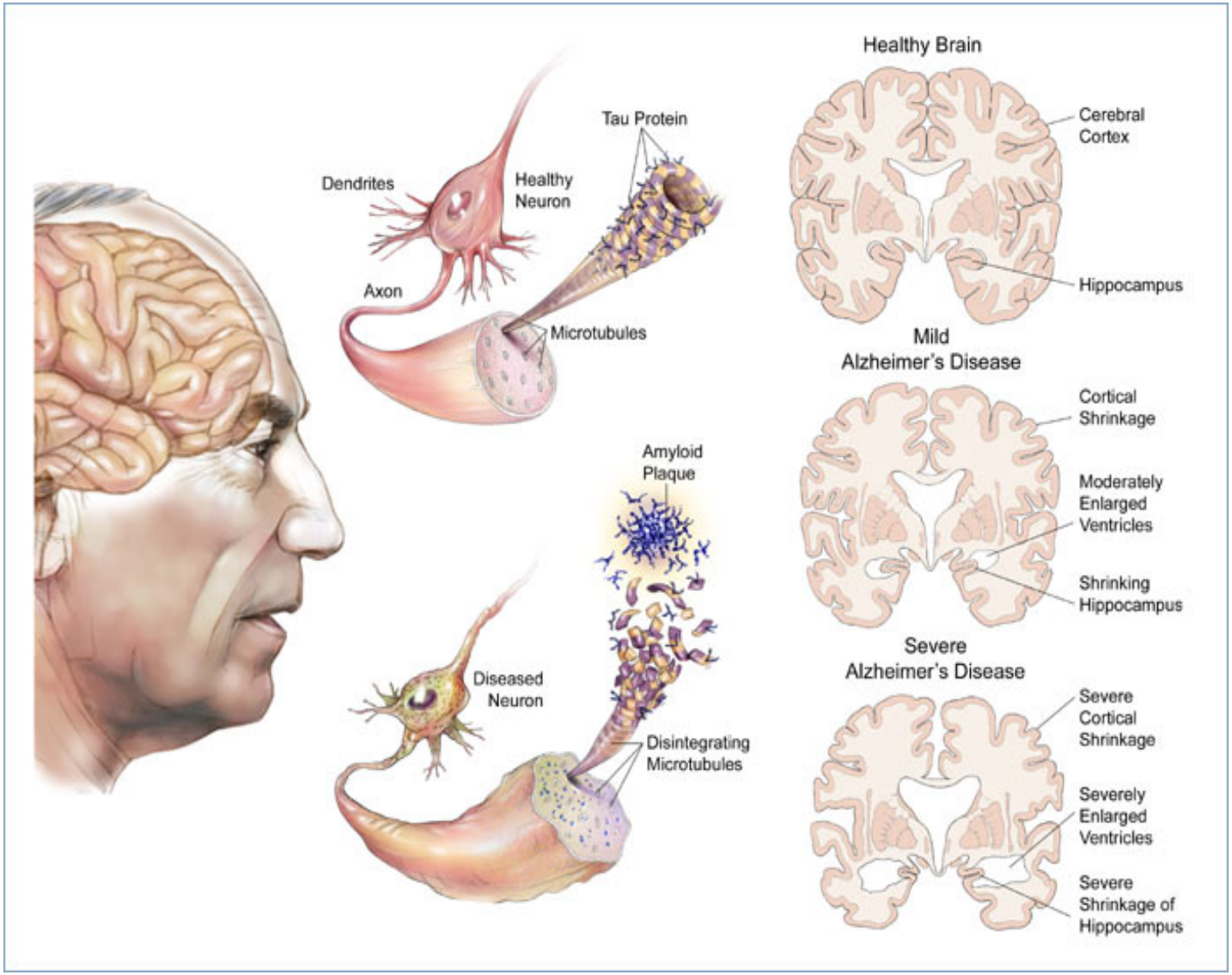
Shrinkage / Atrophy of the brain particularly temporo-parietal areas

Ventricular enlargement

Thinning of gyri

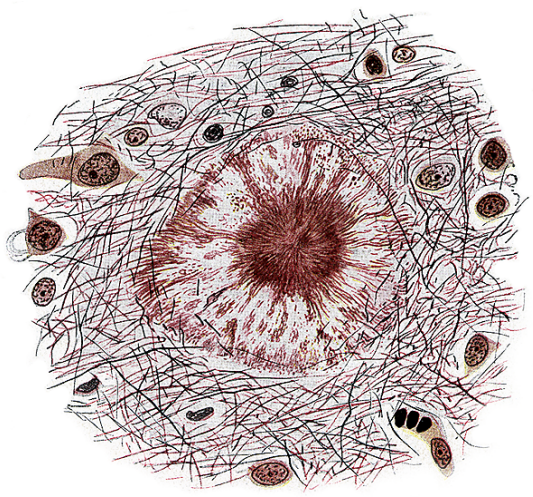
Widened sulci

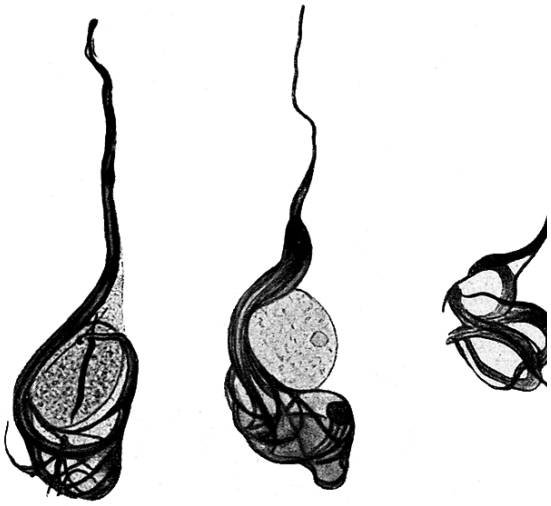



Healthy Brain
Cerebral Cortex
Hippocampus
Mild Alzheimer's Disease
Cortical Shrinkage
Moderately Enlarged Ventricles
Shrinking Hippocampus
Severe Alzheimer's Disease
Severe Cortical Shrinkage
Severely Enlarged Ventricles
Severe Shrinkage of Hippocampus
Tau Protein
Dendrites
Healthy Neuron
Axon
Microtubules
Amyloid Plaque
Diseased Neuron
Disintegrating Microtubules

