

The Diagnosis of Dementia

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Keeping dementia front of mind:

*Incidence and Prevalence
2009 to 2050*

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Prevalence of dementia in Australia

Four-fold rise from: 245,000 (2009)
to: 1,113,000 (2050)

2010: 257,275
2030: 591,531
2050: 1,130,691

Incidence of Dementia in Australia

- 2010 75,336
- 2030 187,443
- 2050 385,176

1.1% of population in capital cities in 2009
(1.2% in the balance)

2.9% of population in capital cities in 2050
(3.8% of balance of the population)

- **Half** of those with moderate to severe dementia **live in their own home** or in the home of their carer

- The other half live in residential facilities

Diagnosis

Autopsy findings show diagnosis of dementia made before death in:

- 3% mild dementia
- 24% moderate dementia

Diagnosis

- In general practice, nearly **75%** of patients with moderate to severe dementia are **unrecognised** by primary care **physicians** as having cognitive impairment
(Gifford, Neurology, 1999)
- **20%** of **family** informants failed to recognise memory problems in those fulfilling the criteria for dementia

How do GPs diagnose dementia?

MMSE

- Average **sensitivity & specificity** for detecting dementia are **83% & 82%**
- If applied to a population of 65-74 year olds, the **false positive rate** would be **93%**
- Is dementia score: **< 20 ?**
< 24 ?
- Is annual decline of **3.4 points** in AD
- **Score correlates** with several clinical outcomes:
 - Functional status
 - Behavioural change
 - Length of time in hospital
 - Urinary incontinence
 - Mortality

DSM III-R

The essential feature of **dementia** is impairment in short- and long-term **memory**, associated with impairment in **abstract thinking**, impaired **judgement**, other disturbances of higher **cortical function**, or **personality** change. The disturbance is severe enough to interfere significantly with *work* or usual *social activities* or *relationships* with others. The diagnosis of dementia is not made if these symptoms occur in...delirium...

Alzheimer's Disease

- *Most common* dementia (two thirds of cases)
- Predominantly a memory problem, early
- Onset is gradual & progression *slow*
- May be early language disturbances (word substitutions, impaired comprehension)
- *Personality lost late*
- Lack of insight
- Delusions & hallucinations in 50%
- "*head turning sign*"

DSM-4 Criteria for Alzheimer's Disease

- A. Multiple cognitive deficits with both
1. Memory impairment
 2. At least one of
 - aphasia (language)
 - apraxia (motor activities)
 - agnosia (recognition)
 - disturbance in *executive function* (planning, organising, sequencing, abstracting)
- B. 3. Gradual onset & *continuing* cognitive decline
- C. 4. Significant impairment of *social* or *occupational* functioning
- D. 5. Exclusion of other causes of the cognitive decline:
- CNS: P.D., Huntington's, NPH, SDH, CVD
 - Systemic illness: hypothyroid, Vit B₁₂ or folate deficiency, HIV, hypercalcaemia
 - Substance induced conditions
- E. 6. Not exclusively due to delirium
- F. 7. Not due to other psychiatric diagnoses

Diagnostic criteria for Alzheimer's disease

Inclusion Factors:

- Gradual onset of poor memory
- Worsening of memory problem
- Failure of function
- Cortical dysfunction:
 - dysphasia
 - agnosia
 - dyspraxia

Exclusion Factors:

- Delirium
- Other organic causes
- Psychiatric illness

Cognitive Assessment: Other Screening Instruments

The Rowland Universal Dementia
Assessment Scale (RUDAS):
A multicultural cognitive
assessment scale

International Psychogeriatrics
Storey JE et al, 2004, 16:13-31

Cognitive Assessment: Other Screening Instruments

GP Cog.

