



Dunedin School of Medicine

# Diagnosing & managing dementia & delirium

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## Aging: Its complex management

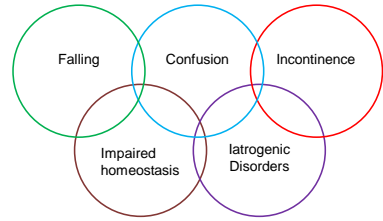
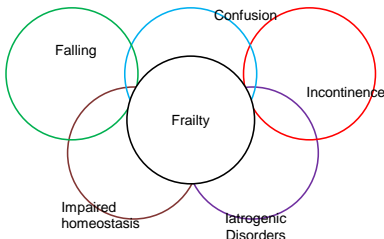


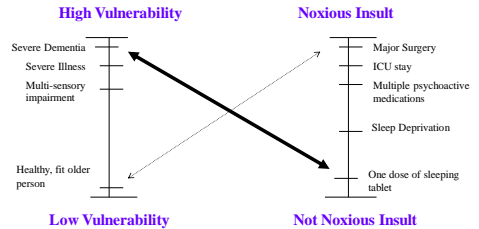
Fig 4-10: O complex of Geriatric Medicine



## Who is affected by delirium?

### Predisposing Factors (Vulnerability)

### Precipitating, Perpetuating, Factors (Insults)



Multifactorial Model of Delirium Inouye 1993

## Overview

- Mild cognitive impairment
- Dementia subtypes
  - Alzheimer's disease
  - Vascular Cognitive Impairment
  - Others
- Treatment / Management
- Delirium

## Aspects of memory which change with age

Endure with age	Worsen with age
Knowledge about people and things	Tip-of-tongue occurrences
Recalling the gist of long-ago events	Remembering with no prompt
Learning and using reminder strategies	Doing more than one thing at a time
Remembering well if more time taken	Remembering under time pressure
Remembering with cue	The source of information

## Mild Cognitive Impairment

- Continuum of cognitive changes with ageing
- No consensus on criteria- usually mild memory loss (>1.5 s.d) +/- other cognitive domains but **no significant functional loss**
- Subtypes – amnesic and multi-domain
- Amnesic may be a prodrome of AD  
10-15% convert per year, 50% over 5 yrs.

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## Dementia definition

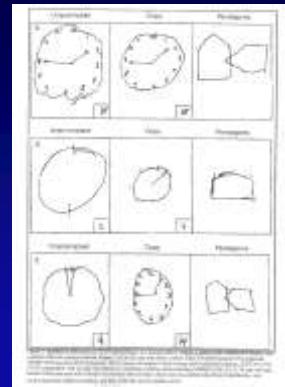
- On basis of hx and mental state exam at least 2 of
  - impaired learning/retention/recall new information
  - impaired handling of complex tasks
  - impaired reasoning
  - impaired spatial ability and orientation
  - impaired language
- Do not occur exclusively during a delirium or are better explained by a major psychiatric diagnosis
- Cognitive impairment interferes with work/usual social activities or relationships
- A decline in cognition from previous level

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## Dementia-diagnosis

- Relies on good collateral history and mental state examination
- History
  - Relative/friend, co-morbidities which may limit function, specific examples of cognitive failure
- Exam
  - MMSE, clockface, generating word lists e.g animals in 60 sec (>12 in 80 with <3 yrs education)
  - Physical exam – general + neurological
- Investigations  
FBC, U+E, Ca, LFTs, glucose, B12, TSH +/- other

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## Dementia-neuropsych

- If presentation atypical
- Young <65 yrs
- High or low premorbid intellect/education
- NART – pronunciation of irreg words is preserved in dementia and can indicate premorbid IQ

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## Dementia-diagnosis

Diagnosis	Function	Cognitive test
Cognitively intact	normal	normal
MCI	normal	impaired
Dementia	impaired	impaired
Consider depression/ frontal dementia	impaired	normal

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## Neuroimaging

- Does not make diagnosis but can be supportive or exclude stroke / tumour / NPH
- Indications
  - age <60
  - Hx seizure/headache
  - rapid decline
  - recent head trauma
  - unexplained neurology
  - history of malignancy or anticoagulation
  - unexplained incontinence/gait disorder