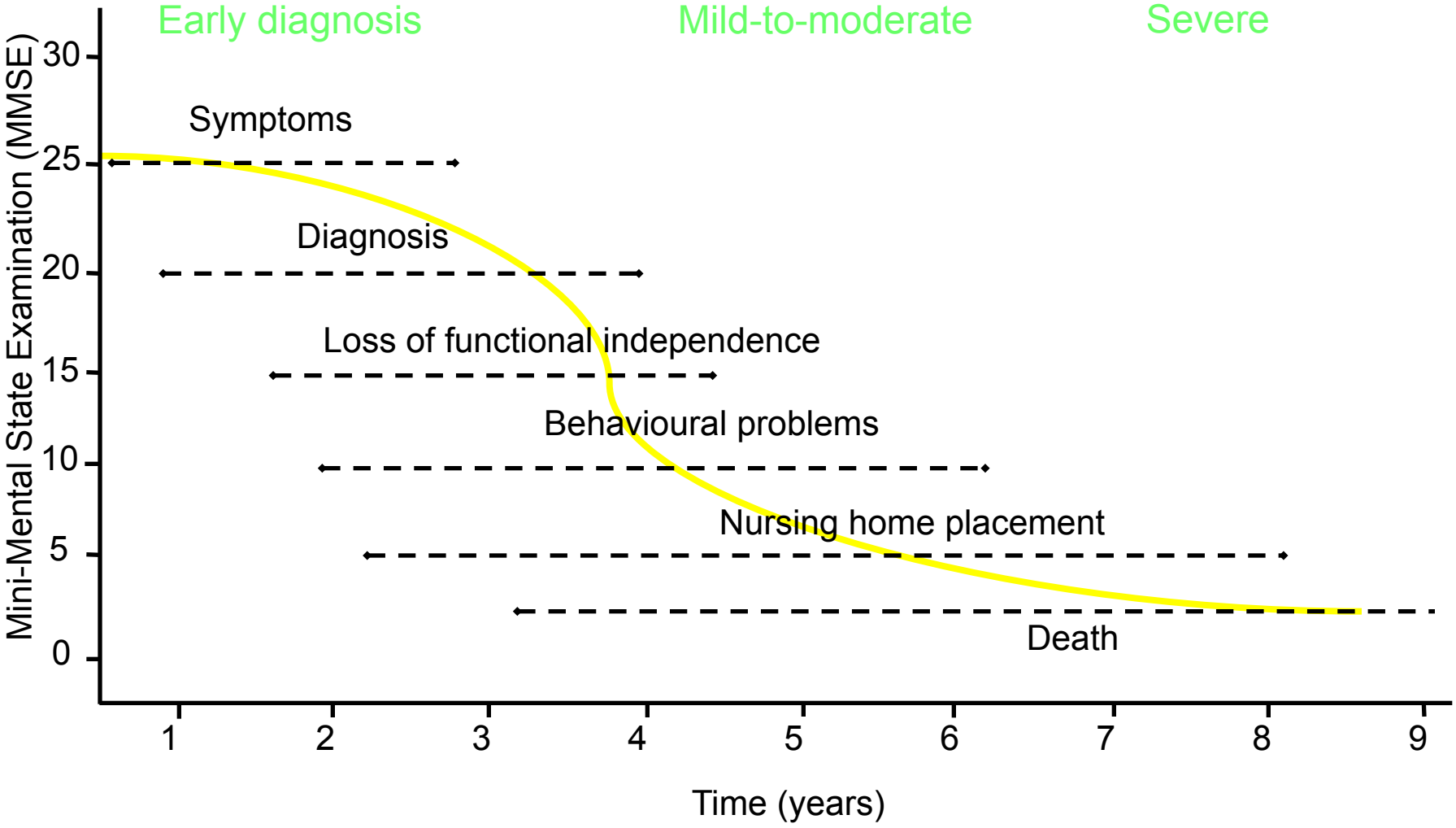
# Histological Markers of Alzheimer's Disease

- Twisted neurofibrillary tangles
- Round clumps of cellular trash forming the neuritic plaques





# Course of Alzheimer's Disease

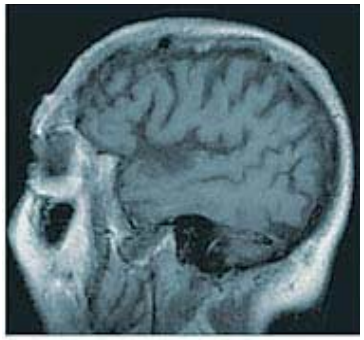



Feldman and Gracon. The Natural History of Alzheimer's Disease. London: Martin Dunitz, 1996

# Mild Stages

## Cognition

- Episodic memory deficits (e.g. delayed recall and recent memory)
- Impaired prospective memory (forgetfulness)
- Reduced autobiographical memory (temporal gradient)
- Word-finding difficulties
- Reduced language output (oral and written)
- Circumlocution
- Reduced insight and judgement
- Impaired ability to cope with novel/ complex tasks (e.g. handling finances, planning a dinner party)



Mild Alzheimer's

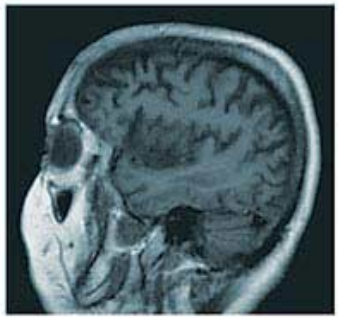
## Adaptive Functioning

- Impaired IADLs (e.g. balancing a checkbook, paying bills, banking, etc.)