A screening tool for cognitive impairment
International Journal of Geriatric Psychiatry
Brodaty, H. et al, 2004, 19:870-874

Vascular Dementia

- Abrupt onset & step-wise decline
- Impaired "executive" function
- Gait disorder
- Emotional lability
- Focal neurological signs
- CT evidence of cerebrovascular disease

Vascular Dementia

Neuropathological analyses indicate that:

- Some vascular pathology exists in **29-41%** of dementia cases coming to autopsy in community based cohorts
- Pure vascular pathology accounts for dementia in only **9-10%**

DSM-IV criteria for the diagnosis of vascular dementia

- A. The development of multiple cognitive deficits manifested by both:
- Memory impairment (impaired ability to learn new information or to recall previously learned information)
 - One or more of the following cognitive disturbances:
 - (a) aphasia (language disturbance)
 - (b) apraxia (impaired ability to carry out motor activities despite intact motor function)
 - (c) agnosia (failure to recognize or identify objects despite intact sensory function)
 - (d) disturbance in executive functioning (i.e., planning, organizing, sequencing, abstracting)

- B. The cognitive deficits in criteria A1 and A2 each cause significant impairment in social or occupational functioning and represent a significant decline from a previous level of functioning.
- C. Focal neurological signs and symptoms (e.g., exaggeration of deep tendon reflexes, extensor plantar response, pseudobulbar palsy, gait abnormalities, weakness of an extremity) or laboratory evidence indicative of cerebrovascular disease (e.g., multiple infarctions involving cortex and underlying white matter) that are judged to be etiologically related to the disturbance.
- D. The deficits do not occur exclusively during the course of a delirium.

Diagnostic criteria for Vascular dementia

Inclusion Factors:

- Gradual onset of poor memory
 - Worsening of memory problem
 - Failure of function
 - Cortical dysfunction:
 - dysphasia
 - agnosia
 - dyspraxia
- and the presence of a neurological sign

Exclusion Factors:

- Delirium
- Other organic causes
- Psychiatric illness

Dementia with Lewy Bodies

- 1912 Lewy body Friedrich Lewy
- 1961 Okazaki Lewy bodies and dementia
- LB in up to 20% of elderly dementia
- 1996 consensus criteria

Dementia with Lewy Bodies (DLB)

Clinically: * *dementia*

- * gait & balance disorder
- * prominent *hallucinations*
- * sensitivity to traditional antipsychotics
- * *fluctuations* in alertness

Consensus criteria for dementia with Lewy bodies

- 1 Progressive cognitive decline
- 2 For a probable diagnosis, two of,
or a possible diagnosis, one of:
 - a fluctuations in attention & alertness
 - b visual hallucinations
 - c spontaneous motor features of parkinsonism

Consensus criteria for dementia with Lewy bodies

- 3 Supportive of a diagnosis:
 - a falls
 - b syncope
 - c transient LOC
 - d neuroleptic sensitivity
 - e systematised delusions
 - f hallucinations in other modalities
- 4 Opposing a diagnosis:
 - a cerebrovascular disease
 - b another physical cause for the illness

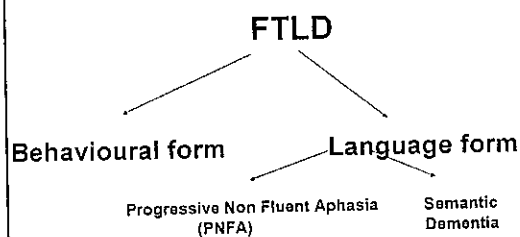
Frontotemporal dementia *Pick's disease*



Frontotemporal dementia

- Aka Pick's disease, frontal dementia, primary progressive aphasia
- *Relative memory sparing*
- Early *behavioural or personality or language* changes
- Insidious onset & slow progression
- Family history in about 45%
- Frequently *affective symptoms*: anxiety, depressions, delusions
- Core features: *disinhibition*, loss of personal hygiene, loss of social awareness, impulsivity
- Stereotyped, perseverative behaviour is common
- Most patients also fulfill the criteria for AD

Frontotemporal dementia



FTLD: progress

- The forms tend to blur and they amalgamate over time
- 50% survive to 8 years
- A small number go on for 20 years
- NFA live longest
- One subset develop MND and die in a mean of 12 months

Epidemiology

- Second most common form of dementia under 65 years

(Ratnavalli, 2002)

Diagnosis

Difficulties are due to:

- Overlap with Asperger's
- Unreliability of witness reports
- Differentiation from psychiatric conditions
- Normal neuropsychiatric testing