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## AD pathology

- Plaques and tangles in the brain along with death of brain cells (atrophy) and vascular changes.
  - Plaques - collections of amyloid (42A $\beta$  amyloid) protein outside of cells
  - Tangles - chains of protein (tau) inside the cell
  - Amyloid angiopathy-amyloid in walls of cerebral blood vessels
  - Begins in hippocampus and spreads to rest of temporal lobe, parietal and frontal cortex

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## AD risk factors

- Age
- Vascular risk factors – type 2 DM, lipids, HT, IHD, obesity
- Stroke
- Family history
- ?Head trauma
- ?Depression
- ?Decreased reserve- low education/occupational attainment, low mental ability in early life (Nun Study)
- ?Reduced mental and physical activity in later life

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## Alzheimer's Disease and Genetics

- 75% of Alzheimer's Disease is sporadic
- 25% Familial
  - 20% Late onset with weak genetic component
  - <5% Early onset with strong genetic component

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## Early Onset AD

- Onset of symptoms before 65yrs of age (usually in 40s and 50s)
- < 5% of all Alzheimer's cases
- ~60% of people with early onset AD will have a positive family history
- Autosomal dominant condition

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## Late Onset Alzheimer's Disease

- Multifactorial - genes plus environment
- Probably many genes involved
  - Apolipoprotein E on c'some 19
  - Possibly others on c'some 12, 10 and 9
- These genes increase a person's susceptibility to AD

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## Apolipoprotein E

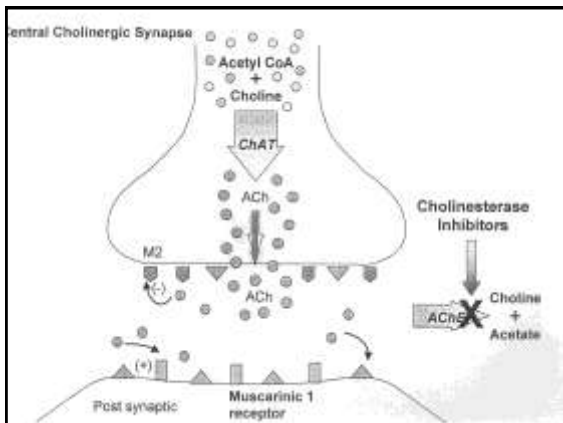
- A protein which binds lipids and carries them from the blood into cells – cholesterol transporter in the brain
- Has a role in stopping Tau protein from forming tangled chains in cells and from stopping amyloid forming plaques
- 3 different forms - E2, E3, E4
- E4 increases risk and E2 decreases risk

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## APO E and Risk of AD

- One E4 gene - risk increased 2-3 times ( appears to modify age of onset)
- Two E4 genes - risk increased 5-10 times
- **BUT** ~50% with E4 genes never develop AD
- **AND** ~50% of people with AD do not have an E4 gene
- **SO** E4 increases risk of AD but testing for it does not help an individual predict whether they will get AD

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## AD treatment- Cholinesterase Inhibitors

- Some evidence for small benefit in cog, ADLs, decreased carer hours, neuropsych symptoms (~1/3 benefit for 6-12 months)
- Contraindicated if poorly controlled asthma, active peptic ulcer, heart block.
- 10% stop due to side effects (GI upset, runny nose, urinary frequency, syncope).
- In practice ~60% stop within 3 months – side-effects/lack of benefit/cost.

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## Vascular Cognitive Impairment

- VCI refers to all forms of cognitive impairment associated with cerebrovascular disease
  - post stroke
  - multi-infarct
  - subcortical ischaemic VD
  - vascular mild cognitive impairment
  - mixed with AD
  - hereditary-CADASIL, amyloid angiopathy