## Behavioural Changes

- Incipient apathy
- Irritability

# Moderate Stages



Moderate Alzheimer's

## Cognition

- Severe episodic memory deficits (i.e. delayed and recent recall)
- Compromised language expression and comprehension
- Repetitive speech
- Compromised orientation even to familiar surroundings

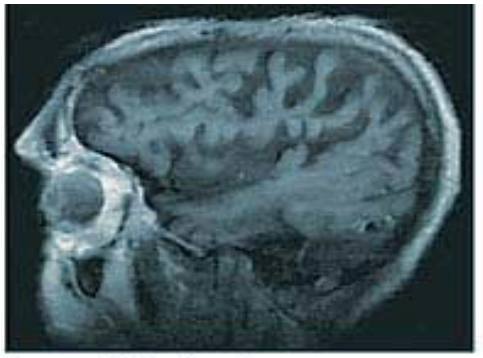
## Adaptive Functioning

- Impaired ADL's
- Needs assistance with dressing, bathing, toileting and community functioning
- Urinary then faecal incontinence

## Behavioural Changes

- Delusions and depression
- Agitation
- Insomnia and wandering can be observed

# Severe Stages



Severe Alzheimer's

## Cognition

- Severely impaired attention, apraxia
- Complete amnesia
- Loss of recognition for familiar faces

## Adaptive Functioning

- Ambulatory ability lost
- Inability to sit up, smile or hold up head

## Behavioural Changes

- Mutism in late stages
- Persistent vocalisations

# Language 1

- **Early Stages**

  Characterized by word-finding and naming difficulties
  - On confrontation Naming Tests (Boston)
    - Tool for hammer or musical instrument for harmonica
  - Poor verbal fluency
  - Semantic fluency worse than phonetic fluency

# Language 2

- **Moderate Stages**
  - Comprehension problems begin to emerge
  - Followed by difficulties repeating information
  - Followed by declines in fluent conversational output resembling a global aphasia

# Visuospatial Functioning

Usually AD patients perform poorly on a number of visuospatial tasks

- Spatial construction
  - Block Design
- Copying
  - Clock Drawing
  - ROCF
  - Pentagons

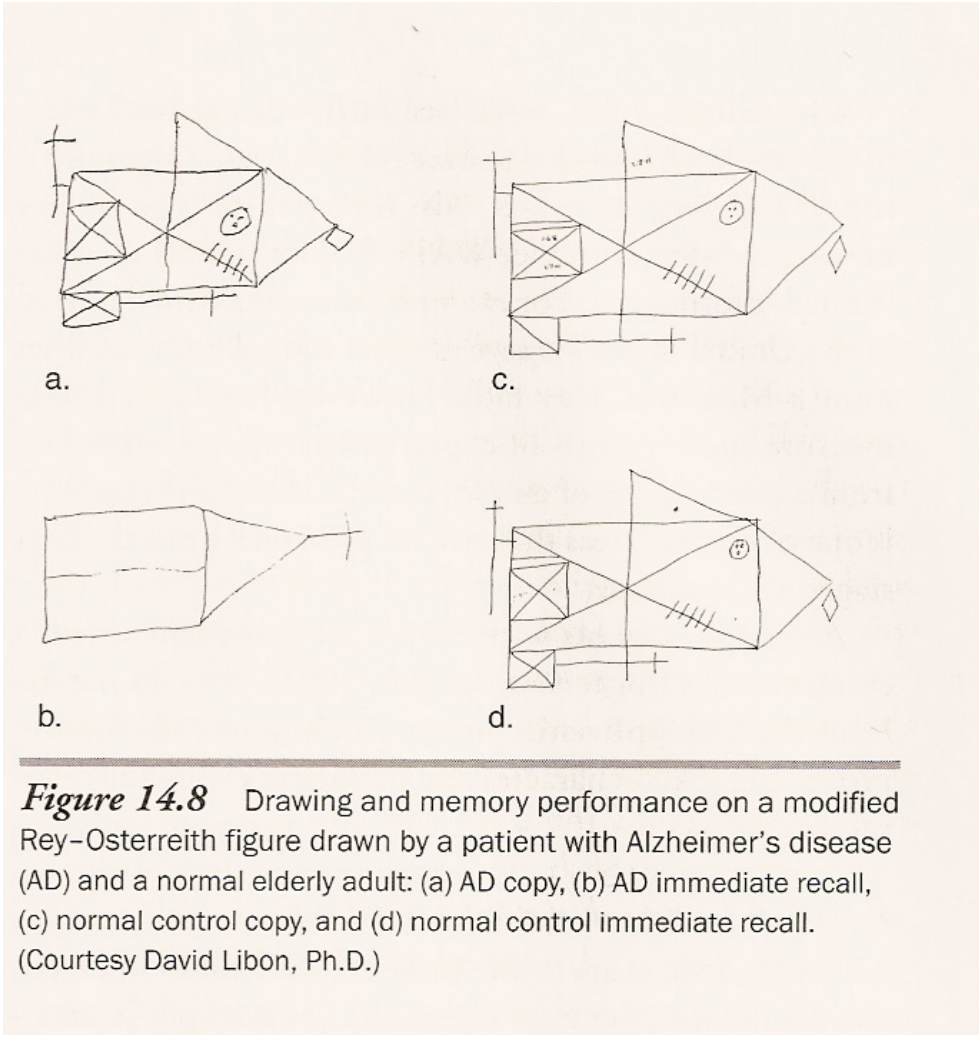



***Figure 14.8*** Drawing and memory performance on a modified Rey–Osterreith figure drawn by a patient with Alzheimer's disease (AD) and a normal elderly adult: (a) AD copy, (b) AD immediate recall, (c) normal control copy, and (d) normal control immediate recall. (Courtesy David Libon, Ph.D.)