FTLD: diagnosis

- Some are really Alzheimer's dementia
- These are usually PNFA

Diagnosis: Behavioural variant

- Insidious onset and slowly progressive
- Insight limited or absent
- Early changes in personality and behaviour (apathy and irritability are non-specific)

Diagnostic criteria: behavioural variant

1. Disinhibition
2. Apathy and inertia
3. Loss of sympathy and empathy
4. Pervasive stereotyped or ritualistic behaviour
5. Hyperorality or dietary changes

Diagnosis of Behavioural variant

Possible diagnosis:

- 3 features early
- Executive deficits on psychiatric testing

Probable diagnosis:

- Above and
- *MRI or Spect or PET changes*

Definite diagnosis:

- Above and
- *Mutation on pathology*

Epidemiology and Natural History of Prion Diseases

- **Incidence** ~ prevalence : 1-1.5/10⁶/year (about 25 cases in Australia each year)
- **Mean survival** is 6 months; median is 4 months; 90% die within a year
- **Mean age of onset** of sporadic CJD is 61 years (younger for nvCJD and some genetic forms)
- **All forms are potentially infectious** (no danger on routine or intimate contact)

Diagnostic Criteria for sporadic CJD

- **Gold standard is histopathology**
- postmortem
- neuronal loss, gliosis without inflammation, vacuolation (spongiform change)
- **Familial CJD** is confirmed by prion protein (PrP) sequencing

Jacob-Creutzfeld Disease

- Rapidly progressive dementia (death < 6/12)
- Associated myoclonus, ataxia & other neurological signs
- EEG (periodic sharp wave complexes) may be helpful
- But **CSF 14 – 3 – 3 protein** has high specificity (99%) & sensitivity (96%)

What clinical findings support a diagnosis of CJD?

Psychiatric and behavioural:

- Depression
- Apathy
- Irritability
- Personality change

Clinical findings of CJD

Neurological:

- Parasthaesia (often early)
- Pain (often early)
- Neuropathy (often early)
- Extrapyrmidal (bradykinesia, rigidity, dystonia)
- Ataxia
- Visual abnormalities
- Seizures (late)
- Myoclonus (late)

Clinical features of CJD

Neuropsychological:

- Amnesia and confusion
- Frontal/ dysexecutive
- Aphasia/ apraxia/ neglect
- Visuospatial abnormalities

CJD: investigations

MRI:

- DWI + FLAIR abnormality in the cortex and deep grey matter

EEG:

- Normal early
- Focal or diffuse slowing
- 1 Hz periodic complexes (not for nvCJD)

CSF:

- Mildly raised protein (<1g/L), acellular
- Raised 14-3-3, tau, NSE

14-3-3 protein in the D_x of CJD

- Marker of neuronal damage (not prion protein)
- If other causes of acute neuronal damage are excluded (HSVE, stroke), was thought to be very sensitive and specific (>90%)

- But now: sensitivity for
 - sCJD*: ~65%
 - familial CJD*: ~70%
 - nvCJD*: <50%
 (Sanchez-Juan, Neurology, 2006)

Diagnostic Criteria for sporadic CJD: clinical

Masters (1979)

Dementia with 2 of:
 myoclonus
 pyramidal
 extrapyramidal
 cerebellar
 typical EEG

WHO Revised (1998)

Possible dementia with 2 of:
 myoclonus
 pyramidal extrapyramidal
 visual/ cerebellar
 akinetic mutism

Probable dementia:
 typical EEG or
 CSF 14-3-3 (if <2 year duration)

Diagnostic Criteria for CJD: MRI

Flair and (especially DWI) are very sensitive and specific for CJD (each ~ 90%):

- Cortical ribboning
- Basal ganglia increased signal
- Pulvinar (posterior thalamus) double hockey stick in nv CJD
- Absence of contrast enhancement

Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy

- Inherited
- Small vessel disease
- Cause of strokes and dementia

Clinical Features

- Migraine with aura (20-35%)
- Cognitive impairment (50%)
- Recurrent ischaemic events (70-85%)

Genetics

- Is related to a mutation of the NOTCH 3 gene (chromosome 19)

Diagnosis

- Skin biopsy
- Notch 3 gene
- ...