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## Multi-infarct Dementia

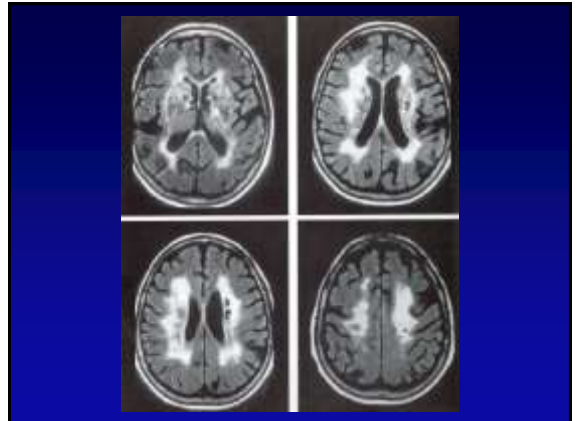
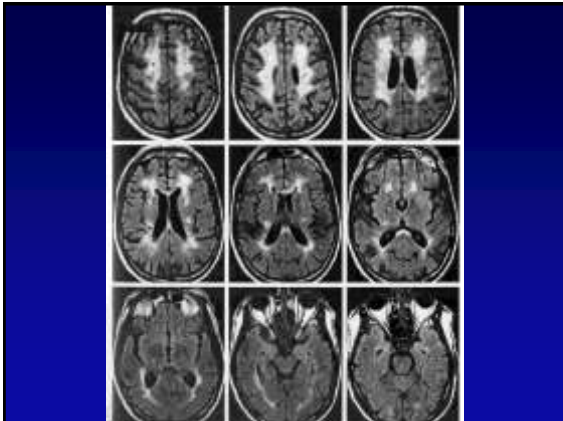
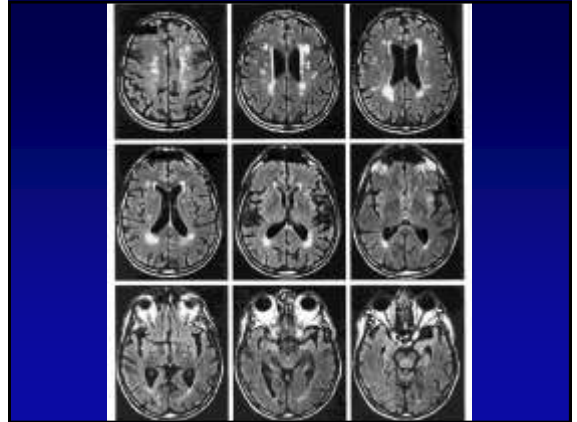
- Traditional view of multiple cortical infarcts causing dementia
- Stepwise
- Focal cognitive deficits

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## White Matter Changes (Leukoarriaosis)

- Increase with age – 70% of 70yr olds
- Subcortical pattern- poor attention/ executive function/apathy/depression
- Often associated with gait apraxia, urinary frequency / incontinence
- Lesion load and location increases risk cognitive impairment

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## Prevention and treatment

- Prevention
  - Minimise vascular risk factors in mid-life but no good evidence for treatment reducing risk.
- Treatment
  - AChEI small benefit (cochrane 2 RCT donepezil, sig improvement in cog/global function/ADL)
  - Memantine- mild-mod VD small benefit in cog and behaviour but no global improvement

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## DLB diagnostic criteria

- Fluctuating cognitive impairment
- Visual hallucinations (VH)
- Parkinsonism (axial)
- 2 or 3 =probable, 1= possible
- Supportive features – falls, syncope, neuroleptic sensitivity, delusions, hallucinations in other modalities, REM sleep disorder, depression
- VH best positive predictor and visuospatial constructional deficits best negative predictor in early disease.

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## DLB/PDD treatment

- Avoid neuroleptics – 50% sensitive with 2-3x mortality
- If absolutely necessary, low dose atypical (Quetiapine)
- CHEI improve fluctuations, apathy, anxiety, hallucinations, sleep (cochrane single RCT, sig improvement NPI, no diff MMSE, well tolerated)
- DLB ~1/3 modest response to L-dopa – worth a trial if EPS significant

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## FTD

- A disorder of language, cognition and behaviour
- Mean age 62 yrs with normal distribution – risk doesn't increase exponentially with age
- 20-40% family history (progranulin mutation)
- Association with MND
- Clinical classification
  - Progressive non-fluent aphasia
  - Semantic dementia- fluent speech but poor semantic memory
  - Behavioural disorder and dysexecutive syndrome.

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## Driving and Dementia

- Older drivers high crash rate/km and injuries sustained.
- Reduced dynamic visual acuity, reaction time, divided attention.
- Patients not reliable, Informants may be.