# Executive Functioning

- Deficits are subtle early on
- Impaired meta-cognitive awareness
  - Inability to self-monitor their own behaviour and performance
  - Little insight into their deficits
  - Generally unaware or unconcerned about the magnitude or consequences of their deficits
- Problems in the ability to organize, plan and use appropriate strategies for problem solving

# Vascular Dementia (VaD)

- VaD is the second (after AD) most common cause of dementia, accounting for 10%-50% of cases
- Since it can and often co-exists with other causes of dementia (e.g. AD), vascular lesions may be the leading cause of cognitive impairment worldwide
- Prevalence increases with age but less steeply than in AD
- More common in men before the age of 75, more common in women over 85 years (Morris et al., 2004)

(NINDS-AIREN) National Institute of Neurological and Communicative Disorders and Stroke-Association Internationale pour la Recherche et l'Enseignment en Neurosciences

Table 4
NINDS-AIREN Diagnostic Criteria for Vascular Dementia*

I. The criteria for the diagnosis of *probable* VaD include *all* of the following:

1. Dementia: Impairment of memory and two or more cognitive domains (including executive function), interfering with ADLs and not resulting from effects of stroke alone.

   Exclusion criteria: Alterations of consciousness, delirium, psychoses, severe aphasia or deficits precluding testing, systemic disorders, *Alzheimer's disease,* or other forms of dementia.

2. Cerebrovascular disease: Focal signs on neurological examination (hemiparesis, lower facial weakness, Babinski sign, sensory deficit, hemianopia, dysarthria) consistent with stroke (with or without history of stroke, *and* evidence of relevant CVD by brain CT or MRI including *multiple large-vessel infarcts* or a *single strategically placed infarct* (angular gyrus, thalamus, basal forebrain, or PCA or ACA territories), as well as *multiple basal ganglia* and *white-matter lacunes* or *extensive periventricular white-matter lesions,* or combinations thereof.

   Exclusion criteria: Absence of cerebrovascular lesions on CT or MRI.

3. A relationship between the above two disorders: Manifested or inferred by the presence of one or more of the following:
   a. onset of dementia within 3 mo after a recognized stroke,
   b. abrupt deterioration in cognitive functions; or fluctuating, stepwise progression of cognitive deficits.

II. Clinical features *consistent* with the diagnosis of *probable* VaD include the following:

1. Early presence of gait disturbances (small step gait or marche à petits pas, or magnetic, apraxic-ataxic, or parkinsonian gait).
2. History of unsteadiness and frequent, unprovoked falls.
3. Early urinary frequency, urgency, and other urinary symptoms not explained by urologic disease.
4. Pseudobulbar palsy.
5. Personality and mood changes, abulia, depression, emotional incontinence, or other deficits, including psychomotor retardation and abnormal executive function.

III. Features that make the diagnosis of VaD uncertain or unlikely include:

1. Early onset of memory deficit and progressive worsening of memory and other cognitive functions, such as language (transcortical sensory aphasia), motor skills (apraxia), and perception (agnosia), in the absence of corresponding focal lesions on brain imaging.
2. Absence of focal neurological signs, other than cognitive disturbances.
3. Absence of CVD on CT or MRI.

*Abbr:* ACA, anterior cerebral artery; ADLs, activities of daily living; CT, computerized tomography; CVD, cerebrovascular disease; MRI, magnetic resonance imaging; PCA, posterior cerebral artery; VaD, vascular dementia.
From G. Román et al *(56).*

# Diagnostic Criteria: Comparison

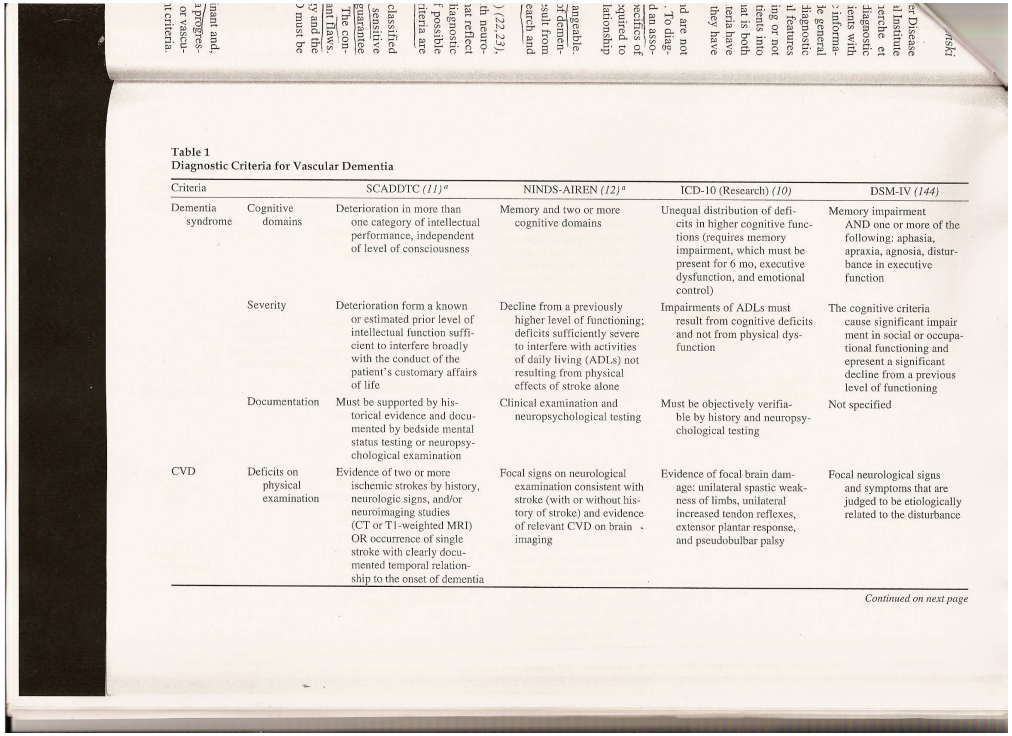


**Table 1**
**Diagnostic Criteria for Vascular Dementia**

| Criteria | | SCADDTC *(11)*[a] | NINDS-AIREN *(12)*[a] | ICD-10 (Research) *(10)* | DSM-IV *(144)* |
|---|---|---|---|---|---|
| Dementia syndrome | Cognitive domains | Deterioration in more than one category of intellectual performance, independent of level of consciousness | Memory and two or more cognitive domains | Unequal distribution of deficits in higher cognitive functions (requires memory impairment, which must be present for 6 mo, executive dysfunction, and emotional control) | Memory impairment AND one or more of the following: aphasia, apraxia, agnosia, disturbance in executive function |
| | Severity | Deterioration form a known or estimated prior level of intellectual function sufficient to interfere broadly with the conduct of the patient's customary affairs of life | Decline from a previously higher level of functioning; deficits sufficiently severe to interfere with activities of daily living (ADLs) not resulting from physical effects of stroke alone | Impairments of ADLs must result from cognitive deficits and not from physical dysfunction | The cognitive criteria cause significant impairment in social or occupational functioning and epresent a significant decline from a previous level of functioning |
| | Documentation | Must be supported by historical evidence and documented by bedside mental status testing or neuropsychological examination | Clinical examination and neuropsychological testing | Must be objectively verifiable by history and neuropsychological testing | Not specified |
| CVD | Deficits on physical examination | Evidence of two or more ischemic strokes by history, neurologic signs, and/or neuroimaging studies (CT or T1-weighted MRI) OR occurrence of single stroke with clearly documented temporal relationship to the onset of dementia | Focal signs on neurological examination consistent with stroke (with or without history of stroke) and evidence of relevant CVD on brain imaging | Evidence of focal brain damage: unilateral spastic weakness of limbs, unilateral increased tendon reflexes, extensor plantar response, and pseudobulbar palsy | Focal neurological signs and symptoms that are judged to be etiologically related to the disturbance |