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## Driving and Dementia

- Medical responsibility for driving safety in dementia is controversial
- NZ “driving may continue in early dementia as long as insight and judgement are not impaired and there is no disorientation or confusion”.
- Poor correlation with neuropsych tests - ? Trails A and block design.
- Assessment with OT best test but expensive.
- Early counselling

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## BPSD

- Antipsychotics small improvement from placebo in trials (discontinued due to SE 3-4x more than placebo- adverse effects outweigh benefit)
- Typical vs atypical probably no more effective but fewer SE with atypical (haloperidol ~25%/yr tardive dyskinesia)

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## BPSD

- ↑mortality with atypical – 3.5% vs 2.3, OR 1.5 at 3/12 and ↑further at 6/12. Mostly ↑cardiac deaths, ↑CVA controversial
- SSRI - ↓depression and irritability, one small trial benefit=antipsychotic with fewer SE
- AChEI – no benefit over placebo

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## BPSD

- Non – drug approaches FIRST
- Consider SSRI
- If symptoms severe consider atypical antipsychotic- start low, go slow, watch for SE and review benefit 2-4 weeks

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## Delirium: essential features

### The Confusion Assessment Method

- 1 Acute onset and fluctuating course
- 2 Inattention
- 3 Disorganised thinking
- 4 Altered level of consciousness

85-90% sensitivity and specificity

The diagnosis of delirium by CAM requires the presence of features 1 and 2 and either 3 or 4

Inouye SK et al Ann Intern Med 1990;113:941-8

## CAM

1. Acute onset – informant history
2. Fluctuation – history and observation
3. Attention – WORLD, months of year backwards, digit span (5=normal), 20 backwards, time of day.
4. Disorganised thinking – conversation illogical/rambling, switches to irrelevant topics
5. Level of consciousness – normal, hyperalert, drowsy.

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## Delirium: associated features

- 1 Perceptual disturbance
- 2 Altered sleep-wake cycle
- 3 Emotional lability
- 4 Psychomotor behavioural changes
  - hyperalert/hyperactive - 30%
  - hypoalert/hypoactive - 25%- underdiagnosed
  - mixed - 45%
  - Inouye SK et al Am J Med 1994;97:278-88

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## Drugs and Delirium

- Psychoactive drugs
  - Withdrawal/Discontinuation syndromes
  - Toxicity
  - Even conservative doses in the vulnerable host
- Non-psychoactive drugs
  - H2 blockers, steroids, cardiac drugs, NSAIDs, antibiotics, B-blockers
- Drugs with anticholinergic effects

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## Anticholinergic Drugs and Delirium

- Tricyclic antidepressants
- Benztropine
- Oxybutynin
- Antihistamines
- Antispasmodics
- Atypical antipsychotics
- Low level but cumulative e.g digoxin, frusemide,....

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## Treatment

- Treat the treatable identified cause(s) of delirium – thorough history (collateral) and examination, obs, UA, ECG, CXR, routine bloods.
- Neuroimaging IF focal neurology, evidence of head trauma, fever with no cause, ?if no other cause found.
- Slowly withdraw contributing and/or unnecessary drugs

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## Treatment

- Remain vigilant for additional aggravating or perpetuating factors
- Supportive care – food/fluids/bowels/pressure care
- Non-drug management of agitation – quiet calm environment, sitter, distraction.
- May require medication for anxiety/agitation if at risk harm to self/others/significant distress/sleep deprivation

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## Pharmacologic Measures

- Consider trial regular paracetamol
- If ETOH withdrawal – benzodiazepines
- If no parkinsonism low dose haloperidol (no anticholinergic activity) e.g 0.5mg BD
- If parkinsonism atypical antipsychotic e.g risperidone, quetiapine
- May require short-acting benzo for night sedation e.g temazepam/oxazepam or if intolerant of antipsychotic e.g lorazepam 0.5mg BD
- Regular review of medications

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## Delirium- “chemical restraint”

- If absolutely necessary for patient safety or administer medical care then consider
  - IM droperidol e.g 2.5-5mg sedation, short acting
  - IM olanzapine e.g 2.5-5 mg sedating, long acting, more extrapyramidal SE
  - Risperidone quicklets e.g 0.5-1mg BD, olanzapine wafers 2.5-5mg BD
- Always close monitoring after administration to watch for sedation/hypotension/falls and frequent review of effect and ongoing dose adjustment

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## Key points

- History key in dementia
  - family and friends
  - push back history by asking about early losses
- Consider multiple contributing factors, particularly in delirium
- Ask specifically about EPA, driving, daily living activities
- Lay the foundation, if possible, for rest home care

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