*Continued on next page*

# Diagnostic Criteria: Comparison

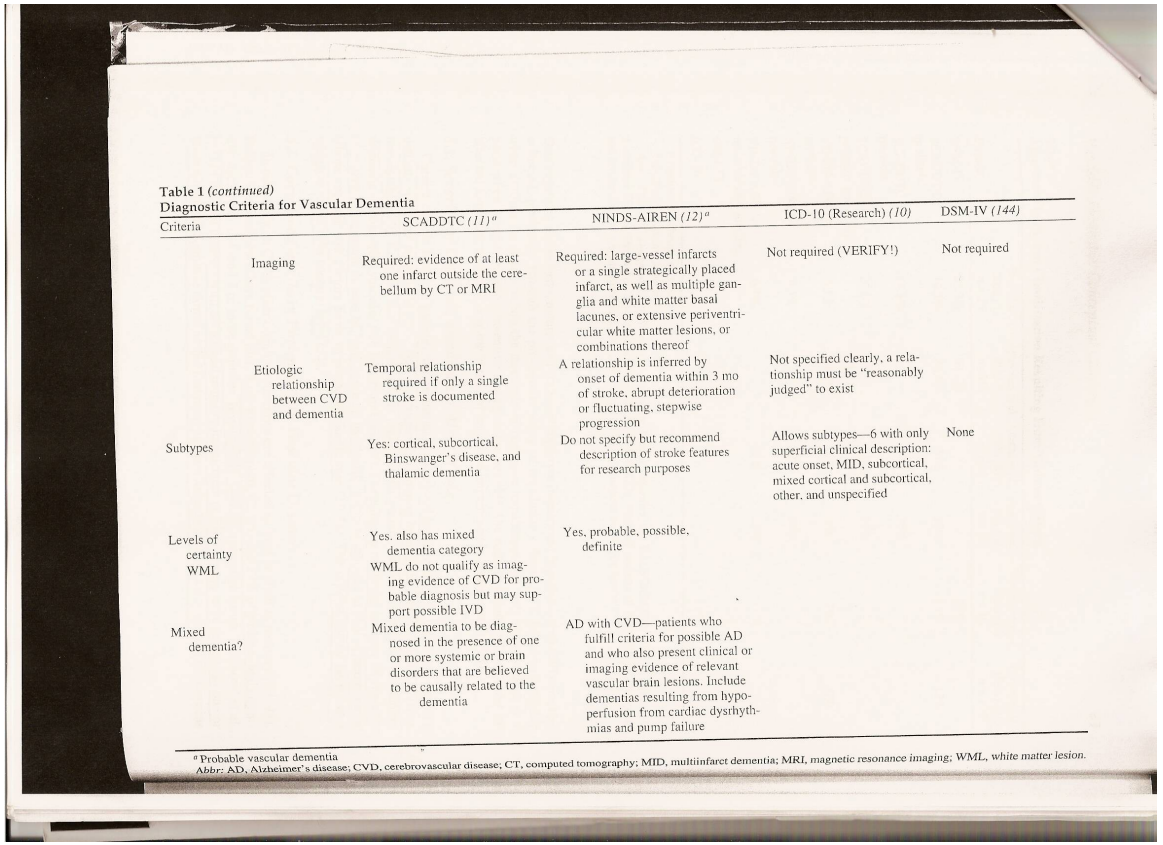


**Table 1** *(continued)*
**Diagnostic Criteria for Vascular Dementia**

| Criteria | | SCADDTC *(11)*[a] | NINDS-AIREN *(12)*[a] | ICD-10 (Research) *(10)* | DSM-IV *(144)* |
|---|---|---|---|---|---|
| | Imaging | Required: evidence of at least one infarct outside the cerebellum by CT or MRI | Required: large-vessel infarcts or a single strategically placed infarct, as well as multiple ganglia and white matter basal lacunes, or extensive periventricular white matter lesions, or combinations thereof | Not required (VERIFY!) | Not required |
| | Etiologic relationship between CVD and dementia | Temporal relationship required if only a single stroke is documented | A relationship is inferred by onset of dementia within 3 mo of stroke, abrupt deterioration or fluctuating, stepwise progression | Not specified clearly, a relationship must be "reasonably judged" to exist | |
| Subtypes | | Yes: cortical, subcortical, Binswanger's disease, and thalamic dementia | Do not specify but recommend description of stroke features for research purposes | Allows subtypes—6 with only superficial clinical description: acute onset, MID, subcortical, mixed cortical and subcortical, other, and unspecified | None |
| Levels of certainty WML | | Yes, also has mixed dementia category<br>WML do not qualify as imaging evidence of CVD for probable diagnosis but may support possible IVD | Yes, probable, possible, definite | | |
| Mixed dementia? | | Mixed dementia to be diagnosed in the presence of one or more systemic or brain disorders that are believed to be causally related to the dementia | AD with CVD—patients who fulfill criteria for possible AD and who also present clinical or imaging evidence of relevant vascular brain lesions. Include dementias resulting from hypoperfusion from cardiac dysrhythmias and pump failure | | |

[a] Probable vascular dementia
*Abbr:* AD, Alzheimer's disease; CVD, cerebrovascular disease; CT, computed tomography; MID, multiinfarct dementia; MRI, magnetic resonance imaging; WML, white matter lesion.

# Risk Factors Related to Vascular Causes of Cognitive Impairment

- Vascular Factors
  - Arterial hypertension
  - Atrial fibrillation
  - Coronary heart disease
  - Diabetes
  - Generalized atherosclerosis
  - Lipid abnormalities
  - Smoking
- Demographic Factors
  - Age and Gender

- Genetic Factors
  - Family history
  - Specific genetic features
- Stroke Related Factors
  - Type of CVD
  - Site and size of stroke

# Cerebrovascular Accident (Stroke)

Stroke itself is not clearly defined and is not a precise medical term

CVD is a more technical term describing a heterogeneous group of vascular disorders that result in brain injury

# Mechanisms and Clinical Subtypes

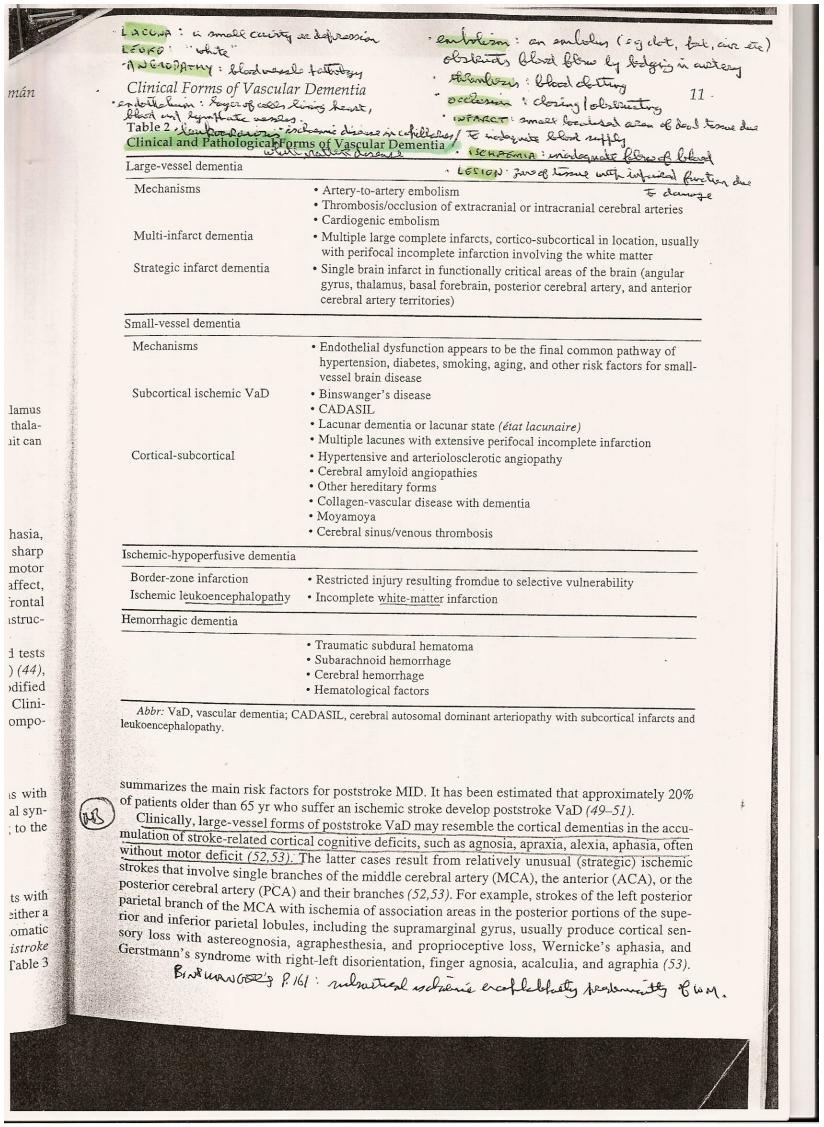
## 3 Main Mechanisms of CVA

- Infarction
- Hemorrhage
- Ischemia

## 3 Main VaD Subtypes (Clinical)

- Large Vessel Dementia
- Small Vessel Dementia
- Strategic Single Infarct Dementia

# Clinical and Pathological Forms of VaD



Clinical Forms of Vascular Dementia

Table 2
Clinical and Pathological Forms of Vascular Dementia

| | |
|---|---|
| **Large-vessel dementia** | |
| Mechanisms | • Artery-to-artery embolism<br>• Thrombosis/occlusion of extracranial or intracranial cerebral arteries<br>• Cardiogenic embolism |
| Multi-infarct dementia | • Multiple large complete infarcts, cortico-subcortical in location, usually with perifocal incomplete infarction involving the white matter |
| Strategic infarct dementia | • Single brain infarct in functionally critical areas of the brain (angular gyrus, thalamus, basal forebrain, posterior cerebral artery, and anterior cerebral artery territories) |
| **Small-vessel dementia** | |
| Mechanisms | • Endothelial dysfunction appears to be the final common pathway of hypertension, diabetes, smoking, aging, and other risk factors for small-vessel brain disease |
| Subcortical ischemic VaD | • Binswanger's disease<br>• CADASIL<br>• Lacunar dementia or lacunar state *(état lacunaire)*<br>• Multiple lacunes with extensive perifocal incomplete infarction |
| Cortical-subcortical | • Hypertensive and arteriolosclerotic angiopathy<br>• Cerebral amyloid angiopathies<br>• Other hereditary forms<br>• Collagen-vascular disease with dementia<br>• Moyamoya<br>• Cerebral sinus/venous thrombosis |
| **Ischemic-hypoperfusive dementia** | |
| Border-zone infarction | • Restricted injury resulting fromdue to selective vulnerability |
| Ischemic leukoencephalopathy | • Incomplete white-matter infarction |
| **Hemorrhagic dementia** | |
| | • Traumatic subdural hematoma<br>• Subarachnoid hemorrhage<br>• Cerebral hemorrhage<br>• Hematological factors |

*Abbr:* VaD, vascular dementia; CADASIL, cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy.

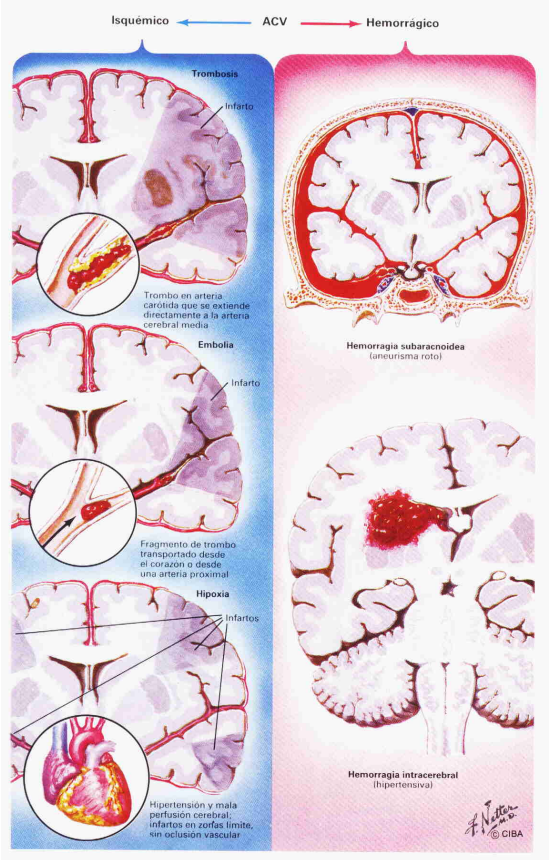
summarizes the main risk factors for poststroke MID. It has been estimated that approximately 20% of patients older than 65 yr who suffer an ischemic stroke develop poststroke VaD *(49–51)*.

Clinically, large-vessel forms of poststroke VaD may resemble the cortical dementias in the accumulation of stroke-related cortical cognitive deficits, such as agnosia, apraxia, alexia, aphasia, often without motor deficit *(52,53)*. The latter cases result from relatively unusual (strategic) ischemic strokes that involve single branches of the middle cerebral artery (MCA), the anterior (ACA), or the posterior cerebral artery (PCA) and their branches *(52,53)*. For example, strokes of the left posterior parietal branch of the MCA with ischemia of association areas in the posterior portions of the superior and inferior parietal lobules, including the supramarginal gyrus, usually produce cortical sensory loss with astereognosia, agraphesthesia, and proprioceptive loss, Wernicke's aphasia, and Gerstmann's syndrome with right-left disorientation, finger agnosia, acalculia, and agraphia *(53)*.

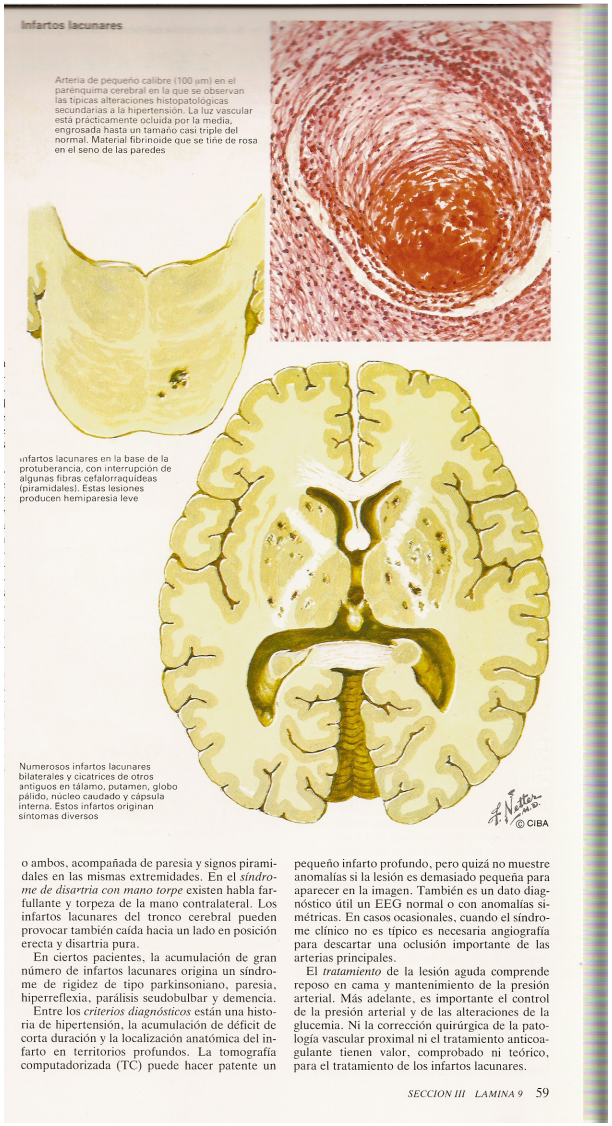
# Infarcts vs. Hemorrhages

- **Embolism**, from the Greek *embolos* meaning 'plug' or 'wedge' refers to a blood clot that has traveled from one part of the body to another

- **Thrombosis**, is the formation of a blood clot or *thrombus* (Greek meaning 'clot')



# Lacunar Infarcts



Infartos lacunares

Arteria de pequeño calibre (100 µm) en el parénquima cerebral en la que se observan las típicas alteraciones histopatológicas secundarias a la hipertensión. La luz vascular está prácticamente ocluida por la media, engrosada hasta un tamaño casi triple del normal. Material fibrinoide que se tiñe de rosa en el seno de las paredes

Infartos lacunares en la base de la protuberancia, con interrupción de algunas fibras cefalorraquídeas (piramidales). Estas lesiones producen hemiparesia leve

Numerosos infartos lacunares bilaterales y cicatrices de otros antiguos en tálamo, putamen, globo pálido, núcleo caudado y cápsula interna. Estos infartos originan síntomas diversos

F. Netter M.D.

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o ambos, acompañada de paresia y signos piramidales en las mismas extremidades. En el *síndrome de disartria con mano torpe* existen habla farfullante y torpeza de la mano contralateral. Los infartos lacunares del tronco cerebral pueden provocar también caída hacia un lado en posición erecta y disartria pura.

En ciertos pacientes, la acumulación de gran número de infartos lacunares origina un síndrome de rigidez de tipo parkinsoniano, paresia, hiperreflexia, parálisis seudobulbar y demencia.

Entre los *criterios diagnósticos* están una historia de hipertensión, la acumulación de déficit de corta duración y la localización anatómica del infarto en territorios profundos. La tomografía computadorizada (TC) puede hacer patente un pequeño infarto profundo, pero quizá no muestre anomalías si la lesión es demasiado pequeña para aparecer en la imagen. También es un dato diagnóstico útil un EEG normal o con anomalías simétricas. En casos ocasionales, cuando el síndrome clínico no es típico es necesaria angiografía para descartar una oclusión importante de las arterias principales.

El *tratamiento* de la lesión aguda comprende reposo en cama y mantenimiento de la presión arterial. Más adelante, es importante el control de la presión arterial y de las alteraciones de la glucemia. Ni la corrección quirúrgica de la patología vascular proximal ni el tratamiento anticoagulante tienen valor, comprobado ni teórico, para el tratamiento de los infartos lacunares.

# Cortical VaD

- **Variable pattern of cognitive deficits depending on territory involved**
- May cause loss of instrumental functions manifested by aphasia, apraxia, or agnosia
- **Memory**
  - Compared to AD patients
    - Superior performance on verbal learning and memory
    - Better delayed recall
    - Lower rates of forgetting
- Generally abrupt onset and fluctuating pattern
- **MCA**
  - Right –Visuo-spatial deficits
  - Left – Aphasia
  - Contralateral limb weakness
- **PCA**
  - Visual and memory deficits

# Subcortical VaD

- Fronto-subcortical involvement
  - Executive dysfunction
  - Attentional deficits
- Reduced verbal fluency (phonetic worse than semantic)
- Reduce speed of information processing
- Slow motor function
- Memory: Poor retrieval and intact recognition
- Apathy and depression

# Dementia with Lewy Bodies

**3 Core Features:**

- Fluctuating cognition with pronounced variation in attention and alertness
- Recurrent visual hallucinations – well-formed and detailed
- Spontaneous features of Parkinsonism

**Suggestive Features:**

- REM sleep Behaviour Disorder
- Severe neuroleptic sensitivity

**Probable DLB:**

- Two core features or
- One suggestive plus one or more core features


OLD LADIES HOME